Associations between cardio-metabolic risk factors and weight status among Canadian children and adolescents using the Canadian Health Measures Survey

Miranda MacPherson

Thesis submitted to the Faculty of Health Sciences in partial fulfillment
of the requirements for the PhD degree in Population Health

Population Health PhD Program
University of Ottawa

TABLE OF CONTENTS

ABSTRACT

Objectives: This thesis examines the risks among Canadian children and adolescents for developing cardio-metabolic diseases, extending evidence that is well-established for adults to pediatric populations. As well, novel indicators and cut-offs for the measurements of disease risks are proposed and associations between physical activity, weight status, socio-economic status and cardio-metabolic health are examined.

Methodology: Secondary data analysis was conducted using data from three[1] cycles of the Canadian Health Measures Survey (CHMS), a nationally representative data set which includes measured anthropometric characteristics. A population health approach was applied throughout, underpinned by the World Health Organization's *Conceptual Framework for Action on the Social Determinants of Health*. The thesis was designed such that a series of four manuscripts successively built on the key findings from each previous research paper:

1. **Establishing the prevalence of Metabolic Syndrome and its risk factors** for 10-18 year olds using the International Diabetes Federation child, adolescent and adult definitions.
2. **Estimating pre-obesity epidemic waist circumference reference values for Canadian children 6-10 years** using reference data from the 1981 Canada Fitness Survey, the Third National Health and Nutrition Examination Survey (1988-1994), and the CHMS through regression of linear, logarithmic and quadratic functions. This work facilitated an expanded age range for the subsequent projects as age- and sex-specific cut-offs based on a Canadian population prior to the obesity epidemic had not been available.

[1] For Project 1, two cycles of the CHMS were used as CHMS Cycle 3 had not been released.

3. **Cardio-metabolic risk by body mass index (BMI), waist circumference (WC), and a combined BMI-WC indicator** quantified the associations between a dichotomous cardio-metabolic risk variable, and obesity, using three indicators of obesity including a novel indicator, for ages 6-18 years.
4. **Association between cardio-metabolic risk and inflammation** quantified the associations between inflammation, using high-sensitivity c-reactive protein (CRP) as a marker, and cardio-metabolic risk to determine if high CRP was a significant predictor of cardiometabolic risk among 6-18 year olds.

Results: For Paper 1 (n=1228), only 2.1% were classified as having the Mets though 38% had at least 1 MetS risk factor. For Paper 2, logarithmic regression predicted WC cut-offs with the lowest degree of error. For Paper 3 (n=2678), 35% were classified as having cardio-metabolic risk with significantly higher levels among those classified as obese and/or having a low level of physical activity. All indicators of obesity had significant associations with cardio-metabolic risk. For Paper 4 (n=1831), 43.6% of children and 62.0% of adolescents with high CRP levels were classified as having cardio-metabolic risk, a significant relationship. Participants from households with moderate to high income and/or education had the lowest prevalence of MetS risk factors and abdominal obesity.

Conclusions: High CRP is a useful indicator of cardio-metabolic risk for pediatric populations. With further research, novel combinations of BMI and WC may be shown to be more predictive for cardio-metabolic risk than these indicators individually. The substantial prevalence of multiple risk factors which predict premature onset of chronic disease foreshadows potential years of morbidity in adulthood for Canada's youth population.

ACKNOWLEDGEMENTS

The pursuit of a doctorate in philosophy with a focus on Population Health has been a fulfilling experience. I wish to express my most sincere gratitude to the many people with whom I share this achievement:

My husband, Steven James, has provided unwavering support and encouragement. My children, Avianna and Connor, have been a constant source of motivation and have blessed me with so much love. My parents, Judith and Terry MacPherson, have provided the inspiration to embark on and complete this endeavour. My parents and my mother-in-law, Eleanor James, have cared for my children and prepared meals so that I may study. My extended family have provided support, including: my grand-parents, Ivan and the late Anne Steeves; Marcia, Bruce, Ella and Owen Graham; and Roberta, John, Beth and Kara Wittmann.

My thesis supervisors, Dr. Lise Dubois and Dr. Denis Prud'homme, have provided brilliant guidance and constant encouragement throughout the doctoral process. It has been a great privilege to learn from them.

My friends with whom I've had many memorable moments: Heather Cudmore, Dana McBain, Runa Das, Craig Brown, Joey Sadler, Jamie Cunningham, and Amy Foster.

My academic colleagues have provided camaraderie throughout this shared learning experience: Maria Benkhalti, Donna Pettey, Liz Darling, Brenda Dogbey, Cecilia Lemus, Debra Cohen, Kerri Mullen, Jason Nickerson and Esther Baum.

My professional colleagues at Health Canada, the Public Health Agency of Canada and the World Health Organization have provided insightful advice, including: Dr. Margaret de Groh, Dr. Ron Wall, Mrs. Xiaohong Jiang, Dr. Heather Orpana, Dr. Beth Jackson, Mr. Gordon Taylor-Lee, Mr. Rodney Ghali, Mr. Marcel Saulnier, Dr. Valerie Walker, Mrs. Barbara Moran, Mrs. Susan Russell, Mr. Jim Ball, Ms. Victoria Saint, Drs Kumanan and Jennifer Rasanathan, Mr. Ted Schrecker, and Mr. Tom Kari

I thank Statistics Canada for conducting the Canadian Health Measures Survey; the University of Ottawa's Population Health Program; and the Public Health Agency of Canada. Finally, I am grateful to the people of Canada who participated in the Canadian Health Measures Survey and to whom I wish good health.

ACRONYMS

BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CFS	Canada Fitness Survey
CHMS	Canadian Health Measures Survey
CI	Confidence interval
CRP	High-sensitivity c-reactive protein
CV	Coefficient of Variation
CVD	Cardiovascular Disease
DF	Degrees of Freedom
DXA	Dual Energy X-ray Absorptiometry
HDL-C	High-Density Lipoprotein Cholesterol
IDF	International Diabetes Federation
IOTF	International Obesity Task Force
MEC	Mobile Examination Centre
MetS	Metabolic Syndrome
MVPA	Moderate-to-Vigorous Physical Activity
NCEP ATP III	National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)
NHANES	National Health and Nutrition Examination Survey
NHES	National Health Examination Survey
NIH	National Institutes of Health
OR	Odds Ratio
SE	Standard Error
SES	Socio-Economic Status
WC	Waist Circumference
WHO	World Health Organization

1. INTRODUCTION

1.1. Situating the Problem

Childhood is a critical life stage for physical, cognitive and emotional development.(1) Childhood is also a period of vulnerability, as children are dependent on their parents, caregivers, communities and governments to provide safe, nurturing environments to enable their healthy development. During the childhood and adolescent years, the socio-economic and environmental conditions have significant influence on the life choices and chances of each child, which in turn, influence their health in the short and long term.(2) A child's pre-conception and gestation periods, as well as their genetic makeup, also have important influences on their health.(3,4) Globally and nationally, the 21st century has seen a marked increase in the prevalence and rate of chronic diseases, such as type 2 diabetes, as well as obesity, even among youth.(5–7) This shift has been attributed to modernity and the accompanying sedentary ways of life, the nutrition transition and structural inequalities.(8) Even among healthy children, we now understand that the impacts of negative socio-economic conditions and health behaviours can, through inflammatory pathways and atherosclerosis for example, initiate physiological changes that will negatively impact future health outcomes.(9–13) Collaborative scientific, medical, policy and societal progress at the individual, family and societal level is critically needed to promote health and prevent chronic disease. The United Nations' *Universal Declaration of Human Rights* and the Constitution of the World Health Organization (WHO) declare health to be a basic human right. The growing rates of diabetes and obesity, among other health problems and risks, point to an urgent need for significant correction for the health of our future generations.(1,14)

1.2. Overview of the Thesis

Briefly, I examined the risk among Canadian children and adolescents for developing cardio-metabolic diseases, such as cardiovascular diseases, diabetes and metabolic syndrome. Further, I examined the associations between their health behaviours, smoking and physical activity; weight status; and socio-economic conditions, household education and income; and their health. Secondary data analysis was conducted using data from three cycles[2] of the Canadian Health Measures Survey, a high-quality, nationally representative data set which includes clinic measurement of anthropometric characteristics. The thesis is structured by chapter as follows:

1. **Introduction** situates the problem that this research endeavour aims to address as well as the theoretical framework underpinning this work;
2. **Literature Review** describes the pertinent literature of child and adolescent health, weight, cardio-metabolic risks and associations with socio-economic status;
3. **Objectives and Hypotheses** outlines the thesis' overarching objectives, as well as the objectives for each research question and the research design to respond to these questions;
4. **Methodology** describes the methodology applied to address the research questions;
5. **Research Results** presents the manuscripts for each of the research questions;
6. **Discussion** provides an interpretation of the results, individually and collectively, and offers policy and clinical recommendations based on the findings.

[2] For Project 1, two cycles of the CHMS were used as CHMS Cycle 3 had not been released.

In fulfillment of the thesis designed to comprehensively study the cardio-metabolic risks among Canadian children and adolescents using the Canadian Health Measures Survey, a series of four research studies were conducted and described in manuscript form:

1. Prevalence of metabolic syndrome and its risk factors in Canadian children and adolescents: Canadian Health Measures Survey Cycle 1 (2007-2009) and Cycle 2 (2009-2011)
2. Estimating pre-obesity epidemic waist circumference reference values for Canadian children 6-10 years using reference data from the 1981 Canada Fitness Survey, the National Health and Nutrition Examination Survey, and the Canadian Health Measures Survey
3. Cardio-metabolic risk by body mass index, waist circumference, and a combined body mass index-waist circumference indicator, among Canadian children and adolescents
4. Cardio-metabolic risk, obesity and c-reactive protein in Canadian children and adolescents

For ease of reference, these projects have been given the short-form titles:

1. Metabolic Syndrome
2. Waist Circumference Cut-offs
3. Cardio-Metabolic Risk
4. Inflammation Marker

1.3. A Population Health Approach

Population health can be defined as a concept and as an approach. While the technical definition and scope of population health as a concept varies by institution and author, the general principle of population health is the socially constructed distribution of health across a defined population.(15,16) Population health affords the recognition that the health and wellbeing of a population is determined by a broad scope of individual, social, environmental and economic factors.(15,16) These determinants of health, such as income, education, living and working conditions, gender, ethnicity and healthy child development, impact the individual and collective chances and choices of a population, which in turn impact their health and wellbeing.(15,17)

A population health approach is intended to address health disparities through action directed at the determinants of health. Given the broad scope of these determinants, a population health approach is often, but not always, a collaborative approach between two or more sectors, such as health, education and environmental sectors, designed to improve the health of a population.(15,18) From a research perspective, the population health approach necessitates disaggregation of the health outcomes under study by socio-demographic and economic variables to understand the socially constructed factors that impact these outcomes. Sir Michael Marmot is widely credited with developing the concept of population health by articulating the relationship between socio-economic status and health outcomes through the Whitehall II longitudinal study of the British civil servants which began in 1985. Sir Marmot identified a social gradient across many chronic illnesses as well as the significant contribution of relative deprivation, in addition to absolute deprivation, to inequitable health outcomes. (19)

1.3.1. Applying a Population Health Approach to Obesity and Cardio-Metabolic Risk

In Canada, despite universal health care and progressive economic policies designed to redistribute wealth, health and social inequities persist. For example, it is estimated that 8-15% of children (<18 years) and 40% of Indigenous children live in poverty.(20–22) Furthermore, low socio-economic status is generally positively associated with chronic diseases, such as cardiovascular diseases and type 2 diabetes, among Canadians.(23) These avoidable disparities in health are attributed to the structural, social and environmental challenges experienced by those with low socio-economic status, as well as the compounding effects of negative health behaviours, such as insufficient physical activity and poor dietary habits.(24)

Applying a population health approach to the research design ensures that the inequities across social groups will be captured and reported and that, through the policy and clinical recommendations, those inequities will not be further exacerbated.

1.4. Theoretical Framework

This doctoral research was underpinned by the WHO's *Conceptual Framework for Action on the Social Determinants of Health*.(18) This framework was published by Drs. Solar and Irwin in their work as part of the WHO Commission on the Social Determinants of Health. (18) This conceptual framework offers a comprehensive depiction of the influence and interplay between determinants of health that give rise to health and social inequities within a population:

- **Structural determinants** – socio-economic and political contexts are macro-level factors within society that establish a basic class status which contribute towards an individual's power and social position in society;
- **Social determinants** – factors that further stratify social class such as sex, gender, ethnicity, education, occupation and income; these factors influence an individual's life choices, chances, income and education level;
- **Intermediary determinants** – factors that determine, to a degree, the exposure and impact of the social determinants of health, specifically material circumstance, behaviours, biological factors and psychosocial factors, on overall health and wellbeing:
    - **Physical environments -** community, neighbourhood and household factors that impact exposures to health risks/characteristics that affect health outcomes and health behaviours; and
    - **Individual factors -** genetics, intrauterine environment, and behavioural factors that can negate or promote health(17,18)

This framework was inspired by the *Social Production of Disease* model by Diderichsen, Evans and Whitehead, which presented the concept of social and economic mechanisms that lead to distributions of power and inequity.(18,25) The WHO conceptual framework was also informed by life course theory, which offers a temporal perspective with which to study population health across the life span. Pertinent to this research endeavour, life course theory posits that the effects of various risk factors for ill health accumulate over time, often with particular emphasis in points in time during childhood and adolescence, potentially leading to the resulting presentation of health problems later in life. Ultimately, the WHO conceptual

framework represents a unification of several predominant, complementary population health theories into one comprehensive framework. (18) For that reason, it is a highly suitable framework with which to study obesity and cardio-metabolic risk factors among children and adolescents from a population health perspective.

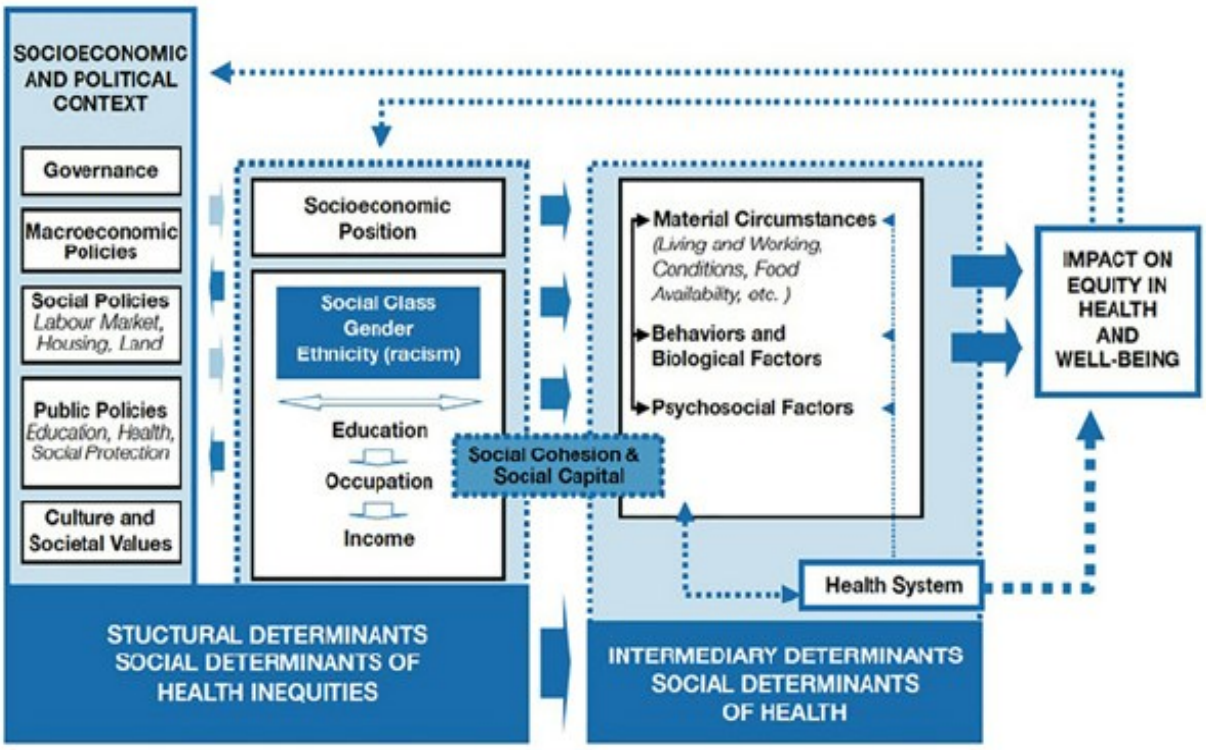


Figure 1. A Conceptual Framework for Action on the Social Determinants of Health, World Health Organization (18)

2. REVIEW OF THE LITERATURE

2.1. Chronic Diseases

Definition

Non-communicable, or chronic, diseases are broadly defined as conditions which last for three months or longer, and are not transmitted through direct or indirect contact but rather progress slowly in response to genetic, socio-economic and behavioural factors.(26) The major chronic diseases fall within five categories: cardiovascular diseases, such as strokes and heart attacks; certain cancers, such as breast and colorectal cancers; chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease; diabetes, particularly 'adult-onset' type 2 diabetes; and mental illnesses, such as depression and anxiety.(26,27)

Causes

Growing rates of chronic diseases have been attributed to shifts in structural, social, economic and individual factors. Structurally, the emergence of a global economy and trade liberalization, industrialization, and urbanization has led to an increasingly unequal distribution of income, as well as drastic changes in dietary patterns and more sedentary time both at home and at work.(2,5,8,28,29) Health behaviours, influenced by both societal and individual factors, also play a prominent role in the changing pattern of chronic disease onset. Health risk behaviours, such as smoking, diets that are nutrient poor and calorie rich, insufficient physical activity, and too much alcohol, contribute to the risk and onset of chronic diseases. Approximately 20% of Canadians aged 12 years and older smoke at least occasionally; fortunately, the prevalence and incidence of smoking is declining, even among adolescents aged 12-18 years.(30) In Canada, less than 10% of children and adolescents meet the Canadian physical activity guidelines of 60

minutes of moderate-to-vigorous physical activity at least six days per week. (31) Less than 50% of Canadians eat a sufficient amount of fruits and vegetables on a daily basis. (32) Sedentary behaviour and poor eating habits contribute towards excess weight gain, which is a substantial risk factor for many chronic diseases and will be discussed in more detail in the following section.

Prevalence in Canada

Chronic diseases now represent the leading cause of morbidity and mortality in Canada, as well as a substantial burden on Canada's universal health care system. (7,33) Among adults in Canada, it is estimated that 38% have a chronic disease with 15% having two or more chronic diseases. The most prevalent chronic diseases being: arthritis (18%), mood disorders and/or anxiety (12%), diabetes (10%), chronic obstructive pulmonary disease (9.7%), asthma (9.5%), cardiovascular diseases (6.2%), and cancer (2.4%). (7) Among Canadians aged 1-19 years, the estimated prevalence of chronic diseases are: asthma (15.7%), mood disorders and/or anxiety (9.7 % for ages 12-19 years only), and diabetes (0.3%). (7)

Trends in Canada

Globally, chronic diseases have increased dramatically during the 21st century at great personal and monetary cost to individuals and governments. (5) In Canada, the prevalence of all major chronic diseases has increased in the past 30 years, with a trend toward starting earlier in adulthood. The Canadian Diabetes Association estimates that the prevalence of diabetes in Canada will more than double in the current twenty year period (4.2% in 2000 to 10.8% in 2020). (6) The prevalence of diabetes in Canada has been growing by 3.5% per year since 1990. (6) The rate of cardiovascular diseases and cancer are estimated to increase by 14%

annually.(7) Notably, the cardiovascular diseases mortality rate has been in decline for the past 60 years, which has been largely attributed to medical and pharmaceutical advances, as well as behavioural modifications to prevent cardiovascular diseases, such as smoking cessation.(34,35) Yet, cardiovascular disease remains one of the primary causes of death in Canada.(36)

2.2. Obesity

Definition

The World Health Organization defines overweight and obesity as *"abnormal or excessive fat accumulation that may impair health".*(37) Though excess weight is a known risk factor for a number of chronic diseases (38), evidence suggests that the type of fat, and the location on the body where this excess fat is primarily stored, has implications on the overall risk to health posed to the individual.(39) Subcutaneous fat is generally stored just below the skin, often on the hips and buttocks, while ectopic fat is stored in the liver, heart or muscles. Ectopic fat has a well-established association with insulin resistance, type 2 diabetes and cardiovascular diseases that extends beyond the relationship between overall adiposity and ill health.(39,40) Visceral, or abdominal, fat is a marker for ectopic fat distribution (41) with substantial evidence indicating that abdominal adiposity is a stronger predictor for cardio-metabolic diseases than BMI for both adult and pediatric populations.(42–45)

Causes

Obesity is generally regarded as the physical consequence of energy imbalance. Basically, obesity can develop when the body's energy expenditure (i.e. physical activity, resting

metabolic rate) are below the level of energy consumption (i.e. calories ingested through diet). While this physiological phenomenon is the main driver for weight gain, consensus is absent on whether reduced physical activity levels or greater intake of energy-dense foods are the primary culprits.(46) The etiology for obesity, however, is much more complex than diet and physical activity, encompassing genetic, hormonal, metabolic, environmental, socio-economic and personal factors.(47) There is increasing recognition of modern society's *'obesogenic environment*', meaning the lifestyle, dietary and activity patterns driven by such factors as technology (e.g. automobiles, computers) and food industry (e.g. larger portion sizes, transformed foods high in fat and sugar), as key explanatory features for increasing rates of obesity.(47)

Obesity as a Chronic Disease

Obesity has recently been labelled as a chronic disease by select medical and stakeholder groups with the argument that a broad range of factors contribute to its development as well as to its association with multiple health problems.(48) In 2015, the Canadian Medical Association declared obesity to be a chronic disease with the intention of drawing support towards the importance of addressing obesity through research, medical and pharmaceutical measures in addition to behavioural modification.(49) This is consistent with the policy direction of the American Medical Association which similarly declared obesity to be a chronic disease in 2013.(50) Re-framed as a chronic disease, treatment for obesity commands both lifestyle and medical interventions, consistent with other chronic diseases such as diabetes.(48)

Health Implications

There are many widely documented health consequences related to obesity as the overall risk of chronic disease for people suffering from obesity is much higher. These diseases are typically considered as 'co-morbidities of obesity', meaning that they have their origins in the presence of excess fat. Persons with obesity are significantly more likely to suffer from such co-morbidities as: type 2 diabetes, cardiovascular disease, high blood pressure, certain types of cancer, osteoarthritis, obstructive sleep apnea, stress urinary incontinence and gallbladder disease.(48,51,52) Beyond the physical health consequences, research indicates a correlation between the presence of psychological disorders and obesity. (52) Mental health problems, social disorders, personal and professional limitations, and disabilities are common, particularly for persons suffering from a severe level of obesity.(51) It is thought that psychological problems may precede and/or succeed the onset of obesity.(53) Obesity is also associated with a reduction in life expectancy, although premature death in persons suffering from obesity is largely due to the presence of serious co-morbidities.(54)

Measurement

Several measures exist for estimating body fat and determining weight class (underweight, normal, overweight or obese). Measurements using dual energy X-ray absorptiometry (DXA) and hydro-densitometry are considered highly precise and reproducible estimates of body fat mass.(55) DXA measures body fat percentage using x-ray technology and is often considered the 'gold standard' of body fat estimation, even among children and adolescents.(55,56) Hydrodensitometry uses a hydrostatic weighing water chamber which compares weight on dry land to weight underwater.(55) Plethysmography, which produces estimates based on air

displacement, is often preferred for the pediatric population (4-18 yrs) as it is a rapid, comfortable test, relative to DXA or underwater weighting. (57,58) Furthermore, plethysmography has been shown to be even more accurate than hydrodensitometry (55,59), which may be partially attributed to the air-displacement mechanism as a positive, fast testing experience. However, while accurate, these methods are complex and require expensive medical equipment, thus best suited for clinical use rather than population estimates.

Body Mass Index

The most common and easy-to-use method to assess body composition is the Body Mass Index (BMI). BMI is an indirect measure of body fat as it represents a height-to-weight ratio calculated using the formula: BMI = [weight(kilograms)/height(meters)^2]. (45) The BMI score is compared to a BMI table, established using population reference data, which indicates the body weight classification of the BMI score.

For adults (≥ 18 years), the body weight classification system developed by the WHO is well-established internationally and endorsed by Health Canada. (38,60,61) There are six weight status categories which correlate with the overall risk of developing health problems and premature mortality:

- Underweight: BMI < 18.5 "increased risk"
- Normal weight: BMI = 18.5 - 24.9 "least risk"
- Overweight: BMI = 25 - 29.9 "increased risk"
- Obese Class I: BMI=30.0-34.9 "high risk"
- Obese Class II=35.0-39.9 "Very high risk"
- Obese Class III= ≥40.0 "Extremely high risk" (38,60,61)

For children and adolescents, sex-specific BMI-for-age curves were developed using reference population to establish defined percentiles. The BMI-for-age score is based on these age- and sex-specific percentiles which define the weight status categories:

- Underweight: BMI<5th percentile
- Normal weight: 5th≤BMI<85th percentile
- Overweight: 85th≤BMI<95th
- Obese: BMI ≥ 95th percentile (62–64)

However, for children and adolescents, there are three prominent body weight classification systems, which differ by their reference populations as well as the precise mathematical techniques applied to generate the percentiles. The existence of multiple systems reflect the complexity in reaching international consensus regarding age- and sex- specific cut-offs that are indicative of the most natural growth patterns of child development and that most accurately reflect the association between weight status and health.(65) For the pediatric population, this challenge is exacerbated by the low prevalence of weight-associated health problems presented in childhood as the co-morbidities of obesity tend to present in adulthood.

The three prominent body weight classification systems for children and adolescents are :

- **United States' Centers for Disease Control and Prevention's (CDC) 2000 Growth Charts**: developed based on population growth patterns estimated from five nationally representative survey data sets (the National Health Examination Survey (NHES) II (1963-1965), the NHES III (1966-1970), the National Health and Nutrition Examination Survey (NHANES) I (1971-1975), NHANES II (1976-1980), and NHANES III (1988-1994) to classify weight status for ages 2-17 years.(64)

- **WHO Growth Reference for School-Aged Children and Adolescents**: developed using nationally representative data from the United States' 1977 National Center for Health Statistics growth charts (based on data from the NHES and NHANES I) to classify body weight status for ages 5-19 years. Complex statistical methods were applied to allow for smooth transition from WHO Child Growth Standards (ages 0-5 years) and to WHO adult cut-offs for ages 18 years and older.(63,65)
- **International Obesity Task Force (IOTF**): developed using nationally representative data from six countries (Brazil, Great Britain, Hong Kong, Netherlands, Singapore, and United States) for the purposes of facilitating international comparisons of prevalence estimates for obesity for ages 2-18 years, though not for clinical or individual use.(66)

There are many studies and evidence reviews which compare the prevalence of overweight and obesity among children and adolescents across these weight classification systems. Among studies comparing IOTF and WHO, a systematic review as well as a study using children and adolescents in the CHMS, found that the IOTF underestimated the prevalence of obesity. (67,68) Among studies comparing the three systems, Lemelin (2013) studied 5 year old children in Quebec and concluded that the prevalence of overweight and obesity differed between the definitions.(69) Further, that the CDC and WHO systems were more similar than IOTF with no sex difference observed between CDC and WHO systems.(69) Similarly, Gonzalez-Casanova (2013) applied the CDC, WHO and IOTF systems to a sample of 5-18 year old children (n=18,265) in Columbia.(70) While the prevalence of obesity differed by each system, logistic regression to predict odds of obesity by age and sex showed no statistically significant difference between the CDC and WHO systems.(70) Finally, among those comparing WHO and

CDC, de Oliveira (2013) reported that the WHO had greater sensitivity at identifying obesity than the CDC system in a sample of Portuguese children (n=200). Yasin (2013) compared the systems in a sample of patients aged 5-20 years (n=4375) at hospital in Ontario. He reported that the prevalence of obesity using the WHO system was twice as high as the CDC, 16.0% and 8.6%, respectively.

Overall, the BMI calculation offers a simple, cost-effective, quick method of estimating weight status category. Evidence indicates that weight status estimates based on BMI are strongly associated with DXA results for children, adolescents and adults. (56,71) A limitation of the BMI is that it is not a measure of body composition and does not differentiate between body fat or muscle mass.(55,72) For example, a very muscular person may be inaccurately classified as overweight or obese using BMI.(38)

- Waist Circumference

Measurement of the waist circumference (WC) is a direct measure of abdominal obesity as well as an indicator of body fat distribution and an especially good indicator of abdominal adiposity.(73,74) Among children and adolescents, evidence indicates that WC has high sensitivity and specificity for abdominal fat estimates in comparison with results using DXA .(74) Further, for both children and adults, obesity estimates by WC have been shown to be a stronger predictor for cardio-metabolic risk than estimated by BMI.(42,44,75)

Among adults, abdominal obesity is defined as: men: WC≥102 cm; and women: WC≥88 cm, which correspond to an "*increased risk of developing type 2 diabetes, coronary heart disease, and hypertension*".(38) Among pediatric populations, abdominal obesity is generally defined using age- and sex-specific cut-offs developed using reference population data. (55,76)

Prevalence in Canada

Recent Statistics Canada estimates, based on measured data (2009) and using the WHO's body weight classification system for adults, indicate that approximately 25% of Canadian adults (18 years and older) are obese (26.0% of men and 24.2% of women). (77) Further, Canadian adult males are significantly more likely to be classified as overweight (42.1%) versus adult females (31.5%).(77) Among Canada's adolescent population (12-17 years), based on measured data (2012-13) and using the WHO Growth Reference for School-Aged Children and Adolescents, Statistics Canada reports that 21% of boys are obese and another 23% are overweight, while for girls, 12% are obese and additional 18% are overweight. Finally, among Canadian children (5-11 years), 19% are overweight with boys more likely than girls to be obese (15% of boys versus 11% of girls).(78)

Trends in Canada

Obesity rates have risen in all age categories over the past 40 years. In 1978, just over 13% of Canadians were obese.(51) The most striking increases are observed among Canada's youngest and oldest adults. Between 1978 and 2009, the prevalence of obesity for young adults (18-35 years) increased from 8.5% to 16.6% and for seniors (65+ years) from 10.6% to 29.2%.(51,77) In 2016, the Standing Senate Committee on Social Affairs, Science and Technology reported, based on expert testimony, that the percent of youth entering adulthood with overweight or obesity has doubled (from 15% to 30%) over the past 30 years.(79) Even more alarming, the Senate Committee also reported that incidence of obesity among children is increasing by 2.0-5.0% annually.(79)

2.3. Metabolic Syndrome

Definition

The understanding and definitions of the Metabolic Syndrome (MetS) have evolved greatly since the concept was first proposed by Dr. Kylin in 1923.(80) MetS is broadly characterized by a constellation of metabolic abnormalities and chronic disease risk factors, with a general consensus that the syndrome originates from obesity and/or insulin resistance.(81) MetS is also known as the *Insulin Resistance Syndrome, Deadly Quartet, Multiple Metabolic Syndrome,* and *Syndrome X.*(82,83) A multitude of competing definitions exist for the diagnosis of MetS, all of which involve excess weight. The prominent definitions are those by the United States' National Institutes of Health National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NCEP ATP III), the WHO, and the International Diabetes Federation (IDF).(84–86) Briefly, the definitions are consistent in that the presence of three of the following five risk factors generally constitutes MetS: abdominal obesity; elevated fasting triglycerides; low high-density lipoprotein cholesterol (HDL-C); elevated blood pressure and/or hypertension; and impaired fasting glucose and/or type 2 diabetes and/or insulin resistance. With the IDF definition, the presence of abdominal obesity is an absolute requirement (85); whereas for the WHO definition, the presence of insulin resistance or type 2 diabetes is required for a MetS diagnosis.(87) The WHO definition also includes microalbuminuria as a potential risk factor for MetS.(87) The NCEP ATP III does not have a required risk factor.(88) The IDF MetS criteria for children, adolescents and adults are provided in the Methodology chapter.

Diagnosing the MetS among children and adolescents proves particularly challenging given the difficulty in establishing accurate and meaningful diagnostic criteria for this population, as well as quantifying the association between MetS and the increased relative risk for cardio-metabolic disease. In particular, there is a lack of consensus regarding the diagnosis of MetS among children under the age of 10 years among the multiple definitions of MetS, as well as the investigators and clinicians who apply these definitions in their research and medical practices. The IDF MetS criteria for children and adolescents does not allow for the diagnosis of MetS for those less than 10 years of age, whereas the NCEP is intended for ages 12-19 years.(89,90) Consequently, prevalence of MetS and MetS risk factors among children and youth vary greatly depending on the adopted definition.(91)

Risks Factors

The clinical criteria that define MetS typically include a measure of excess body fat (obesity, WC or visceral adiposity index)(92); insulin resistance; glucose intolerance (presented as type 2 diabetes, impaired glucose tolerance or impaired fasting glycaemia); dyslipidaemia; and hypertension.(81) With multiple definitions for MetS, there is some discussion among researchers and health professionals as to whether it's best defined by insulin resistance and obesity, elevated risk of cardiovascular diseases, or a collection of statistically related factors.(85) Most experts point to insulin resistance and/or obesity as the most significant risk factors for this condition.(81,84) Disentangling the effects of excess weight and insulin resistance on MetS proves incredibly complex as the two risk factors not only influence the likelihood of MetS but also of each other.(93)

Though insulin resistance is understood to be an important risk factor for MetS, differing views point to insulin resistance being, *"the most accepted and unifying hypothesis to describe MetS"*(81) or an *"underlying feature...although a significant proportion of these (MetS) patients do not have insulin resistance."*(94) Rising rates of insulin resistance among the population are generally attributed to escalating levels of obesity, although there are a select group of insulin resistant individuals who are not overweight or obese (93,95), which may be attributed to genetics, age, low physical activity or a high-for-body weight level of abdominal adiposity.(95)

Prevalence in Canada

Recent national estimates for the MetS are 19.1% for Canadian adults (96) and 3.5% for youth (12-19 years).(97) Prior to these data, findings from the Canadian Heart Health Surveys (1986-1992) pointed to a MetS prevalence of 17% among Canadian adults.(98) Regarding North American children and youth (2-18 years), Kranz (2007) estimated prevalence of 0.7%, 2% or 23%, depending on the defining criteria used to diagnose MetS.(99)

More than the sum of its risks?

The premise of the MetS is that its level of risk for morbidity and mortality is compounded beyond the expected risk of each of its risk factors individually.(100,101) Evidence consistently supports a strong association between MetS and an increased risk of many chronic diseases, particularly cardiovascular disease and type 2 diabetes, and all-cause mortality.(81,101) It is important to note that while consensus exists that the presence of any of these factors presents a serious health risk, not all experts agree that MetS is a stand-alone medical condition. Despite MetS presentation co-occurring more often than chance, some experts argue that this syndrome is nothing more than the sum of its parts. For example, after

modelling national data from the United States (NHANES), Eddy (2008) concluded that the MetS diagnosis, using NCEP ATP III definition, the IDF Criteria or the WHO definition, added little to no value regarding future risk for cardiovascular diseases beyond each individual risk factor for adults. As another example, following a systematic review regarding associations between the risk factors for MetS and atherosclerosis, Bayturan (2010) attributed atherosclerosis progression to the additive contributions of each individual risk factor, rather than MetS.(102) Yet, substantial counter-evidence in support of the concept of MetS indicates that the contribution of individual risk factors are multiplicative, meaning that the risk for cardiometabolic diseases among those with MetS is higher than would be attributed to the sum of risks carried by each risk factor individually.(103)

2.4. Cardio-Metabolic Risk

Definition

Given the overall consensus of the significance of each individual risk factor, coupled with the lack of consensus regarding MetS diagnoses for those aged less than 10 years (89), the concept of cardio-metabolic risk offers an alternative approach to assessing overall risk for cardiovascular diseases and metabolic abnormalities.

Risk Factors

Similar to MetS, cardio-metabolic risk facilitates early recognition of potential onset of cardio-metabolic diseases through a comprehensive list of risk factors.(104) These risk factors are both traditional cardiovascular disease risk factors, such as hypertension, smoking, physical inactivity, dyslipidemia, glycaemia (diabetes and impaired fasting glucose), and emerging

factors, such as insulin resistance, genetic predisposition and inflammatory markers, such as high sensitivity c-reactive protein (CRP).(104) However, with cardio-metabolic risk, the risk factors are considered individually, with the rationale being that the presence of any of these risk factors requires treatment and signals the need to test for the presence of other cardio-metabolic risk factors.(104)

2.5. Socio-Economic Status and Chronic Diseases

As discussed in the Introductory Chapter, health status is determined by a plethora of factors that extend well beyond the availability and quality of health care.(17) For this research endeavour, I examined the social gradient present in cardio-metabolic risk using household income and education as indicators of socio-economic status (SES).

Household Income and Education – Indicators of Socio-Economic Status

Household income and education are robust indicators of SES and are the most commonly applied indicators in epidemiological analyses which incorporate the determinants of health.(2,105–108) Further, household income and education are fairly straightforward to measure relative to other potential indicators of SES, such as social class, occupation or neighbour deprivation index.(109,110)

Accordingly to the WHO, high income is related to improved health status and the disparities by income are often mirrored by disparities in health status.(2) Broadly, the income level of an individual or household greatly determines quality and influence of other determinants of health, such as housing and diet. Further, low income is associated with negative health behaviours, such as tobacco use and unhealthy alcohol consumption patterns.(111)

Unfortunately, a 2008 report by the Organisation for Economic Co-operation and Development indicated that Canada has had one of the greatest increases of income inequality between 1990-2000 among comparable countries.(112)

Low education levels are generally associated with poorer health outcomes, although the relationship between education and health is multifaceted. Education and income are related as those with higher education tend to earn higher incomes.(113) In Canada, primary and secondary education is publically available to all citizens but the substantial tuition costs for college and, particularly, university can be a barrier for those of lower economic position. However, compared to income, education tends to remain more stable throughout the life course and is less influenced by one's health status.(114) Higher education also tends to support improved health literacy and the adoption of health promoting behaviours.(111)

Socio-Economic Status of Canada's Child and Adolescent Population

Children and adolescents represent 6.54% and 8.68% of Canada's population, respectively, (based on the 2011 Census which is not fully representative of Indian reserves or settlements).(115) Estimates from Statistics Canada (based on 2011 Census) indicate that 8.4% of children (< 18 years) live in households classified as low-income (after tax).(20) However, estimates of child poverty in Canada by the Conference Board of Canada are much higher at 15% of all children (<18 years).(21) Disproportionately higher levels of low income are experienced by children in female lone-parent families (23.0%), in Aboriginal families (40%), and in families that have recently immigrated to Canada (48%).(20,22) Notably, regarding socio-economic conditions and childhood, in 2005 article in The Lancet, Sir Michael Marmot stated

that child mortality is *"the health outcome most sensitive to the effects of absolute material deprivation*".(116)

Social Gradient in Chronic Disease

In Canada, even with our universal health care system and progressive social benefits, poor health outcomes are disproportionately high among those of a lower SES.(23) Among Canadians living in Census Metropolitan Areas, those classified as having low SES (versus high SES) are significantly more likely to be hospitalized for (rate per 100,000): diabetes (102 versus 43), Chronic Obstructive Pulmonary Disorder (301 versus 113), mental health issues (596 versus 256) and substance-related disorders (100 versus 29).(9) The relationship between obesity and SES is sex-specific, as an inverse relationship is observed among females, but not males.(117) Indigenous Canadians have established their own set of determinants of health, termed the 'social determinants of aboriginal peoples' health' which build on the existing concepts of structural and social determinants of health but also include historical and cultural determinants specific to the Indigenous Peoples, such as colonialism and self-determination.(118) Unfortunately, the health disparities between non-Indigenous and Indigenous Canadians are disparagingly high. For example, almost 20% of adults living on First Nations reserves have diabetes compared to only 5.4% of the Canadian adult population.(118) Kaler (2006) reported a prevalence of MetS of approximately 50% for adults living in First Nations communities in Western Canada (119), the national average among adults being approximately 19%.(96)

Health outcomes are also socially patterned. Children with asthma living in households classified as low-income adequacy are significantly more likely to be hospitalized for asthma-

related health complications than those of higher income adequacy. (12) Children with low SES are also significantly more likely to be hospitalized for unintentional injuries than those of high SES.(9) Finally, the prevalence of MetS is estimated at 50% for youth (ages 6-17 years) living on First Nations Reserves (119) and national estimates based on data from 2007-2009 suggest that approximately 3.5% of adolescents (aged 12-19 years) have MetS.(97) Oliver (2005) reported that children living in a neighbourhood defined as low SES, using Statistics Canada's 2001 Dissemination area datasets, were significantly more likely to be overweight (versus high SES).(11)

2.6. Childhood: A Foundational Stage for Lifelong Health

Epidemiological studies have repeatedly shown the substantial influence of childhood health on chronic disease outcomes in adulthood. (4,120) The application of a lifecourse approach to epidemiological analysis has generally focused on the childhood and adolescent phases of development in recognition of the critical periods, as well as the cumulative efforts, of repeated exposures to conditions experienced during those years that may increase future disease risk.(121)

Specific to this research endeavour, children and adolescents classified as having obesity are predisposed to remaining obese during adulthood. (122) Some evidence suggests that the presence of fat cells gradually increase during childhood and adolescence and then remain static during adulthood, regardless of weight status and fluctuations.(123) Consequently, those with obesity in childhood are predisposed to the chronic diseases that are associated with obesity. Given current prevalence and trends in pediatric obesity, one can postulate that the

millennial and Y generations may be subject to increasing rates of chronic diseases in their adulthood.

Further, there is substantial evidence to suggest that atherosclerosis and other precursors to chronic disease begin to develop during childhood and adolescence.(124) In a longitudinal study of the association between cardiovascular risk factors and atherosclerosis completed using data from the 'Young Finns' study in Finland (1980-2002), Raitakari (2003) concluded that childhood and adolescent levels of blood pressure, BMI, smoking, and cholesterol were positively associated with atherosclerosis, with a stronger link observed between adolescents (12-18 yrs) and adulthood (versus childhood (3-12yrs) and adulthood).(120)

Following a systematic review regarding associations between SES in childhood and measured risk for cardiovascular disease in adulthood, Galobardes (2003) concluded children with lower SES showed greater risk for cardiovascular diseases and more advanced atherosclerosis, versus those of higher SES, regardless of their SES in adulthood.(10) Thus, it is critically important to recall that risk factors for chronic diseases are influenced by the SES of each child, which in turn will have influence over the SES experienced in their adult life.

3. OBJECTIVES AND HYPOTHESES

3.1. Overall Objective

The overarching objective of this research endeavour is to contribute towards an improved understanding of the current state of health and risk for onset of cardio-metabolic diseases in Canadian children and adolescents. More specifically, to measure and examine the prevalence of traditional risk factors for cardio-metabolic diseases, as well as the behavioural, demographic and socio-economic factors that contribute to these risks, using the Canadian Health Measures Survey (CHMS), a relatively recently available national, measured health dataset.

3.2. Specific Objectives

To achieve this broad objective, a series of four research projects were undertaken with specific objectives:

1. **Metabolic Syndrome**: To investigate the prevalence of MetS and its risk factors, and the associations between SES and these risk factors, in Canadian children and adolescents (10–18 years).
2. **Waist Circumference Cut-Offs**: To establish pre-obesity epidemic waist circumference reference values for children (aged 6-10 years) using established, measured, national anthropometric data from Canada and the United States.
3. **Cardio-Metabolic Risk**: To assess the cardio-metabolic risk profile of Canadian children (6-11yrs) and adolescents (12-18 yrs) and to identify which obesity indicator (BMI versus WC) is the stronger predictor for cardio-metabolic risk, using a dichotomous cardio-metabolic risk variable. As well, to investigate if the generation of a new obesity

indicator, resulting from a combination of both BMI and WC values, is a superior predictor than each traditional obesity indicator.

4. **Inflammation Marker**: To quantify the association between inflammation, with high CRP as a marker, and a dichotomous cardio-metabolic risk variable to determine if high CRP was a significant predictor of cardiometabolic risk among Canadian children (6-11yrs) and adolescents (12-18 yrs).

3.3. Hypotheses

Following a literature review, the following hypotheses were proposed for the four research projects:

1. **Metabolic Syndrome**: *The prevalence of MetS will be approximately 4-8% with a significantly higher prevalence among female, Aboriginal and older participants, as well as those with obesity and having a lower socio-economic status, based on previous national studies of MetS among children and adolescents in Canada and the United States .*
2. **Waist Circumference Cut-Offs**: *Regression of linear, logarithmic and quadratic functions will generate sound reference data that is consistent with trends observed from the Canadian Health Measures Survey and National Health and Nutrition Examination Survey. As compared to linear and quadratic functions, the logarithmic function will generate reference data with the smallest degree of error and highest degree of sensitivity and specificity.*

3. **Cardio-Metabolic Risk**: *The prevalence of cardio-metabolic risk among children and adolescents will be approximately 25-35%, based on previous regional-level studies among children and adolescents in Canada, with significantly higher prevalence among adolescents and smokers, as well as those with obesity, low levels of physical activity, insufficient sleep and with low socio-economic status. All three obesity indicators (BMI, WC, and Combined BMI-WC) will be positively associated with cardio-metabolic risk with the 'combined BMI-WC' being the strongest predictor for cardio-metabolic risk.*
4. **Inflammation Marker**: *High levels of CRP, a blood marker for inflammation, will be a significant predictor for cardio-metabolic risk.*

4. METHODOLOGY

4.1. Overview

This doctoral research endeavour was conducted using data from the CHMS through a series of four research projects conducted over the period of 2011-2016. Project 1 was conducted from 2012-2013 using CHMS Cycle 1 data, collected from 2007-2009, and Cycle 2 data, collected from 2009-2011. Projects 2-4 were conducted from 2015-2016 using CHMS Cycles 1, 2 and 3, with Cycle 3 data collected from 2012-2013. Project 2 also referenced data from the 1981 Canadian Fitness Survey and the Third NHANES (1988-1994).

Project 1 presented a descriptive analysis regarding the prevalence of the MetS among Canadian youth (10-18 years). Project 2 established age- and sex- specific 90^{th} percentile WC reference data for Canadian children aged 6-10 years. This project facilitated an expanded age range for the subsequent two projects. Project 3 examined the association between cardio-metabolic risk and obesity, using three indicators of obesity including a novel indicator, among Canadian children and adolescents (6-18 years) through both description and regression analysis. Project 4 further studied cardio-metabolic risk by examining its association with inflammation among Canadian children and adolescents (6-18 years).

This chapter describes the overall methodology for the dissertation, as well as the statistical analyses applied and specific statistical commands performed for each research project. The manuscripts for each research project provide concise descriptions of the research methods for each endeavour and are provided in Chapter V Research Results.

4.2. Data Source

Description of the Canadian Health Measures Survey

The CHMS is a comprehensive, nationally-representative survey designed to collect information on the health of Canadians.(125–128) The survey is conducted by Statistics Canada in partnership with Health Canada and the Public Health Agency of Canada. The survey covers Canadians living at home and residing in the 10 provinces and three territories, excluding those living on reserves and other Aboriginal settlements, in institutions, in certain remote regions and full-time members of the Canadian Forces; in total, this represents 96% of the Canadian population.(125–128) The CHMS cycle 1 (2007-2009; n=5604) collected data on ages 6-79 years, with Cycle 2 (2009-2011; n=6395) and Cycle 3 (2012-2013; n=5785) expanding to cover ages 3-79 years.(125–128)

The CHMS consists of an in-home interview and a physical assessment conducted at a mobile examination centre (MEC). The interview collects demographic, socio-economic, family history and general health information. The physical assessment at the MEC includes measures of anthropometry, spirometry, blood pressure, fitness, oral health and biological specimens. (125–128) Participants were randomly assigned to either morning or afternoon MEC appointments; those assigned to morning appointments were requested to fast overnight. (126–128) A phlebotomist performed the blood draw following a standardized venipuncture technique.(126–128) The volume of blood collected increased with increasing age thus enabling more laboratory analyses for older participants.(126–128) Laboratory analyses of the biological samples were performed to calculate estimates of disease and markers for disease, nutrition and environmental toxins.(126–128)

Participants were requested to wear Actical accelerometers (activity monitor) for a seven day period following their visit to the MEC to measure their level of physical activity.(126–128) The activity monitor sits on a belt across the hips and measures the intensity of physical activity at intervals of 1 minute. The results from participants who wore the activity monitors for a minimum of 4 days for at least 10 hours each were included in the CHMS accelerometry sub-sample.(126–128)

The CHMS statistical research collection is legislated under the federal *Statistics Act* and approved by the Health Canada Research Ethics Board.(126) Participation in the survey is voluntary and ongoing consent is obtained throughout the household interview and assessment at the MEC.(126–128) For participants 13 years and younger, written consent from a parent or guardian, as well as written asset from the child (when feasible), is required.(126–128)

Sampling Strategy and Weighted Data

The CHMS produces reliable estimates at the national level by age group and sex through a multistage sampling strategy and survey weight adjustment.(126–129) The selection of collection sites for each cycle is informed by the Labour Force Survey sampling frame.(126–129) A multitude of practices are employed to minimize non-response; the combined response rate for home and clinic visits were 51.7%, 55.5% and 51.7% for cycles 1, 2 and 3, respectively.(126–128)

Each survey participant represents a number of Canadians and is assigned a sample weight to facilitate these national estimates. Statistics Canada calculated the sample weights by multiplying the selection weights for collection sites by the selection weights for dwellings,

followed by a series of adjustments for non-response at the initial contact, household interview and MEC stages.(126–129)

Greater details regarding the CHMS methodology have been published elsewhere.(126–129)

The CHMS User Guides for Cycles 1, 2, and 3 provide more detailed descriptions of the measurement procedures for all variables in this study.(126–128)

4.3. Analytical Approach

Data Preparation

Access to the CHMS was approved by the Public Health Agency of Canada's Data Coordination and Access Program. In combining multiple CHMS Cycles, the instructions provided by Statistics Canada were strictly followed. To create the final dataset for Project 1, the CHMS Cycle 1 and Cycle 2's fasting, household and clinic data files were merged for each cycle, and then Cycles 1 and 2 were combined using a Clinic Identifier. Similarly, the final dataset for Projects 2-4 was created by merging the fasting, household, clinic and activity monitor and laboratory data files for each cycle, and then Cycles 1-3 combined using a Clinic Identifier. In instances where identical variables were not combined due to different names across cycles, data manipulation was performed to combine each of these variables. With each of these final datasets, data cleaning was performed to identify, correct and/or remove errors in the data.

Study Population

For project 1, all CHMS respondents aged 10-18 years who provided fasting blood samples for Cycles 1-2 were included (n=1228). For project 2, all CHMS respondents aged 6-18 years were included (n=5922), as well participants from the 1981 Canadian Fitness Survey (n=3064) and the

Third NHANES (n=9713). For project 3, all CHMS respondents aged 6-18 years who provided fasting blood samples for Cycles 1-3 were included (n=2679). For project 4, all CHMS respondents aged 6-18 years who provided fasting blood samples and laboratory results for CRP for Cycles 1-3 were included (n=1831). There were no pregnant participants in any of the studies.

The University of Ottawa Research Ethics Board approved the secondary data analyses.

Project-Specific Derived Variables

The CHMS data files include variables that are raw as well as derived, meaning variables that were created by Statistics Canada using 2 or more raw CHMS variables. The list of raw and derived variables that were used in completion of this doctoral thesis is provided in APPENDIX A. A multitude of variables were derived for specific use for these research projects. The list of 'project derived variables' is provided in APPENDIX B. The criteria that were applied for defining these project derived variables are elaborated upon below.

Defining the determinants and outcome variables

The key variables as well as the cut-offs that were applied to establish categories are described below.

- **Socio-Demographic Profile**: A participant's demographic and socio-economic profile was assessed by self-report. Parents or guardians responded to questions about their children (6-11 years) by proxy and adolescents (12-17yrs) responded in private, with parental/guardian consent. The variables that constituted the socio-demographic profile were:

- **Age Group**: For the purposes of this thesis, I have categorized participants aged 6-11 years as 'children' and those aged 12-18 years as 'adolescents'[3]. With the age of majority ranging from 18-19 years in Canada, I chose to define 19 years as the start of adulthood.
- **Aboriginal Origin or Identity**: Participants were identified as having an Aboriginal origin or identity by self-report or proxy self-report.
- **Immigrant Status**: Participants were identified as being an immigrant to Canada by self-report or proxy self-report.
- **Socio-Economic Status**: SES was captured through household income adequacy and educational attainment variables. Education and income are key determinants of health and the most frequently used indicators of SES. (2,107,130)
    - **Household Income Adequacy**: Statistics Canada calculated income adequacy by classifying each participant into categories based on total household income from all sources and the number of people living in the household for CHMS Cycles 1-2.(126,127) I applied this approach to generate income adequacy for CHMS Cycle 3. To allow for greater statistical power and comparability across CHMS Cycles 1-3, I combined the household income adequacy categories of 'lowest income' and 'lower middle income' resulting in three categories for income adequacy (lowest and lower middle income, upper middle and highest).

[3] For Project 2 Waist Circumference Cut-Offs, adolescents were defined as ages 11-18 years to align with our reference data

- **Household Educational Attainment**: Derived by Statistics Canada, this variable represents the highest level of education attained by any member of the household. For participants not living with parents or guardians (5.1%), their responses pertained to their current household.(126–128) To allow for greater statistical power and comparability across CHMS Cycles 1-3, I re-classified the household educational attainment variables. The categories of 'less than secondary school graduation', 'secondary school graduation' and 'some post-secondary' were combined resulting in two categories (secondary school graduation or less and post-secondary graduation).

- **Weight Status**: Classified using BMI, WC, and a 'combined BMI-WC' indicator.

Body Mass Index

- **BMI**: Statistics Canada derived BMI using measured of weight and height (weight (kg)/height (m^2)).
- Statistics Canada also classified BMI using: (i) growth charts prepared by the CDC for ages 6-17 years; (ii) the WHO cut offs ages 5-18 years (Cycles 2-3 only); and (iii) the WHO body weight classification (for ages ≥ 18 years).(126–128,131–133)
- For ages 6-17 years, I chose to use the BMI variable derived by CDC growth charts for several reasons: (1) This variable was available for CHMS Cycle 1, which was the only existing cycle at the beginning of this research endeavour; (2) For Cycle 3, Statistics Canada only applied the United States' National Institutes of Health protocol to measure waist circumference, thus the CDC cut-offs allowed for greater alignment and consistency between the BMI and WC estimates, which is particularly important

for the analysis in the third paper, Cardio-Metabolic Risk, when these variables are combined as one variable (discussed below); (3) Application of the CDC BMI growth curves permits more accurate comparisons between the results of these projects and related studies in the United States using the NHANES data; (4) Finally, although studies show differences in prevalence of obesity between the CDC and BMI growth curves, to my knowledge, these definitions are not significantly different in terms of their association with measured health outcomes.

- For age 18 years, I used the international body weight classification system that was established by the WHO and is endorsed by Health Canada(38,60,61)

Waist Circumference

- **Waist Circumference** (to define abdominal obesity): I applied a prediction equation to CHMS Cycles 1 and 2 to the WC data (collected following the WHO protocol) to align it to the CHMS cycle 3 WC data (collected following the United States' National Institutes of Health protocol).(134) Abdominal obesity was defined as measured WC ≥ 90th age- and sex- specific percentile for ages 11-18 years based on reference data from the 1981 Canada Fitness Survey.(76) For ages 6-10 years, national reference data from the same time period was unavailable. I generated age- and sex-specific reference points using data from the 1981 Canada Fitness Survey and supplemented with trend lines from the CHMS Cycles 1-3 WC measurements (sex- and age- specific 90th percentile reference points). The methodology for this approach to generating reference data is elaborated upon in a separate paper.(135)

Combined BMI-WC

- **Combined BMI-WC**: I derived the combined BMI-WC indicator into 4 categories using the following cut-offs:
    - Normal: BMI<85th and WC<90th;
    - BMI Normal with Abdominal Obesity: BMI<85th and WC≥90th;
    - BMI Overweight with Abdominal Obesity: BMI≥85th and WC≥90th; and
    - BMI Obese with Abdominal Obesity: BMI≥95th and WC≥90th.

Behaviour

- **Physical Activity**: A participant's average daily moderate-to-vigorous physical activity (MVPA) was derived by Statistics Canada using an intensity cut-point which is equivalent to approximately >3 metabolic equivalents.(126–128) Participants aged 6-17 years were determined to meet physical activity guidelines if they accumulated ≥ 60 minutes of MVPA at least 6 days per week.(126–128,136) Participants aged 18 years were determined to meet physical activity guidelines if they accumulated ≥ 30 minutes of MVPA at least 5 days a week.(126–128,136)
- **Sleep**: Sleep duration per 24 hour period was ascertained by self-report or by proxy for participants aged 6-11 years.(126–128) Adequate sleep was defined as 9 or more hours for ages 6-13 years, 8 or more hours for ages 14-17 years and 7 or more hours for 18 years.(137)
- **Smoking Status**: This was determined using self-reported smoking behaviour, available for participants aged 12-18 years.(126–128) I re-categorized participants into two groups: ever

smoked, which included all past and present smokers, and never smoked, which included all participants who had never smoked.

- **Cardio-Metabolic Risk factors**:
    - Elevated fasting triglycerides defined as ≥1.25mmol/L.(104,124)
    - Low HDL-C defined as using appropriate age- and sex- specific criteria: (1) males and females 6-15 years: <1.03mmol/L; (2) males 16-18 years: <1.03mmol/L; and (3) females 16-18 years: <1.3 mmol/L.(104,124,138)
    - Impaired fasting glucose defined as ≥5.6mmol/L)and/or the presence of diabetes.(104,124,139)
    - Insulin resistance: Calculated using the homeostasis model assessment of insulin resistance (fasting insulin concentration (μU/mL) × fasting glucose concentration (mmol/L)/22.5≥3.16).(104,124,140)
    - **Elevated Blood Pressure** (BP) defined by age (104,124,141):
        - Participants aged 6-17 years: elevated BP was defined using age-, sex and height-specific reference data by the National High BP Education Program Working Group on High BP for Children and Adolescents; participants with pre-hypertension were included.(141)
        - Participants aged 18 years were defined as systolic BP≥130mm Hg and/or a diastolic BP≥85 mm HG.(142) Participants who reported taking medication for high BP were also classified as having elevated BP.

- **Dichotomous Cardio-metabolic Risk**: Participants were dichotomized as having 'no cardio-metabolic risk' or 'cardio-metabolic risk', defined as the presence of adverse levels of one or more of the cardio-metabolic risk factors.
- **Metabolic Syndrome**: defined using criteria established by the International Diabetes Federation (IDF)
    - Participants 10-15 years: The IDF consensus definition of MetS for children and adolescents defines MetS as having: abdominal obesity and the presence of two or more of the following clinical features: elevated fasting triglycerides; low HDL-C; elevated BP and/or diagnosis of hypertension; and impaired fasting glucose and/or diagnosis of type 2 diabetes.(89)
    - Participants 16-18 years: The IDF worldwide adult criteria define MetS as having abdominal obesity and the presence of two or more of the following clinical features: elevated fasting triglycerides; low HDL-C; elevated BP and/or diagnosis of hypertension; and impaired fasting glucose and/or diagnosis of type 2 diabetes.(143)
- **Inflammatory Marker**: In a joint scientific statement, the United States' CDC and the American Heart Association recommended CRP be applied in clinical practice as the marker of inflammation for prediction of cardiovascular risk.(144)
    - High serum levels of CRP were defined as ≥75th (mg/L) age- and sex-specific percentiles calculated using the study population data.(145)

4.4. Statistical Analysis

Computing Programs

The statistical analysis was primarily conducted using SAS version 9.3 (SAS Institute Incorporated, Cary, North Carolina, United States). For paper 2 only, Waist Circumference Cut-Offs, Microsoft Excel 2007 was also used (Redmond, Washington, United States).

Generalizing Study Findings to the Canadian Population

Sampling weights were applied to produce weighted estimates that are representative of each specific study population to allow for generalization for the Canadian population. As recommended by Statistics Canada, data manipulation and variance estimation (Standard Error and 95% confidence intervals) and significance testing ($p<0.05$) were conducted using the bootstrap method to produce accurate national estimates.(126–128) The bootstrap method employs a re-sampling approach to generate a series of estimates for sub-samples of the full dataset.(146)

With each additional CHMS Cycle, the number of degrees of freedom (DF), the quantity of allowable variations in each estimate, increased which allowed for increasingly powerful and accurate statistical calculations. For the first paper, Metabolic Syndrome, CHMS Cycles 1 and 2 allowed for 24 DFs to estimate the variance in the cross-tabulation analyses and regression models, where for papers 2-4, using CHMS Cycles 1-3, applied 35 DFs.(126–128) Results with $16.6<$Coefficient of Variation (CV) ≤ 33.3 were published with reservation and results with a cell frequency of <10 or a CV≥ 33.3 were withheld and represented with an F.

Statistical Analysis: Paper 1 Metabolic Syndrome

Prevalence estimates for MetS and its risk factors were generated using PROC SURVEYFREQ and expressed as a frequency and percentage. Chi-Square tests were performed using PROC SURVEYFREQ to determine if there were statistically significant differences among the prevalence of MetS and each risk factor among groups established by sex, Aboriginal status, immigrant status, household education and income adequacy. PROC UNIVARIATE was applied to generalize the study findings to the Canadian population.

Statistical Analysis: Paper 2 Waist Circumference Cut-Offs

Regression was performed using linear, logarithmic and quadratic functions to extrapolate predicted WC for ages 6-18 years using measured WC for 11-18 year olds from the NHANES and CHMS, and ages 6-10 years for 11-18 years from the CFS, respectively. Error values were calculated to reflect the % difference between measured and predicted WC to determine the predictive power of each function for all three data series.

Prevalence estimates of abdominal obesity were calculated for CHMS participants using the predicted WC values (6-10 years) and the reference values from the 1981 CFS (11-18 years). Sensitivity and specificity analyses were performed to compare the predictive accuracy of the linear, logarithmic function extrapolated WC values.

Statistical Analysis: Paper 3 Cardio-Metabolic Risk

Prevalence estimates for cardio-metabolic risk, expressed as a dichotomous variable; each cardio-metabolic risk factor; and obesity, using three indicators; were determined using PROC SURVEYFREQ. The associations between cardio-metabolic risk and obesity indicators were estimated using chi-square tests by PROC SURVEYFREQ. PROC UNIVARIATE commands were

used to generalize results to entire population using sample weights, as well as to generate detailed summary statistics to inform the regression analysis. PROC CORR was also performed to determine the correlation between variables to help inform the variables included in the multivariate regression models. Regression analyses were informed to determine the factors that predict cardio-metabolic risk. Initially, a series of binary analyses were performed using PROC SURVEYLOGISTIC to understand the relationship between the independent variables, the obesity indicators and behaviours, and cardio-metabolic risk factors. Next, multi-variable regression using PROC SURVEYLOGISTIC was performed to develop a model using the multiple predictors for cardio-metabolic risk. In PROC SURVEYLOGISTIC, a CLASS statement was applied to define the reference levels for each of the predictors. For example, the reference level for body mass index was normal weight.

Statistical Analysis: Paper 4 Inflammatory Marker

Weighted means, percentiles, and standard errors for CRP were generated using PROC MEANS. Prevalence estimates for cardio-metabolic risk, expressed as a dichotomous variable, each cardio-metabolic risk factor and high levels of CRP using PROC SURVEYFREQ. Pearson correlation coefficients were calculated using PROC CORR to examine the relationshi p between each individual cardio-metabolic risk factor with CRP. The associations between cardio-metabolic risk and the inflammation were estimated using X^2 tests by PROC SURVEYFREQ and independent t-tests. PROC UNIVARIATE commands were used to generalize results to entire population using sample weights, as well as to generate detailed summary statistics to inform the regression analysis. Generalized logistic regression models by PROC SURVEYLOGISTIC were used to develop models for predicting cardio-metabolic risk using obesity and CRP.

5. RESEARCH RESULTS

5.1. Prevalence of Metabolic Syndrome and its risk factors in Canadian children and adolescents: Canadian Health Measures Survey Cycle 1 (2007-2009) and Cycle 2 (2009-2011)[4]

Authors References: Miranda MacPherson (1,2), Margaret de Groh (1), Lidia Loukine (3), Denis Prud'homme (4) Lise Dubois(5)

1. Social Determinants and Science Integration Directorate, Public Health Agency of Canada, Ottawa, Ontario, Canada
2. Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
3. Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, Ottawa, Ontario, Canada
4. Institut de recherche de l'Hôpital Montfort, Ottawa, Ontario, Canada; Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
5. School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

This manuscript was published in the Health Promotion and Chronic Disease Prevention Journal on February 18, 2016 and is publically available online:
http://www.phac-aspc.gc.ca/publicat/hpcdp-pspmc/36-2/ar-03-eng.php

Suggested citation:

MacPherson M, de Groh M, Loukine L, Prud'homme D, Dubois L. Prevalence of metabolic syndrome and its risk factors in Canadian children and adolescents: Canadian Health Measures Survey Cycle 1 (2007-2009) and Cycle 2 (2009-2011). Health Promot Chronic Dis Prev Can. 2016 Feb 18;36(2):32–40.

[4] To read this paper on a computer screen, double click the image on each page to display a larger, clearer view in Acrobat

Prevalence of metabolic syndrome and its risk factors in Canadian children and adolescents: Canadian Health Measures Survey Cycle 1 (2007-2009) and Cycle 2 (2009-2011)

M. MacPherson, MBA (1, 2); M. de Groh, PhD (1); L. Loukine, MSc (3); D. Prud'homme, MD (4, 5); L. Dubois, PhD (6)

This article has been peer reviewed.

Abstract

Introduction: We investigated the prevalence of metabolic syndrome (MetS) and its risk factors, and the influence of socioeconomic status, in Canadian children and adolescents.

Methods: Canadian Health Measures Survey cycle 1 (2007–2009) and cycle 2 (2009–2011) respondents aged 10 to 18 years who provided fasting blood samples were included (n = 1228). The International Diabetes Federation (IDF) consensus definition for children and adolescents (10–15 years) and worldwide adult definition (≥ 16 years) were used to diagnose MetS. Prevalence of MetS and its risk factors were calculated and differences by socioeconomic status were examined using χ^2 tests.

Results: The prevalence of MetS was 2.1%. One-third (37.7%) of participants had at least one risk factor, with the most prevalent being abdominal obesity (21.6%), low HDL-C (19.1%) and elevated triglyceride levels (7.9%). This combination of abdominal obesity, low HDL-C and elevated triglyceride levels accounted for 61.5% of MetS cases. Participants from households with the highest income adequacy and educational attainment levels had the lowest prevalence of one or more MetS risk factors, abdominal obesity and low HDL-C.

Conclusion: The prevalence of MetS (2.1%) was lower than previously reported in Canada (3.5%) and the USA (4.2%–9.2%), potentially due to the strict application of the IDF criteria for studying MetS. One-third of Canadian children and adolescents have at least one risk factor for MetS. Given that the risk for MetS increases with age, these prevalence estimates, coupled with a national obesity prevalence of almost 10% among youth, point to a growing risk of MetS and other chronic diseases for Canadian youth.

Keywords: Canadian Health Measures Survey, metabolic syndrome, health surveys, cardiometabolic risk factors, prevalence, adolescent, child

Key findings

- Having metabolic syndrome (MetS) increases the risk for chronic disease—cardiovascular disease by two and type 2 diabetes by five.
- Only 2.1% of Canadian youth have MetS. However, one-third of Canadian youth have one or more risk factors for MetS.
- The biggest risk factor for MetS is abdominal obesity. As more youth are becoming obese, MetS will probably increase among Canadian youth.
- Risk of MetS increases with age. As a result, the risk for chronic diseases will probably increase as the Canadian population ages.
- Youth who live in better off or better educated households have the lowest risk for MetS.

Introduction

Chronic diseases constitute the leading cause of preventable death in Canada and the world as well as the largest avoidable burden on the public health care system.[1] The metabolic syndrome (MetS) is a constellation of cardiometabolic risk factors that are predictive for chronic disease and all-cause mortality.[2-4] It is estimated that risk of cardiovascular disease (CVD) doubles and the risk of type 2 diabetes increases fivefold if MetS is present.[3-5]

MetS is characterized by the presence of different combinations of risk factors including obesity, hypertension, elevated fasting triglycerides, insulin resistance, low total cholesterol, high low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol (HDL-C), elevated apolipoprotein B, elevated C-reactive protein and elevated homocysteine.[7-9] These clinical features of MetS, if present together, tend to suggest a common etiology; the proposed mechanisms underlying MetS and its influence on health outcomes are discussed elsewhere.[7,10,11]

The global prevalence of obesity and diabetes has increased dramatically in the past quarter century.[12] This increase, in

Author references:

1. Social Determinants and Science Integration Directorate, Public Health Agency of Canada, Ottawa, Ontario, Canada
2. Faculty of Graduate and Postdoctoral Studies, University of Ottawa, Ottawa, Ontario, Canada
3. Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, Ottawa, Ontario, Canada
4. Institut de recherche de l'Hôpital Montfort, Ottawa, Ontario, Canada
5. Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
6. Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

Correspondence: Miranda MacPherson, Social Determinants and Science Integration Directorate, Public Health Agency of Canada, 9168-785 Carling Avenue, Ottawa, ON K1A 0K9; Tel.: 613-668-4018; Fax: 613-960-0921; Email: miranda.macpherson@phac-aspc.gc.ca

turn, has contributed to a higher prevalence of MetS.[15] Worldwide estimates of the prevalence of MetS range from 1.2% to 22.6% for youth and 9.0% to 35.0% for adults, depending on the definition of MetS used, the region, the study design, the years of the study, and the age group and study population.[14-16] In Canada, the prevalence of MetS among adults is between about 11.4% and 22.2%, which is greater than the prevalence estimates of 10% to 15% measured in adults in the early 1990s.[17-22] In comparison, the prevalence of MetS among adults in the USA is between about 24% and 34%.[23-25] It is widely accepted that the prevalence of MetS increases significantly with age.[17,20,21] The national prevalence among youth aged 12 to 19 years is 3.5% in Canada (based on a 2012 study using the Adult Treatment Panel III criteria for MetS) and 4.2% to 9.2% in the USA, with about 42% to 63% of youth in the USA having one or more MetS risk factors.[19,27-29] Further examination of national prevalence among youth will help us understand the progression of MetS and its risk factors among Canadians.

There is substantial evidence supporting an inverse relationship between socioeconomic status (SES) and CVDs, conditions that share some risk factors with MetS.[30-32] Studies examining the relationship between SES and MetS reveal a similar pattern in which people with a lower social status experience a significantly higher prevalence of MetS.[17,19,20,33,34] Canadian national studies have shown that the prevalence of MetS is significantly lower among people from households with postsecondary education compared to those with less education, a relationship that is particularly evident in women.[17,19,20] This inverse relationship remains consistent between household income and MetS, albeit less pronounced, with Canadian households with the lowest quartiles of income having a higher prevalence of MetS than households with average and higher incomes.[17,20]

A challenge in determining the prevalence of MetS has been the use of multiple criteria and definitions for identifying this condition. In response, the International Diabetes Federation (IDF) released the *IDF Consensus Worldwide Definition of the Metabolic Syndrome* as a single, universally accepted tool.[35] The IDF defines MetS as the presence of abdominal obesity (measured by waist circumference) and 2 or more of the following risk factors: low levels of HDL-C, hypertension, elevated fasting triglyceride levels and elevated glucose concentration.[35,36] Before the IDF consensus definition, the most recognized definitions were criteria established by the World Health Organization, the European Group for the Study of Insulin Resistance, and the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III criteria) (NCEP ATP III).[5,37,38]

Diagnosing MetS among children and adolescents proves particularly challenging given the difficulty in establishing accurate, meaningful and harmonized criteria for this population. Consequently, prevalence estimates of MetS among children and youth vary greatly depending on the adopted definition.[6] In 2007, the IDF released their *Consensus Definition of the Metabolic Syndrome in Children and Adolescents*.[36] This criterion provides an age- and sex-specific definition for youth aged 10 to 15 years. The IDF definition further stipulates that the worldwide adult definition of MetS should be applied for individuals aged 16 years or older and that MetS should not be diagnosed in children less than 10 years old.[36]

The main objectives of this study were to investigate the prevalence of MetS and its risk factors, and the influence of SES on these risk factors, in Canadian children and adolescents (10–18 years) using nationally representative data from the Canadian Health Measures Survey (CHMS). This study builds upon an earlier national analysis of Canadian youth

- by including those aged 10 and 11 years;
- by calculating the prevalence of one or more risk factors for MetS among youth;
- by examining the patterns of risk presentation; and
- by using data from two cycles of the CHMS.[39]

This is the first national study to strictly apply the IDF consensus definition of MetS in children and adolescents, the most current and universally accepted definition of MetS for youth; and to use Canadian age- and sex-specific waist circumference reference data to determine abdominal obesity in Canadian children and youth.

Methods

Data source

The CHMS is a nationally representative survey designed to collect information on the health of Canadians.[39-41] Conducted by Statistics Canada, the CHMS consists of an in-home interview and a physical assessment conducted at a mobile examination centre. The interview collects demographic, socioeconomic, family history and general health information. The physical assessment includes measures of anthropometry, spirometry, blood pressure, fitness and oral health and involves collecting biological specimens.[39-41] The survey covered Canadians living at home in the 10 provinces and 3 territories, although people living on reserves and other Aboriginal settlements, in institutions and in certain remote regions as well as full-time members of the Canadian Forces were excluded.[39-41] The CHMS cycle 1 (2007–2009) collected data on people aged 6 to 79 years, with cycle 2 (2009–2011) expanding to cover those aged 3 to 79 years.[40-42] In total, this represents 96.3% of the Canadian population.[39-41]

The CHMS produces reliable estimates at the national level by age group and sex through a multistage sampling strategy.[39,42] The selection of collection sites was informed by the Labour Force Survey sampling frame. A multitude of practices were used to minimize non-response; the combined response rate for home and clinic visits was 51.7% for cycle 1 and 55.5% for cycle 2.[39,42] Statistics Canada calculated the sampling weights by multiplying the selection weights for collection sites by the subsample weights for dwellings, followed by a series of adjustments for non-response at the initial, interview and MEC stage.[42]

Study population

All 10- to 18-year-old CHMS respondents who provided fasting blood samples for

cycle 1 (2007–2009) or cycle 2 (2009–2011) were included (n = 1228). No participants were pregnant. Sample weights specific to the fasting subgroup were provided by Statistics Canada to ensure appropriate representativeness of the population level.

Criteria for diagnosing MetS

We applied the IDF consensus definition of MetS for children and adolescents to participants aged 10 to 15 years and the IDF worldwide adult definition adult criteria to participants aged 16 to 18 years.

The IDF consensus definition for children and adolescents defines MetS as having abdominal obesity (waist circumference equal or greater than the 90th percentile by age and sex) and the presence of two or more of the following clinical features: elevated triglycerides (≥ 1.7 mmol/L); low HDL-C (< 1.03 mmol/L); high blood pressure (systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg and/or diagnosis of hypertension); and elevated glucose (≥ 5.6 mmol/L and/or diagnosis of type 2 diabetes).[35]

The IDF worldwide adult criteria define MetS as having abdominal obesity and the presence of two or more of the following clinical features: high triglycerides (≥ 1.7 mmol/L), low HDL-C (< 1.03 mmol/L in males and < 1.29 mmol/L in females); high blood pressure (systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg and/or diagnosis of hypertension); and high glucose (≥ 5.6 mmol/L and/or diagnosis of type 2 diabetes).[36]

We defined abdominal obesity using the 90th percentiles from the age- and sex-specific waist circumference reference data established from the 1981 Canadian Fitness Survey.[37] We applied the waist circumference cut-offs for 11-year-olds to those aged 10 to 11 years since this reference provided estimates for those aged 11 to 18 years only.

Variables for assessing demographic and socioeconomic status

A respondent's demographic and SES was assessed through the variables of household educational attainment, household income adequacy, Aboriginal status, and immigrant status. The use of household education and household income variables in this study is consistent with previous studies examining the relationship between SES and MetS.[17,19,20,24] Education is the most frequently used indicator of SES in epidemiological studies and, among indicators of SES, it tends to have the strongest and most consistent relationship with cardiovascular health.[22,31,44] Household income is another well-established SES indicator and determinant of health.[44-46] Statistics Canada calculated income adequacy by classifying each participant into categories based on total household income from all sources and the number of people living in the household.[35,40]

To allow for greater statistical power, we reclassified both the household educational attainment and income adequacy variables from 4 categories into 3. For income adequacy, we combined the "lowest income" and "lower middle income" categories, resulting in "lowest and lower middle," "upper middle" and "highest" categories. For household educational attainment, we combined the "less than secondary school graduation" and "secondary school graduation" categories, resulting in "secondary school graduation or less," "some postsecondary" and "postsecondary graduation" categories.

Statistical analysis

We conducted statistical analyses using SAS version 9.3 [SAS Institute Inc., Cary, NC, US] for data manipulation and variance estimation using the bootstrap method.[47] The prevalence of MetS and each risk factor were estimated and expressed as a frequency and a percentage with a 95% confidence interval (CI). χ^2 tests were used to examine differences in MetS and each risk factor by gender, Aboriginal status, immigrant status, household education and income adequacy. The analyses were conducted using weighting and bootstrapping. Statistical significance was set at a p value of less than .05.

We obtained ethics approval for this project from the University of Ottawa's Research Ethics Board.

Results

Description of study sample

To be able to evaluate the criteria for MetS, of the original sample of child and adolescent respondents aged 10 to 18 years, we included in our study only those participants who provided fasting blood samples. This resulted in a final sample of 1228 participants. The sample included slightly more males (51.5%) than females (48.5%).

Table 1 shows an overview of the sample by demographic and SES.

Prevalence of MetS

Only 26 study participants were diagnosed with MetS, which represents 2.1% of participants (95% CI: 0.8–3.3)* (Table 2). This small number of participants with MetS prevented accurate disaggregation by sex, age or SES.

Prevalence of individual risk factors

Over one-third (37.7%; 95% CI: 33.8–41.6) of children and adolescents had at least one of the clinical features of MetS (1 or more risk factors) (Table 2). Risk factors in order of prevalence were abdominal obesity (21.6%; 95% CI: 16.6–26.7), low HDL-C (19.1%; 95% CI: 16.6–21.8), elevated triglycerides (7.9%; 95% CI: 4.8–11.0) and elevated glucose (1.7%; 95% CI: 0.7–2.8)†. The prevalence of elevated blood pressure was too low to provide an accurate statistical estimate. There were no gender differences for the prevalence of each risk factor.

Pattern of risk factor combinations

The most prevalent single risk factors were abdominal obesity (10.7%), low HDL-C (9.8%) and elevated triglycerides (2.7%) (Table 3). The most prevalent distinct combinations of two risk factors were abdominal obesity coupled with low HDL-C (5.1%) and abdominal obesity and elevated triglycerides (1.5%). Among distinct combinations of three risk factors, the most prevalent combination was abdominal obesity, low HDL-C

*This result is published with caution due to a coefficient of variation (CV) of 25%.
†Due to small cell sizes, not all risk factors and SES categories could be reported.

Unfiled Notes Page 1

TABLE 1
Sample profile, 10–18 years*

Characteristics	Study sample, n	Percentage of study sample, %
Demographic profile (n = 1240)		
Sex		
Male	632	51.5
Female	596	48.5
Age, years		
10	172	14.0
11	184	15.0
12	127	10.4
13	151	12.3
14	115	9.4
15	117	9.5
16	131	10.7
17	121	9.8
18	110	9.0
Socioeconomic profile		
Income adequacy (n = 1170)		
Lowest and lower middle	247	19.7
Upper middle	333	25.0
Highest	590	50.4
Household education (n = 1193)		
Secondary school graduation or less	126	11.0
Some postsecondary	81	6.6
Postsecondary graduation	986	78.3
Aboriginal origin or identity (n = 1227)		
Aboriginal	46	4.4
Not Aboriginal	1181	95.5
Immigrant status		
Immigrant	120	10.2
Not immigrant	1103	89.8

*Figures are based on raw data.

and elevated triglycerides (1.3%). This combination of these risk factors accounted for 61.5% of MetS cases (Table 3).

Associations between SES (household educational attainment and income adequacy) and risk factors

Participants from families with the highest income had the lowest percentage of one or more risk factor(s) (35.5%; 95% CI: 29.8–41.2), abdominal obesity (18.4%; 95% CI: 11.7–25.1) and low HDL-C (17.5%; 95% CI: 14.2–20.6) versus those from families with the lowest and lower middle incomes (Table 4). Educational attainment results showed that participants with a household member with postsecondary graduation had the lowest percentage of one or more risk factor(s) (35.3%; 95% CI: 31.0–39.6), abdominal obesity (19.8%; 95% CI: 14.6–25.0) and low HDL-C (17.5%; 95% CI: 14.8–20.2) versus those from households with some postsecondary education or secondary school graduation or less. Due to small cell sizes, the results could not be disaggregated by Aboriginal or immigrant status.

Discussion

The prevalence for MetS among children and adolescents (2.1%) was lower than previously reported in Canada (3.5%) and the USA (4.2%–9.2%).[19,27,29] Assuming our sample is representative of the Canadian population, this prevalence of 2.1% would be equivalent to about 54 832 children and adolescents. The prevalence of one or more risk factors (37.7%) among children and adolescents was also lower than reported in the USA (42%–63%).[29] In comparison to earlier national estimates on Canadian youth, our study's lower prevalence may be attributed to our applying the IDF definition of MetS, which has slightly more stringent criteria, including the required presence of abdominal obesity.[5,6,9,19,31] Furthermore, MetS is known to increase with age and our sample included younger ages (10–11 years) and had greater numbers of younger participants (n = 356 for 10–11 years) than older, adolescent participants (n = 281 for 17–18 years).[17,29]

The lower prevalence estimates we found compared to those in the USA may be attributable to several factors. Obese youth have a higher prevalence of MetS than do those of normal weight and the prevalence of obesity among youth is higher in the USA than in Canada.[32–34] The prevalence estimates in the USA were calculated using data from the National Health and Nutrition Examination Survey with variation in the periods of data collection (ranging from 1988–2006), the MetS definition (all variations of ATP III) and criteria for abdominal obesity. Our study followed a strict application of the IDF MetS definition including age- and sex-specific cut-offs. Finally, our study does not include Canadian residents living on reserve or in other Aboriginal settlements, populations shown to have a higher prevalence of MetS.[35–37]

Despite the overall low prevalence of MetS, note that one-third (37.7%) of study participants had at least one risk factor for MetS. This finding, coupled with a prevalence of obesity of almost 10% among Canadian children and youth, is disconcerting as the probability of MetS also increases with obesity.[29] Further, given that age is one of the most significant predictors for MetS, it is reasonable to assume that children and adolescents with one or more risk factors are more susceptible to MetS and, consequentially, chronic disease as adults.[2–4] Evidence indicates that, in the long term, adults with MetS have an elevated risk of CVD-attributed mortality, although a moderate-to-high level of cardiorespiratory fitness has been shown to mitigate some of this risk.[38,39]

Unfiled Notes Page 1

TABLE 2
Prevalence of metabolic syndrome and risk factors[a], 10–18 years[a] (n = 1228)

Condition	Total Sample		Male		Female		p value
	Frequency n	% (95% CI) CV	Frequency	% (95% CI) CV	Frequency	% (95% CI) CV	
MetS	25	2.1 (1.0–3.1) 1.26[b]	—	—	—	—	—
Number of risk factors							
≥ 2	123	10.8 (7.4–14.2) 3.15	71	6.1 (3.5–8.7) 0.02	52	4.7 (2.8–6.5) 0.93	.3658
≥ 1	420	37.7 (33.8–41.6) 0.05	212	18.1 (15.4–20.8) 0.07	208	19.6 (16.4–22.9) 0.08	.3179
Abdominal obesity	340	21.6 (16.6–26.7) 0.11	110	12.6 (9.1–11.9) 0.15	110	11.0 (7.5–14.5) 0.16[b]	.7441
Low HDL-C	218	19.1 (16.6–21.8) 0.06	107	8.8 (6.6–11.0) 0.12	111	10.54 (8.4–12.5) 0.09	.2861
Elevated triglycerides	82	7.9 (5.8–11.0) 1.19[b]	42	4.7 (2.2–7.3) 0.28[b]	40	3.2 (1.7–3.2) 0.22[b]	
Elevated glucose	22	1.7 (0.7–2.8) 1.34[b]	—	—	—	—	—

Abbreviations: BP, blood pressure; CC, waist circumference; HDL-C, high-density lipoprotein cholesterol.

Note: Blank cells (—) indicate that the results cannot be published because of a coefficient of variation (CV) ≥ 0.333 and/or a CV ≥ 0.556. The prevalence of elevated BP was too low to provide an accurate statistical estimate.

[a] These figures are based on weighted data.

[b] These figures are published with reservation as 0.16 ≤ CV ≤ 0.33.

Our findings support the conclusions of previous studies that abdominal obesity, low HDL-C and elevated triglycerides are the most prevalent risk factors of MetS among children and adolescents;[18] in fact, this combination accounted for 61.5% of all MetS cases in this study. The most prevalent risk factor was abdominal obesity (21.6%), which may be attributed to over one-quarter of Canadian youth being overweight or obese.[19] The IDF considers abdominal obesity as a prerequisite for MetS given that it is associated with an increased risk of cardiovascular disease and an independent predictor of insulin resistance, lipid levels and high blood pressure.[3,5,6,8,9] Our study defined abdominal obesity using age- and sex-specific reference data established from the 1981 Canadian Fitness Survey (90th percentile).[14] Domestic prevalence estimates of obesity among youth have almost doubled in the past 25 years, meaning that these predefined cut-offs represent norms for the Canadian population before this dramatic increase in body fat.[20,21]

Consistent with previous studies on youth, hypertension is not highly prevalent in the early onset of this syndrome.[25]

Participants from families in the highest income adequacy and household educational attainment groups had the lowest prevalence of one or more risk factors, abdominal obesity and low HDL-C, which is consistent with earlier findings between SES and MetS risk factors.[17,19,20,22] For abdominal obesity, a dose–response relationship was present for household education. The relationship between household education and prevalence of risk factors appeared to be more sensitive than household income, which is also consistent with previous findings.[17,20,22] This may be attributed to the influence of education on health literacy and behaviour, such as nutrition and physical activity, which are related to abdominal obesity and MetS.[22,26] Further, household education is considered

TABLE 3
Pattern of metabolic syndrome risk factor combinations[a]

Risk factor combination (n = 1228)	Frequency (%)
Presence of 1 risk factor	
Abdominal obesity	131 (10.7)
Low HDL-C	121 (9.8)
Elevated TG	33 (2.7)
Presence of 2 risk factors	
Abdominal obesity + low HDL-C	63 (5.1)
Abdominal obesity + elevated TG	19 (1.5)
Presence of 3 risk factors	
Abdominal obesity + low HDL-C + elevated TG	16 (1.3)
Risk factor combination in participants with MetS (n = 25)	**Frequency (%)**
Presence of 3 risk factors	
Abdominal obesity + low HDL-C + elevated TG	16 (61.5)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

Note: Risk factor combinations with cell sizes (n) < 10 were not published as prevalence was too low to provide accurate statistical estimates.

[a] These figures are based on weighted data.

TABLE 4
Relationship between metabolic syndrome risk factors and socioeconomic status, fasting sub-sample ages 10–18 years[a]

Condition	Presence of ≥ 1 risk factor(s) % (95% CI) CV	Abdominal obesity % (95% CI) CV	Low HDL-C % (95% CI) CV
Income Adequacy (50 missing)			
Lowest and lower middle	35.9 (25.9–46.0) 0.14	21.4 (11.8–30.9) 0.22[b]	19.4 (12.7–26.1) 0.17[b]
Upper middle	41.8 (34.4–49.3) 0.09	28.1 (19.7–36.6) 0.15	20.2 (15.2–25.2) 0.13
Highest	35.5 (29.8–41.2) 0.08	18.4 (11.5–25.3) 0.17[b]	17.5 (14.5–20.6) 0.09
Household education (85 missing)			
Secondary school graduation or less	43.2 (29.1–58.0) 0.16	31.8 (17.6–46.0) 0.22[b]	19.3 (10.9–31.9) 0.31[b]
Some postsecondary	42.8 (32.4–53.2) 0.12	28.1 (13.7–42.5) 0.25[b]	26.1 (15.1–37.1) 0.21[b]
Postsecondary graduation	35.1 (31.3–39.0) 0.06	19.0 (14.6–23.4) 0.11	17.5 (14.8–20.2) 0.08

Abbreviations: HDL, blood cholesterol; HDL-C, high-density lipoprotein cholesterol; SES, socioeconomic status.

Note: Small cell sizes prohibited further analysis of BP, glucose and triglyceride risk factors and Aboriginal and immigrant status SES factors.

[a] These figures are based on weighted data.

[b] These figures are being published with coefficients of 0.16 ≤ CV ≤ 0.33.

to be more stable, and less influenced by health status, than household income over the life course.[30] More broadly, participants from households with lower education and income levels are more likely to experience unfavourable social, physical and economic environments that can contribute to poorer health outcomes, including a higher rate of mortality attributed to CVDs.[30,31] These results point to a need for interventions, including public policy, public education, research and medical care that focus on mitigating the impact of lower levels of education and income on health outcomes. Research focussed on elucidating the causal pathways through which SES influences the risk for MetS and CVDs throughout the life course would be useful in designing effective, targeted interventions.

Future studies using more cycles of CHMS data may have the statistical power with which to examine MetS and its risk factors in Canadian children and adolescents in greater detail. The sex differences in MetS in relation to SES should be examined to better understand the sex-specific ways in which unfavourable socioeconomic conditions affect MetS outcomes. Further, regression analyses are needed to comprehensively examine the relationship between MetS, its risk factors, behaviour such as physical activity and sleep, and SES.

Strengths

This is the first national study to apply the IDF consensus definition of MetS to children and adolescents and to use Canadian age- and sex-specific waist circumference reference data for determining abdominal obesity in Canadian children and youth. Strictly applying the IDF criteria for studying MetS at the population level in Canada will allow for more accurate comparisons with future studies on MetS in children and adolescents.

This study was conducted using government survey data that is both high quality and representative of 96% of Canadians.

Limitations

Descriptive statistics was the only method we could use to examine MetS using this dataset of Canadian children and adolescents because the sample size was small; only those participants from whom fasting blood samples were taken were included. The sample size and low prevalence of MetS did not allow for an analysis of the relationship between each risk factor and MetS. The small sample size also prohibited a robust statistical analysis of the influence of demographic and SES variables on MetS and allowed only limited analysis of the influence of these variables on risk factors with no distinction by sex. It was not feasible to disaggregate by sex, age, Aboriginal status or immigrant status. Furthermore, the cross-sectional design of the CHMS limits inference about causal pathways underlying the observed relationships. Consequently, the study focussed on the prevalence of each MetS risk factor.

Nonetheless, the study results improve the understanding of the current landscape of cardiometabolic risks among Canadian children.

Conclusions

By investigating the prevalence of MetS and its risk factors among Canadian children and adolescents, this study highlights important health and socioeconomic considerations for Canada's child and adolescent population. The results affirm previous findings of a low prevalence of MetS among youth. The results also highlight important indicators of future health risk among Canadian youth by showing that one in three have at least one risk factor for MetS, one in five have abdominal obesity, and one in five have low HDL-C. Efforts to prevent, diagnose and treat MetS and its risk factors among youth are important to prevent type 2 diabetes, cardiovascular diseases and premature mortality.

Acknowledgements

We are grateful to Statistics Canada for conducting the Canadian Health Measures Survey and to the people of Canada who participated in the study.

There were no competing interests.

We acknowledge the support of the University of Ottawa's Department of Epidemiology

Unfiled Notes Page 1

and Community Medicine and the Public Health Agency of Canada.

References

1. Public Health Agency of Canada. Working together globally: Canada's World Health Organization (WHO) Collaborating Centre on Chronic Non-communicable Disease Policy [Internet]. Ottawa (ON): Public Health Agency of Canada; 2014 Sep 7; [cited 2014 Feb 11]. Available from: http://www.phac-aspc.gc.ca/about_apropos/whocc-ccoms/index-eng.php

2. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care. 2005;28(7):1769-78.

3. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care. 2001;24(4):683-9.

4. McNeill AM, Rosamond WD, Girman CJ, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities study. Diabetes Care. 2005;28(2):385-90.

5. Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin resistance syndrome (Syndrome X). Diabetes. 1992;41(6):715-22.

6. Alberti KG, Zimmet PZ, Shaw J. Metabolic syndrome – a new world-wide definition. Lancet. 2005;366(9491):1059-62.

7. Huang TT, Ball GD, Franks PW. Metabolic syndrome in youth: current issues and challenges. Appl Physiol Nutr Metab. 2007;32(1):13-22.

8. Haffner SM. The metabolic syndrome: inflammation, diabetes mellitus, and cardiovascular disease. Am J Cardiol. 2006;97(2A):3A-11A.

9. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. part 1: provisional report of a WHO consultation. Diabetes Med. 1998;15(7):539-53.

10. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595-607.

11. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes and inflammation. Circulation. 2005;111(11):1448-54.

12. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414:782-7.

13. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;365(9468):1415-28.

14. Goodman E, Daniels SR, Morrison JA, Huang B, Dolan LM. Contrasting prevalence of and demographic disparities in the world health organization and national cholesterol education program adult treatment panel III definitions of metabolic syndrome among adolescents. J Pediatr. 2004;145(4):445-51.

15. Tailor AM, Peeters PH, Norat T, Vineis P, Romaguera D. An update on the prevalence of the metabolic syndrome in children and adolescents. Int J Pediatr Obes. 2010;5(3):202-13.

16. Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. Endocrinol Metab Clin North Am. 2004;33(2):351-75.

17. Riediger ND, Clara I. Prevalence of metabolic syndrome in the Canadian adult population. CMAJ. 2011;183(15):E1127-34.

18. Statistics Canada. Health Fact Sheets – Metabolic syndrome in Canada: 2009-2011. Ottawa (ON): Statistics Canada; 2012 [Statistics Canada, Catalogue No.: 82-625-X].

19. Setayeshgar S, Whiting SJ, Vatanparast H. Metabolic syndrome in Canadian adults and adolescents: prevalence and associated dietary intake. ISRN Obesity. 2012;2012:1-8.

20. Ardern CI, Katzmarzyk PT. Geographic and demographic variation in the prevalence of the metabolic syndrome in Canada. Can J Diabetes. 2007;31(1):34-46.

21. Brenner D, Arora P, Karmali M, Badawi A. The impact of the metabolic syndrome on cardiometabolic and inflammatory profiles among Canadian adults. J Epidemiol Community Health. 2011;65(A):A228-9.

22. Brien SE, Katzmarzyk PT. Physical activity and the metabolic syndrome in Canada. Appl Physiol Nutr Metab. 2006;31(1):40-7.

23. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among US adults. Diabetes Care. 2004;27(10):2444-9.

24. Ervin RB. Prevalence of metabolic syndrome among adults 20 years of age and over, by sex, age, race and ethnicity, and body mass index: United States, 2003–2006. Natl Health Stat Report. 2009;13:1-7.

25. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287(3):356-9.

26. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med. 2003;163(4):427-36.

27. De Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the third National Health and Nutrition Examination Survey. Circulation. 2004;110(16):2494-7.

28. Johnson WD, Kroon JJ, Greenway FL, Bouchard C, Ryan D, Katzmarzyk PT. Prevalence of risk factors for metabolic syndrome in adolescents: National Health and Nutrition Examination Survey (2001-2006). Arch Pediatr Adolesc Med. 2009;163(4):371-7.

29. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med. 2003;157(8):821-7.

30. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation. 1993;88(4):1973-98.

31. Marmot M. Income inequality, social environment, and inequities in health. J Policy Anal Manage. 2001;20(1):150-9.

32. Hemingway H, Shipley M, Macfarlane P, Marmot M. Impact of socioeconomic status on coronary mortality in people with symptoms, electrocardiographic abnormalities, both or neither: the original Whitehall study 25 year follow up. J Epidemiol Community Health. 2000;54(7):510-6.

33. Brunner EJ, Marmot MG, Nanchahal K, et al. Social inequality in coronary risk: central obesity and the metabolic syndrome. Evidence from the Whitehall II study. Diabetologia. 1997;40(11):1341-9.

34. Santos AC, Ebrahim S, Barros H. Gender, socio-economic status and metabolic syndrome in middle-aged and old adults. BMC Public Health. 2008;8:62.

35. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome [Internet]. Brussels: IDF Communications; 2006 [cited 2014 Sep 10]. Available from: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf

36. International Diabetes Federation. The IDF consensus definition of the metabolic syndrome in children and adolescents [Internet]. Brussels: IDF Communications; 2007 [cited 2014 Sep 10]. Available from: http://www.idf.org/webdata/docs/Mets_definition_children.pdf

37. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance. Diabetes Med. 1999 May;16(5):442-3.

38. National Heart Lung and Blood Institute, National Cholesterol Education Program Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults. Third report of the National Cholesterol Education Program Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). Circulation. 2002 Dec;106(25):3143-421.

39. Statistics Canada. Canadian Health Measures Survey - Data User Guide: Cycle 2 [Internet]. Ottawa (ON): Statistics Canada. 2013 April [cited 2013 Dec 1]. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V2-eng.htm

40. Statistics Canada. Canadian Health Measures Survey - Data User Guide: Cycle 1 [Internet]. Ottawa: Statistics Canada. 2011 April [cited 2013 Dec 1]. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.htm

41. Tremblay MS, Connor Gorber S. Canadian Health Measures Survey: Brief Overview. C J Public Health. 2007 Nov-Dec;98(6):453-6.

42. Giroux S. Canadian Health Measures Survey: sampling strategy overview. Ottawa (ON): Statistics Canada; 2007 [Statistics Canada Health Reports: 18(82-003-S):31-6].

43. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11-18 years of age. Eur J Clin Nutr. 2004 Jul;58(7):1011-5.

44. Winkleby MA, Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. Am J Public Health. 1992 Jun;82(6):816-20.

45. Liberatos P, Link BG, Kelsey JL. The measurement of social class in epidemiology. Epidemiol Rev. 1988 Jan;10(1):87-121.

46. Duncan GJ, Daly MC, McDonough P, Williams DR. Optimal indicators of socioeconomic status for health research. Am J Public Health. 2002 Jul;92(7):1151-7.

47. Commission on Social Determinants of Health. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health - Final Report of the Commission on Social Determinants of Health. World Health Organization (Switzerland);2008.

48. McIntosh CN, Finès P, Wilkins R, Wolfson MC. Income disparities in health-adjusted life expectancy for Canadian adults, 1991 to 2001. Ottawa (ON): Statistics Canada; 2009 [Statistics Canada Health Reports, No: 20(4): 55-64].

49. Efron B, Tibshirani R. Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. Statist Sci. 1986 Feb;1(1):54-75.

50. Jolliffe CJ, Janssen I. Development of age-specific adolescent metabolic syndrome criteria that are linked to the Adult Treatment Panel III and International Diabetes Federation criteria. J Am Coll Cardiol. 2007 Feb;49(8):891-8.

51. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med. 2011 May;9(48):1-13.

52. Weiss R, Dziura J, Burgert TS, et al. Obesity and the metabolic syndrome in children and adolescents. New Engl J Med. 2004 Jun;350:2362-74.

53. Katzmarzyk PT, Church TS, Janssen I, Ross R, Blair SN. Metabolic syndrome, obesity, and mortality: impact of cardiorespiratory fitness. Diabetes Care. 2005 Feb;28(2):391-7.

54. Lee S, Bacha F, Arslanian SA. Waist circumference, blood pressure, and lipid components of the metabolic syndrome. J Pediatr. 2006 Dec;49(6):809-16.

55. Pollex RL, Hanley AJ, Zinman B, Harris SB, Khan HM, Hegele RA. Metabolic syndrome in Aboriginal Canadians: Prevalence and genetic association. Atherosclerosis. 2006 Jan;184(1):121-9.

56. Liu J, Young TK, Zinman B, Harris SB, Connelly PW, Hanley AJ. Lifestyle variables, non-traditional cardiovascular risk factors, and the metabolic syndrome in an Aboriginal Canadian population. Obesity (Silver Spring). 2006 Mar;14(3):500-8.

57. Kaler SN, Ralph-Campbell K, Pohar S, King M, Laboucan CR, Toth EL. High rates of the metabolic syndrome in a First Nations Community in western Canada: prevalence and determinants in adults and children. Int J Circumpolar Health. 2006 Dec;65(5):389-402.

58. Hunt KJ, Resendez RG, Williams KW, Haffner SM, Stern MP. National Cholesterol Education Program versus World Health Organization Metabolic Syndrome in relation to all-cause and cardiovascular mortality in the San Antonio Heart Study. Circulation. 2004 Sep;110:1251-7.

59. Tremblay MS, Willms JD. Secular trends in the body mass index of Canadian children. CMAJ. 2000 Nov;163(11):1429-33.

50. Burke V, Beilin LJ, Simmer K, et al. Predictors of body mass index and associations with cardiovascular risk factors in Australian children: a prospective cohort study. Int J Obesity. 2005 Sept;29:15-23.

51. Public Health Agency of Canada, Canadian Institute for Health Information. Obesity in Canada. A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. Ottawa (ON):2011.

52. Loucks EB, Rehkopf DH, Thurston RC, Kawachi I. Socioeconomic disparities in metabolic syndrome differ by gender: evidence from NHANES III. Ann Epidemiol. 2007 Jan;17(1):19-26.

53. Dallongeville J, Cottel D, Ferrières J, et al. Household income is associated with the risk of metabolic syndrome in a sex-specific manner. Diabetes Care. 2005 Feb;28(2):406-13.

Unfiled Notes Page 1

5.2. Estimating pre-obesity epidemic waist circumference reference values for Canadian children 6-10 years using reference data from the 1981 Canada Fitness Survey, the National Health and Nutrition Examination Survey, and the Canadian Health Measures Survey

Authors References: Miranda MacPherson (1,2), Margaret de Groh (1), Ron Wall (1), Denis Prud'homme (3), XiaoHong Jiang (1), Lise Dubois (4)

1. Social Determinants and Science Integration Directorate, Public Health Agency of Canada, Ottawa, Ontario, Canada
2. Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
3. Institut de recherche de l'Hôpital Montfort, Ottawa, Ontario, Canada; Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
4. School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

This manuscript will be submitted for publication in the *Health Promotion and Chronic Disease Prevention Journal* in January 2017.

ABSTRACT

Objectives: This ecological study was designed to establish pre-obesity epidemic waist circumference 90th percentile reference values for 6-10 year olds using national anthropometric reference data from Canada and the United States.

Methods: The analysis was based on reference data from a study of the 1981 Canadian Fitness Survey (CFS) (11-18 years; n=3064). Reference data from a study using the United States' National Health and Nutrition Examination Survey (NHANES) (1988-1994) (6-18 years; n=9713) and data from the Canadian Health Measures Survey (CHMS) (2007-2009, 2010-2011, 2012-2013)(6-18 years; n=5922) were also applied. Consistent with our studies of reference, abdominal obesity was defined as ≥ 90th age- and sex- specific percentile. The slopes of the 90th waist circumference by age were plotted for both NHANES and CHMS for ages 6-18 years with application of linear, logarithmic and quadratic trend lines to examine reliability of fit. Regression was performed using linear, logarithmic and quadratic functions to extrapolate waist circumference values for ages 6-18 years for the NHANES and CHMS and for 11-18 years for the CFS. The degree of error (%) between the measured and predicted values was calculated to determine and compare the predictive performance of each function.

Results: The logarithmic function had the strongest predictive power as its extrapolated values had the smallest degree of error, particularly for the NHANES and CHMS, as compared to the linear and quadratic functions.

Conclusions: The age- and sex- specific cut-offs predicted by the logarithmic function, using national reference data established prior to the surge in obesity rates, will facilitate measurement of abdominal obesity among children in Canada at the national level.

INTRODUCTION

The prevalence of obesity among Canada's children and adolescents is unprecedented. Nearly 10% of these youth are classified as obese, a prevalence that has more than doubled since 1978-79.(1,2) This alarming increase mirrors an almost-global epidemic of obesity worldwide with the prevalence of obesity increasing from 5%-9% (ages 2-19 years) in developed countries since 1980.(3,4) Children with obesity have an elevated risk of the development, and early onset, of chronic diseases such as cardiovascular diseases, diabetes and the metabolic syndrome.(4–6) Some studies suggest that abdominal obesity is a stronger predictor for cardio-metabolic diseases than body mass index (BMI) for both adult and pediatric populations.(7–11) Further, the presence of abdominal obesity is an absolute requirement for the International Diabetes Federation's definitions for Metabolic Syndrome.(6,12) Among adults, the inclusion of abdominal obesity, using waist circumference (WC) thresholds specific to BMI categories, has been shown to strengthen the measured association between obesity and cardiovascular disease risk versus BMI alone.(13,14)

Measured WC and BMI are the most prominent indicators for estimating body fatness. BMI is an efficient, inexpensive indicator that is easily applied at the population level, however, as it is not a direct measures of adiposity, it does not distinguish between lean muscle and body fat.(15,16) Measurement of the WC offers a more direct estimate of abdominal adiposity and overall estimation of body fatness.(17) Weight classification estimates from both measures have been shown to be highly correlated with estimates using dual emission x-ray absorptiometry (DXA) which recognized as the 'gold standard' measurement technique for producing very accurate and reliable body fatness estimates for paediatric and adult

populations.(18–20) Through comparison by DXA estimates, BMI estimates have been shown to have a moderate sensitivity, meaning a moderate propensity to misclassify overweight or obese children as normal weight, and high specificity, meaning BMI is very unlikely to misclassifying a child with low body fat as obese, for children 8-12 years.(21–23) Estimates using WC have been shown to have a high sensitivity and high specificity even among children and adolescents by comparison with DXA estimates.(24)

In 2004, Katzmarzyk published WC percentiles for ages 11-18 years using the 1981 Canada Fitness Survey.(25) The study offers important insight regarding the age- and sex- body composition as well as growth pattern of Canadian adolescents prior to the obesity epidemic that has emerged over the past 30 years. To our knowledge, comparable, national, measured WC percentiles for Canadian children from this time period, for the purposes of estimating abdominal obesity, are absent. Further, WC percentiles calculated using the Canadian Health Measures Survey, our current source for measured anthropometric data, as the reference population would underestimate the prevalence of abdominal obesity given the substantial increase in overweight and obesity in the past thirty years.(2,26)

Our primary objective with this ecological study was to establish pre-obesity epidemic WC reference values for children ages 6-10 years using established, national, anthropometric data from Canada and the United States. To achieve this outcome, our methodological objectives were to determine: (1) whether regression of linear, logistic and quadratic functions of adolescent WC would extrapolate reference data for children that were statistically sound; and (2) which of these functions predicted reference values that were closest to the measured WC.

We hypothesize that the logarithmic slope will generate reference data with the least degree of error. A linear and quadratic function would suggest a continual increase or an eventually decrease, respectively, neither of which are applicable to WC progression by age over the life span. From a mathematical and theoretical perspective, the logarithmic transformation is widely applied where non-linear data violate the assumption of linearity for ordinary regression analysis in order not to bias estimation.

METHODS

Subjects: Our ecological analysis was completed using subjects from three data sources:

1981 Canada Fitness Survey (CFS) - a nationally representative survey designed to collect fitness levels, activity patterns and anthropometric measures on Canadians aged 7-69 years from 13,400 households.(27) The survey's 88% participation rate resulted in data collection from 11,844 households across Canada.(27) The survey was funded by Fitness Canada and conducted by Statistics Canada. The CFS was comprised of demographic and lifestyle questions (ages 10-69 years only) and a physical measures assessment for all participants. For the physical measures assessment, the exact ages of participants under 10 years cannot be determined due to the methodological challenges of obtaining accurate self-reported age and date of birth from participants of that age group.(25,28) We based our ecological analysis on a study of 1981 CFS participants aged 11-18 years (n=3064) that was published in 2004.(25)

Canadian Health Measures Survey (CHMS) - a nationally-representative survey designed to collect information on the health of Canadians.(29–31) Conducted by Statistics Canada, the CHMS consists of an in-home interview, focused on demographic, socio-economic, family history and general health information, and a physical assessment which captures measures of

anthropometry, spirometry, blood pressure, fitness, oral health and biological specimens.(29–31) The survey covers Canadians living at home and residing in the 10 provinces and three territories; in total this represents 96.3% of the Canadian population.(29–32) People living on reserves and other Aboriginal settlements, in institutions, in certain remote regions and full-time members of the Canadian Forces are excluded.(29–31) Data on participants aged 6-18 years from the CHMS Cycles 1 (2007-2009), 2 (2009-2011) and 3 (2012-2013) were included in our study, excluding those who were pregnant, for a total of n=5922 participants.

National Health and Nutrition Examination Survey (NHANES) - a series of studies that examine the health and nutritional status of children, adolescents and adults in the United States. (33) The survey is led by the National Center for Health Statistics within the Centers for Disease Control and Prevention.(33) Data collection for the NHANES program commenced in the 1960s and became a continuous program in 1999.(33) NHANES data is collected through an interview and physical examination with the former collecting socio-demographic, dietary and health-related information and the latter collecting medical, dental and laboratory information. NHANES collects data on approximately 5000 persons each year to create a nationally representative sample of all ages.(33) We used reference data from a study based on NHANES III (1988-1994) that had calculated WC profiles for ages 2-18 years (n=9713).(34)

Anthropometric Variables:

Waist Circumference - Consistent with our reference studies, abdominal obesity was defined as ≥90th percentile age- and sex- specific WC.(25,34) For each of these sources, WC was measured in millimetres by a trained technician and reported in cm.(35,29–31,36) The 1981 CFS obtained WC measurements with a non-rigid tape measure at the narrowest part of the waist.(35) The

CHMS followed the World Health Organization (WHO) protocol in Cycles 1-2 and the United States' National Institutes of Health (NIH) protocol in Cycles 2-3 to obtain WC measurements.(29–31,37) With the WHO Protocol, the mid-point between the bottom of the rib cage and the top of the iliac crest is measured whereas with the NIH Protocol, the uppermost point of the iliac crest is measured.(29–31,36,38) The NHANES III measured WC in accordance with the NIH Protocol.(36) We applied a prediction equation developed by Statistics Canada to adjust the CHMS Cycle 1 WC to align with the CHMS Cycles 2-3 WC.(39) We also chose to apply this prediction equation to the 1981 CFS data, as its measurement procedure was comparable to the WHO protocol, to facilitate comparisons across the CFS, CHMS and NHANES data.

Body Mass Index - Statistics Canada derived BMI using measured of weight and height (weight (kg)/height (m^2)) and classified BMI using growth charts prepared by the Centers for Disease Control and Prevention for ages 6-17 years and the international body weight classification system recommended by Health Canada and the WHO for ages ≥18 years.(29–31,40–42)

Table 1. 90th percentile waist-circumference measurements from the reference data

	CFS (1981) (cm)		NHANES (1988-1994) (cm)		CHMS 1-3 (2007-2013) (cm)	
Age (y)	Male	Female	Male	Female	Male	Female
6	POINTS OF INTEREST		66.1	62.5	61.6	61.0
7			69.0	68.4	69.5	66.3
8			70.9	69.0	71.7	73.3
9			78.0	80.8	80.2	76.5
10			80.0	79.0	82.5	76.5
11	72.7	70.6	84.2	80.9	83.0	82.3
12	74.0	72.3	85.9	81.2	91.9	84.9
13	75.9	74.7	90.0	89.5	89.1	87.3
14	78.8	76.9	96.0	91.9	93.2	88.6
15	81.6	78.7	95.9	89.0	94.8	91.2
16	83.3	79.8	90.2	92.1	96.2	92.8
17	84.6	81.4	98.0	94.6	95.8	96.5
18	85.7	83.6	97.6	92.8	106.9	97.3

Notes:

- *Abbreviations:* cm, centimetres; CFS, Canada Fitness Survey; CHMS, Canadian Health Measures Survey; NHANES, National Health and Nutrition Examination Survey

Statistical Analysis: The 90th WC values by age were plotted for both NHANES and CHMS data for ages 6-18 years. Linear, logarithmic and quadratic trend lines were imposed and the reliability of fit (R^2) was calculated to verify that each function was appropriate for further study. For each data series, regression was performed using linear, logarithmic and quadratic functions using measured WC for 11-18 years to extrapolate predicted WC for ages 6-18 years from the NHANES and CHMS, and 11-18 years from the CFS, respectively. Error values were calculated to reflect the % difference between measured and predicted WC to determine the predictive power of each function for all three data series. Next, regression using the three functions was performed on measured WC for 11-18 year olds from the 1981 CFS to extrapolate WC values for ages 6-10. Prevalence estimates of abdominal obesity were calculated for CHMS participants using the extrapolated WC values (6-10 years) and the

reference values (11-18 years) from the CFS. Sensitivity and specificity analyses were performed to compare the predictive accuracy of the linear, logarithmic function extrapolated WC values. The estimated prevalence of abdominal obesity was examined against BMI using the CHMS. The sensitivity and specificity of the prevalence of abdominal obesity for CFS reference data (11-18 years) was also established as a point of reference.

RESULTS

The predicted WC for 6-10 years generated using regression which applied linear, logarithmic and quadratic functions to WC measurements for 11-18 years from the NHANES and CHMS, respectively, are presented in Tables 2 and 3. Also presented are comparisons of relative errors regarding predictive performance of regressions estimated for ages 11-18 years for ages 6-10 for NHANES and CHMS. Errors exceeding 10% were deemed as unacceptable and those under 3.0% as acceptable. For both data series, the logarithmic function extrapolated WC values were the most accurate, with linear and quadratic functions having several error values greater than 10% for the younger ages. Table 4 presents the predicted WC values for 6-10 years olds based on 11-18 year olds for the CFS, as well as the corresponding degrees of error. As compared to the NHANES or CHMS predictions, the errors are much smaller with none greater than 3.0%. For the CFS, all three regression functions exhibit good fit though there are greater deviations in predictions by the linear and quadratic regressions versus the logarithmic regression. Overall, the logarithmic functional form fits all three data series for both males and females. Figures 1-4 graphically display WC versus age for males and females for the three data series, individually and collectively.

The predicted age- and sex- specific 90th percentile references points for ages 6-10 years using linear, logarithmic quadratic and logarithmic regression are presented in Table 5. The prevalence of abdominal obesity among CHMS participants' aged 6-10 years was calculated using the predicted reference values. The weighted prevalence of abdominal obesity calculated using the linear predictions was the lowest (M: 17.00%, F: 19.21%), followed by quadratic (M: 26.17%, F: 23.25%) with the logarithmic values resulting in the highest prevalence (M: 30.71%, F: 32.05%)(Tables 6 and 7).

Table 8 presents the sensitivity and specificity of reference points using the CHMS. For all three functions, the specificity was very high (>99%) with no statistical significance between them. These findings indicate that it would be extremely unlikely for these WC reference values to classify a non-obese child or adolescent as obese. Among children (6-10 years), the sensitivity among the functions was lower-moderate and statistically significant with logarithmic, followed by quadratic, followed by linear having the lowest specificity, respectively. These results indicated that the reference values predicted by the logarithmic function would be significantly more likely to classify an overweight or obese child or adolescent as normal weight. Among adolescents (11-18 years), the specificity between the functions, as well as a compared to the established reference values for 1981 CFS, were not statistically significant and all between lower to moderate levels (29-45%). Overall, the proposed logarithmic cut-offs have equivalent or greater sensitivity and specificity as the reference values for the 1981 WC.

DISCUSSION

Our primary aim with this ecological study was to establish pre-obesity epidemic WC reference values for children ages 6-10 years using national, anthropometric data from Canada and the United States. As an initial step, we established that regression of adolescent WC measurements using linear, logistic and quadratic functions would extrapolate predicted WC values for children that were statistically sound within reasonable degree of error for the NHANES, CHMS and CFS. To our knowledge, this is a novel approach to generating proposed cut-offs for abdominal obesity, though this extrapolation technique has been applied to derive reference values for pediatric populations from adults in other contexts, such as clinical neurology and laboratory studies regarding medical devices.(43,44)

Subsequently, we determined whether the linear, logistic or quadratic function predicted reference values that were closest to the measured WC by comparing the degrees of error, examining the theoretical basis of each mathematical function and conducting a sensitivity and specificity analysis. Compared to the linear and quadratic functions, the logistic function extrapolated WC values that were closest to the measured values and with a degree of error that was consistently in an acceptable range. The predicted values from both linear and quadratic functions increasingly deviated from the measured values as the regression moved further away from age 11 years with unacceptably high errors for ages 6-8 years for the NHANES and CHMS data series.

Furthermore, the logarithmic function is the most suitable as it is destined to level off over time, which is consistent with WC reference values across the life span with established WC cut-offs for adults. Presently, multiple WC cut points exist for adulthood, ranging from lower

thresholds (male:≥94.0cm, female: ≥80.0cm)(4) to higher thresholds (male: ≥102.0cm, female: ≥88.0 cm)(42), with a rich, ongoing international discourse regarding appropriate modifications for application to various races and ethnicities, and further research required to reach consensus of the optimal thresholds for predicting relative cardio-metabolic risk.(38)

Multiple large scale studies of children and adolescents which have applied a linear slope to report age- and sex- specific WC percentiles have noted that a non-linear function may be more suitable. In a landmark paper that established WC percentiles for American children and adolescents of various ethnicities using NHANES III, Fernandez (2004) applied complex regression to model WC such that the resulting percentiles are linear.(45) Fernandez (2004) also noted that WC increased as function of age and sex at "non-constant rates" which is consistent with the 90th percentiles generated from the raw data presented in our reference study for NHANES III.(34,45) In a report by the Centers for Disease Control and Prevention, McDowell (2008) presented national WC percentiles using NHANES 2003-2006.(46) The slope of WC over age is consistent with our other data series of reference showing that, while a linear slope could be applied, a non-linear function is more suitable to model the growth pattern. Cook (2009) established WC smoothed sex-specific percentile curves using the Lamba, Mu and Sigma method (LMS method) for the combined 90th percentiles from the NHANES III, NHANES (1999-2006), Bogalusa Heart Study (1992-1994) and the Fels Longitudinal Study (1976-1996) which are also appear best suited for non-linear function.(47) Taken together, these studies consistently show that WC growth during childhood and adolescence progresses at non-linear, sex-specific function of age.

A sensitivity and specificity analyses was performed to further test the accuracy of the predicted WC values. All extrapolated WC values had a very high specificity, meaning that the likelihood of misclassifying a child with low body fat as having abdominal obesity was very low for the values extrapolated by all three functions. The extrapolated WC values exhibited low-moderate sensitivity, meaning that the values would misclassify many overweight or obese children as normal weight. In fact, of the three functions, the logarithmic function generated WC values with the lower sensitivity which was small, but significantly different. However, the extrapolated values by logarithmic function predicted as well, or slightly better, than the established, measured reference values for ages 11-18 years.

Strengths, Limitations and Future Research

Our study offers a comparative analysis of three national, anthropometric data series of WC at three different points in time over the past 40 years. The CFS data represents national norms prior to the obesity epidemic,(2,25) whereas the NHANES (1988-1994) was taken as obesity rates began to increase and the CHMS (2007-2013) taken over 30 years later.(2,25) Yet, all data series show a relatively similar slope, suggesting that the pattern of WC among children and adolescent is relatively consistent, although intercept increased over time due to emerging obesity epidemic, which supports our approach. The predicted CFS measurements had the smallest degree of error compared to the NHANES or CHMS. Much of this can be attributed to our CFS reference study's age standardization of the WC measures to represent values at the half way point between each age (i.e. 11 years refers to exact 11.5 years of age). Thus, for the CFS data, age is a stronger predictor for WC than it is for NHANES or CHMS. Application of a prediction equation facilitated alignment and comparability across the data series. Researchers

have noted that challenges exist when striving to compare WC reference values across populations and to make international comparisons due to variations in the site of measurement as dictated by varying measurement protocols. A study comparing measurement of WC following four protocols concluded that the magnitude of WC differed by protocol in a sex-specific manner and that measured WC was highly correlated with body fat mass in a sex-specific manner.(48) Overall, that comparison between measurements that have been taken by different protocols is not recommended.(48)

Extrapolating reference values is subject to a degree of uncertainly. Without the raw data of the CFS, we are limited in the statistical techniques, prediction and power with which to analyse the data. Furthermore, the relative contribution of intra-abdominal fat mass to total body fat is influenced by sex, age, race-ethnicity, physical activity, total adiposity and puberty, however, age and sex were the only available predictors in our case. Fortunately, studies have shown that age and WC are highly correlated for both male and female children and adolescents.(49)

These WC reference values for children ages 6-10 years, representing Canada's pre-obesity epidemic population, offer a starting point from which future studies can continue to examine and refine these estimates, particularly for ethnically-specific subpopulations. The *2006 Canadian Clinical Practice Guidelines on the Management and Prevention and Obesity in Adults and children* call for research efforts to establish Canadian-specific WC reference data that is associated with measured health outcomes.(50) Thus, studies which perform data linkages between measured WC and health outcomes over time will be essential towards establishing reference values to serve as medical diagnostic tools.

CONCLUSION

In conclusion, the regression of the logarithmic function extrapolated usable age- and sex-specific WC reference values for measuring and studying abdominal obesity among children in Canada. We hope to inspire further study of these reference values to support the establishment of ethnically-specific WC cut points that are predictive of health outcomes for children in Canada.

ACKNOWLEDGMENTS

We are grateful to Statistics Canada for conducting the Canadian Health Measures Survey and to the people of Canada who participated in the study.

There were no competing interests.

We acknowledge the support of the School of Epidemiology, Public Health and Preventative Medicine in the Faculty of Medicine with University of Ottawa and the Public Health Agency of Canada.

TABLES AND FIGURES

Table 2: Predicting waist circumference for ages 6-10 years using trend for ages 11-18 years, NHANES

Age (y)	NHANES Measured WC (cm)	Predicted WC (cm)			Error (%) Predicted vs Measured		
		Lin	LN	QF	Lin	LN	QF
Males							
6	**66.1**	76.6	69.0	59.1	15.8	4.4	-10.6
7	**69.0**	78.4	73.1	65.1	13.6	5.9	-5.7
8	**70.9**	80.2	76.7	70.5	13.2	8.1	-0.5
9	**78.0**	82.1	79.8	75.5	5.2	2.3	-3.2
10	**80.0**	83.9	82.6	79.9	4.9	3.3	-0.1
11	**84.2**	85.8	85.2	83.9	1.9	1.2	-0.4
12	**85.9**	87.6	87.5	87.3	2.0	1.9	1.6
13	**90.0**	89.5	89.6	90.1	-0.6	-0.4	0.2
14	**96.0**	91.3	91.6	92.5	-4.9	-4.6	-3.6
15	**95.9**	93.1	93.5	94.3	-2.9	-2.5	-1.6
16	**90.2**	95.0	95.2	95.7	5.3	5.5	6.1
17	**98.0**	96.8	96.8	96.5	-1.2	-1.2	-1.6
18	**97.6**	98.7	98.3	96.8	1.1	0.8	-0.9
Females							
6	**62.5**	73.3	65.6	50.3	17.3	4.9%	-19.5
7	**68.4**	75.1	69.7	57.7	9.9	1.9%	-15.7
8	**69.0**	77.0	73.3	64.3	11.6	6.3%	-6.8
9	**80.8**	78.8	76.5	70.3	-2.4	-5.3%	-13.0
10	**79.0**	80.7	79.3	75.5	2.1	0.4%	-4.4
11	**80.9**	82.5	81.9	80.1	2.0	1.2%	-1.0
12	**81.2**	84.4	84.2	84.0	3.9	3.8%	3.5
13	**89.5**	86.2	86.4	87.2	-3.7	-3.5%	-2.5
14	**91.9**	88.1	88.4	89.8	-4.2	-3.8%	-2.3
15	**89.0**	89.9	90.3	91.6	1.0	1.4%	2.9
16	**92.1**	91.8	92.0	92.8	-0.4	-0.1%	0.7
17	**94.6**	93.6	93.6	93.3	-1.0	-1.0%	-1.4
18	**92.8**	95.5	95.2	93.0	2.9	2.6%	0.3

Notes:

- Abbreviations: Cm, centimetres; Lin, linear; LN, Natural logarithm; NHANES, National Health and Nutrition Examination Survey; QF, Quadratic function; WC, Waist circumference; Y, Years.
- Colours: green, error ≤3.0%; ; red, error≥10% unacceptable range

Table 3: Predicting waist circumference for ages 6-10 years using trend for ages 11-18 years, CHMS

Age (y)	CHMS Measured WC (cm)	Predicted WC (cm)			Error (%) Predicted vs Measured		
		Lin	LN	QF	Lin	LN	QF
Males							
6	**61.6**	72.6	63.2	81.1	17.9	2.5	31.6
7	**69.5**	75.1	68.6	81.5	8.1	-1.3	17.3
8	**71.7**	77.6	73.3	82.3	8.3	2.3	14.8
9	**80.2**	80.1	77.5	83.3	-0.1	-3.4	3.8
10	**82.5**	82.6	81.2	84.5	0.2	-1.6	2.4
11	**83.0**	85.1	84.6	86.0	2.6	1.9	3.6
12	**91.9**	87.6	87.6	87.7	-4.7	-4.6	-4.5
13	**89.1**	90.1	90.5	89.7	1.1	1.5	0.7
14	**93.2**	92.6	93.1	92.0	-0.6	-0.1	-1.3
15	**94.8**	95.1	95.5	94.5	0.3	0.7	-0.3
16	**96.2**	97.6	97.8	97.2	1.5	1.7	1.1
17	**95.8**	100.1	99.9	100.2	4.5	4.3	4.6
18	**106.9**	102.6	101.9	103.5	-4.0	-4.6	-3.2
Females							
6	**61.0**	71.7	63.3	71.4	17.5	3.8	17.1
7	**66.3**	73.9	68.1	73.6	11.4	2.7	11.1
8	**73.3**	76.0	72.2	75.9	3.7	-1.5	3.5
9	**76.5**	78.2	75.8	78.1	2.2	-0.9	2.1
10	**76.5**	80.4	79.1	80.3	5.0	3.3	5.0
11	**82.3**	82.5	82.0	82.5	0.3	-0.4	0.2
12	**84.9**	84.7	84.7	84.7	-0.2	-0.3	-0.3
13	**87.3**	86.9	87.1	86.9	-0.5	-0.2	-0.5
14	**88.6**	89.0	89.4	89.0	0.5	0.9	0.5
15	**91.2**	91.2	91.6	91.2	0.0	0.4	0.0
16	**92.8**	93.4	93.5	93.4	0.6	0.8	0.6
17	**96.5**	95.5	95.4	95.5	-1.0	-1.1	-1.0
18	**97.3**	97.7	97.2	97.7	0.4	-0.1	0.4

Notes:

- Abbreviations: CHMS, Canadian Health Measures Survey; Cm, centimetres; Lin, linear; LN, Natural Logarithm; QF, Quadratic function; WC, Waist circumference; Y, Years.
- Colours: green, error ≤3.0%; ; red, error≥10% unacceptable range

Table 4: Predicting waist circumference for ages 11-18 years by regressing linear, logarithmic and quadratic functions based on 11-18 years, CFS

Age (y)	CFS Measured WC (cm)	Predicted WC (cm)			Error (%) Predicted vs Measured		
		Lin	LN	QF	Lin	LN	QF
Males							
11	**72.7**	72.5	72.0	72.0	-0.2	-0.9	-1.0
12	**74.0**	74.5	74.5	74.5	0.8	0.7	0.7
13	**75.9**	76.6	76.8	76.8	0.8	1.1	1.1
14	**78.8**	78.6	78.9	79.0	-0.3	0.1	0.2
15	**81.6**	80.6	80.9	81.0	-1.3	-0.9	-0.8
16	**83.3**	82.6	82.8	82.8	-0.9	-0.7	-0.6
17	**84.6**	84.6	84.5	84.5	0.0	-0.1	-0.1
18	**85.7**	86.6	86.2	86.1	1.1	0.6	0.5
Females							
11	**70.6**	70.9	70.4	70.5	0.3	-0.4	-0.2
12	**72.3**	72.7	72.7	72.6	0.5	0.5	0.5
13	**74.7**	74.5	74.7	74.7	-0.2	0.1	0.0
14	**76.9**	76.3	76.7	76.6	-0.8	-0.3	-0.5
15	**78.7**	78.2	78.5	78.4	-0.6	-0.3	-0.4
16	**79.8**	80.0	80.2	80.1	0.2	0.4	0.4
17	**81.4**	81.8	81.7	81.8	0.6	0.4	0.5
18	**83.6**	83.7	83.2	83.3	0.0	-0.5	-0.4

Notes:

- Abbreviations: Cm, centimetres; CFS, Canada Fitness Survey; Lin, linear; LN, Natural logarithm; NHANES, National Health and Nutrition Examination Survey; QF, Quadratic function; WC, Waist circumference; Y, Years.
- Colours: green, lowest error; orange, error≥1%

Table 5:90th percentile waist circumference reference values for ages 6-10 years, 1981 Canadian Fitness Survey

	Linear	Logarithmic	Quadratic (cm)
Age (y)	**Predicted (cm)**	**Predicted (cm)**	**Predicted (cm)**
Males			
6	62.5	**54.6**	57.2
7	64.5	**59.0**	60.5
8	66.5	**62.9**	63.6
9	68.5	**66.2**	66.5
10	70.5	**69.3**	69.3
Females			
6	61.7	**54.6**	58.6
7	63.6	**58.6**	61.2
8	65.4	**62.1**	63.7
9	67.2	**65.2**	66.0
10	69.0	**67.9**	68.3

Notes:

- Abbreviations: Cm, centimetres; Y, Years.

Table 6: Prevalence of abdominal obesity among males, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013) in CHMS (2007-2013)

Prevalence of Abdominal Obesity % (95% CI)			
	Male		
Age (y)	**Linear**	**Logarithmic**	**Quadratic**
6	F	39.92 (26.96-52.89	21.80[R] (12.84-30.77)
7	19.60[R] (10.34-28.86)	33.20 (23.31-43.09	29.20[R] (18.58-39.82)
8	14.63[R] (8.54-20.73)	25.15 (17.69-32.62	23.89 (16.72-31.07)
9	21.93 (14.6-29.27)	28.06 (18.85-37.27	28.06 (18.85-37.27)
10	24.20 (17.20-31.32)	27.65 (19.96-35.34)	27.65 (19.96-35.34)
Total 6-10 y (n=1280)	17.00 (13.95-20.06)	30.71 (26.39-35.02)	26.17 (22.44-29.90)
Age (y)	**Measured**		
11	23.35 (16.45-30.24)		
12	32.27 (22.18-42.35)		
13	36.15[R] (23.79-48.50)		
14	33.03[R] (20.09-45.97)		
15	33.44 (22.57-44.30)		
16	27.66 (18.50-36.82)		
17	33.34 (23.91-41.78)		
18	42.00 (30.83-53.16)		
Total 11-18 y (n=1727)	32.67 (28.39-26.96)		

Notes:

- Abbreviations: CI, Confidence Interval; Cm, centimetres;; Y, Years.
- Prevalence for ages 6-10 years was calculated using references points established from the 1981 Canadian Fitness Survey using linear, logarithmic and quadratic slopes (reference points from Table 5)
- Prevalence for ages 11-18 years was calculated using references points established from the 1981 Canadian Fitness Survey
- R denotes figures are being published with reservation as 0.16 ≤ Coefficient of Variation (CV)≥0.33
- F denotes figures may not be published due to CV≥0.33

Table 7: Prevalence of abdominal obesity among females, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013) in CHMS (2007-2013)

Prevalence of Abdominal Obesity % (95% CI)			
	Female		
Age (y)	Linear	Logarithmic	Quadratic
6	8.53[R] (3.34-13.72)	43.15 (33.37-52.94)	16.40[R] (9.98-22.82)
7	12.83[R] (6.70-18.96)	31.29 (21.48-41.10)	18.72[R] (11.26-26.19)
8	25.98 (18.19-33.78)	35.30 (28.28-42.33)	28.37 (21.37-35.36)
9	24.29 (17.03-31.54)	26.49 (18.67-34.31)	26.09 (18.23-33.94)
10	22.06[R] (14.39-29.72)	26.49 (18.62-34.37)	25.20 (17.50-32.90)
Total 6-10 y (n=1250)	19.21 (16.00-22.41)	32.05 (27.60-36.47)	23.25 (19.79-26.71)
Age (y)	Measured		
11	32.11 (24.83-39.38)		
12	45.32 (34.06-56.57)		
13	40.87 (29.82-51.93)		
14	28.12 (18.96-37.28)		
15	34.90 (23.93-45.86)		
16	26.20 (18.48-33.91)		
17	36.89 (27.02-46.76)		
18	23.60 (15.96-31.25)		
Total 11-18 y (n=1665)	33.08 (29.00-37.16)		

Notes:

- Abbreviations: CI, Confidence Interval; Cm, centimetres;; Y, Years.
- Prevalence for ages 6-10 years was calculated using references points established from the 1981 Canadian Fitness Survey using linear, logarithmic and quadratic slopes (reference points from Table 5)
- Prevalence for ages 11-18 years was calculated using references points established from the 1981 Canadian Fitness Survey
- R denotes figures are being published with reservation as $0.16 \leq CV \geq 0.33$

Table 8. Sensitivity and Specificity of the reference values

	Sensitivity % True Positive (95% CI)	Specificity % True Negative (95% CI)
Children 6-10 years (n=2530)		
· **Males - Linear**	69.62 (63.33-75.41)	98.18 (97.17-98.90)
· **Males – LN**	46.53 (41.49-51.63)	99.66 (99.02-99.93)
· **Males – Quadratic**	53.55 (48.07-58.96)	99.68 (99.07-99.93)
· **Females - Linear**	43.65 (37.44-50.2)	99.30 (98.56-99.72)
· **Females – LN**	27.82 (23.57-32.39)	99.88 (99.33-100.0)
· **Females – Quadratic**	43.65 (37.44-50.02)	99.30 (98.56-99.72)
Adolescents 11-18 years (n=3392)		
· **Males - Linear**	42.91 (38.65-47.25)	100.0 (99.96-100.0)
· **Males – LN**	42.81 (38.65-47.25)	100.0 (99.69-100.0)
· **Males – Quadratic**	44.31 (39.98-48.76)	100.0 (99.70-100.0)
· **Males – 1981 CFS**	**42.91 (38.65-47.25)**	**100.0 (99.69-100.0)**
· **Females - Linear**	31.85 (27.94-35.97)	99.91 (99.51-100.0)
· **Females - LN**	31.85 (27.94-35.97)	99.91 (99.51-100.0)
· **Females - Quadratic**	29.30 (25.65-33.17)	99.91 (99.48-100.0)
· **Females – 1981 CFS**	**31.85 (27.94-35.97)**	**99.91 (99.51-100.0)**

Notes:

· Abbreviations: CI, Confidence Interval; Lin, Linear; LN, natural logarithm; QF, quadratic function

Figure 1. Waist circumference measurements and regression predictions for males and females, CFS

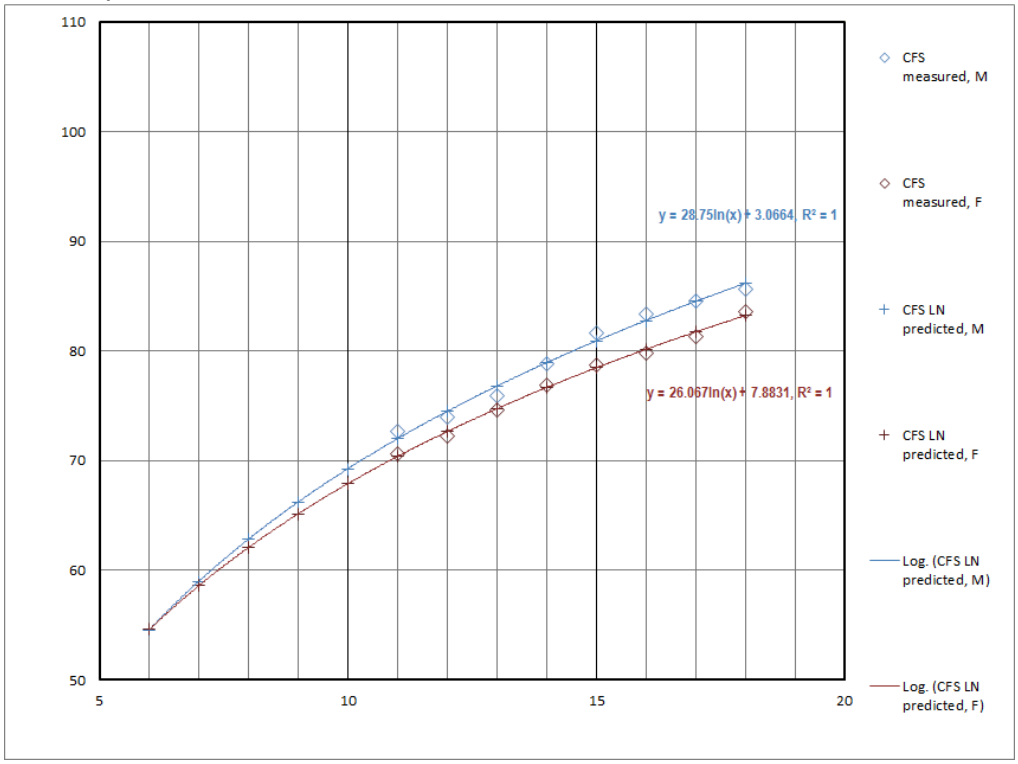


Figure 2. Waist circumference measurements and regression predictions for males and females, CHMS

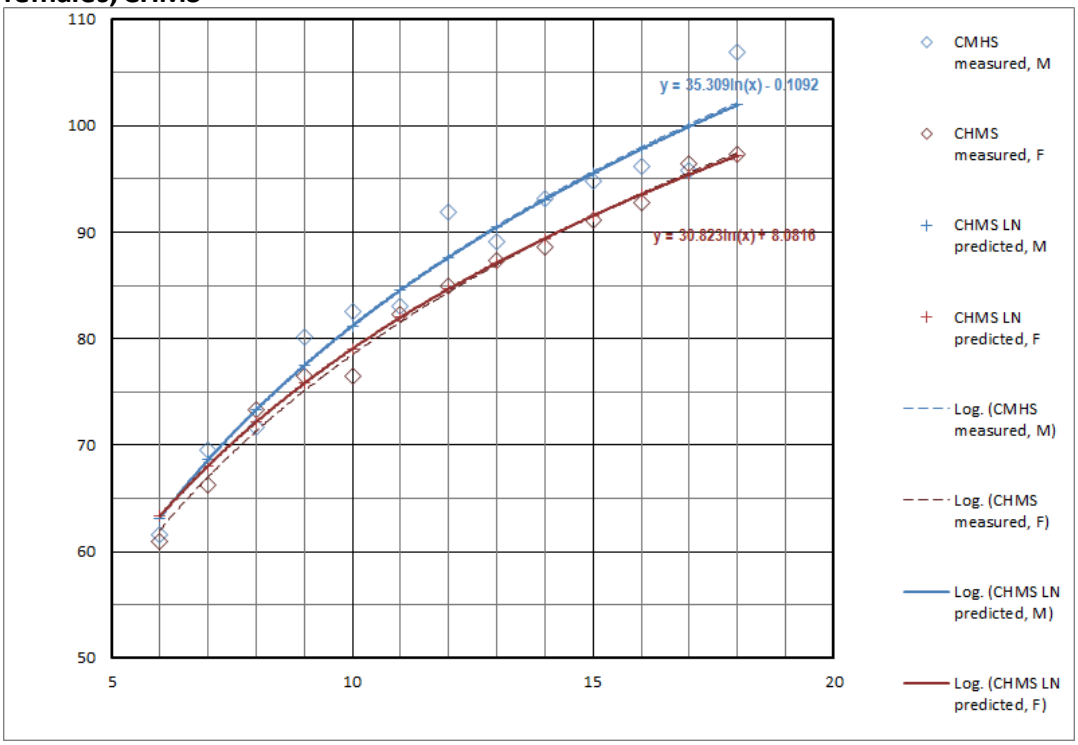


Figure 3. Waist circumference measurements and regression predictions for males and females, NHANES

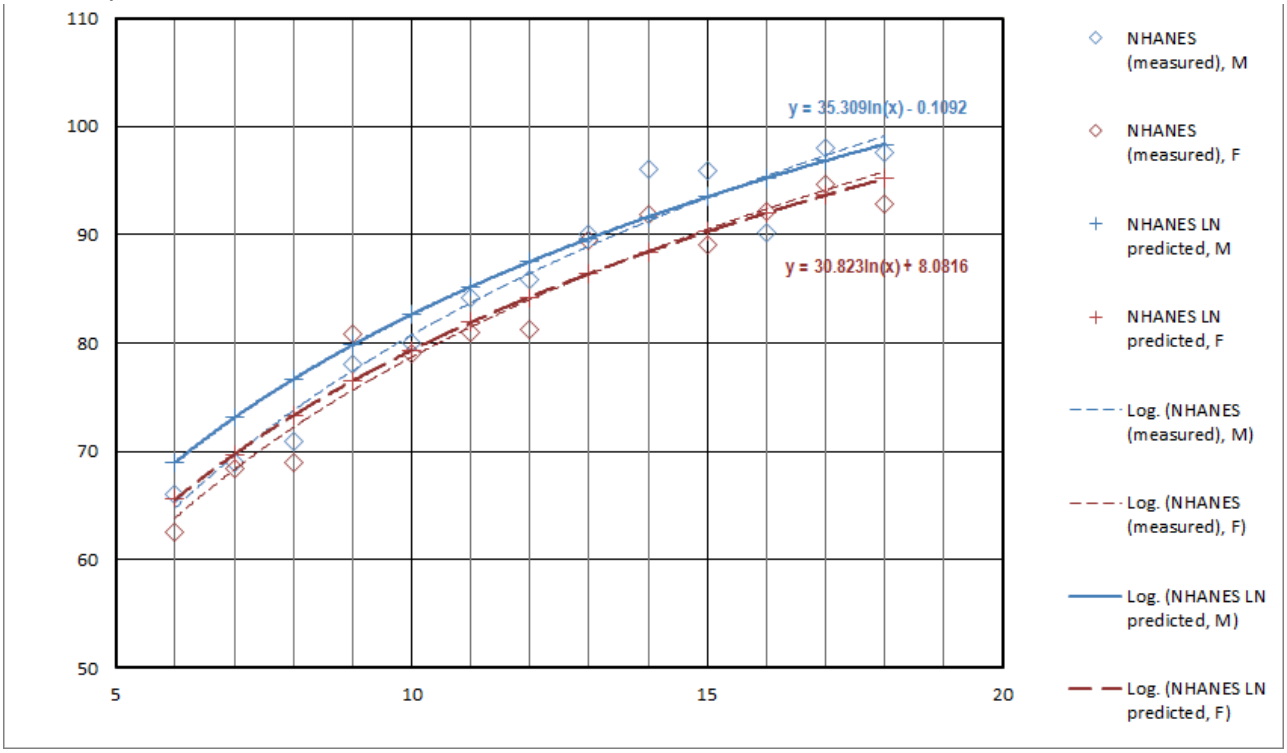
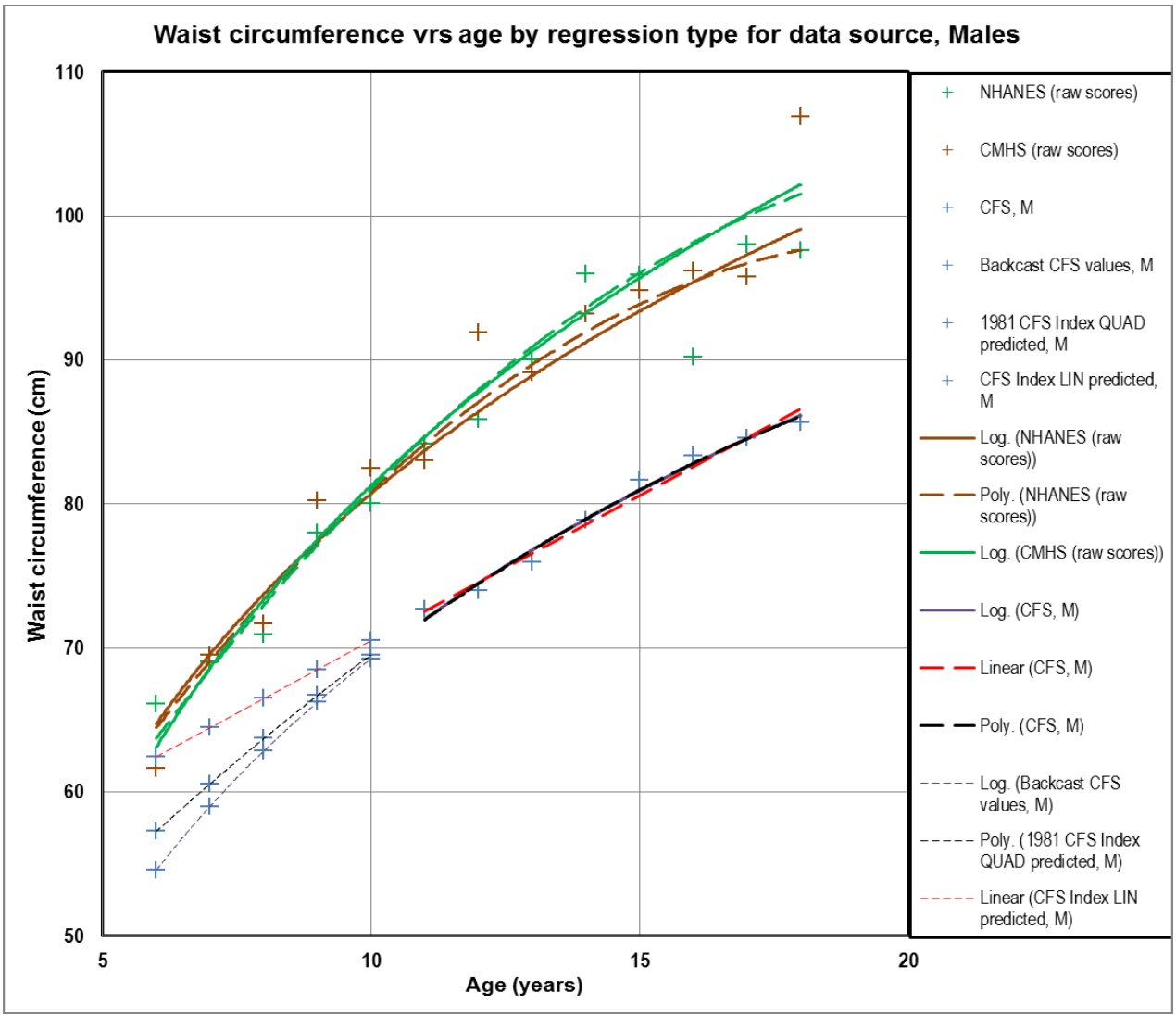


Figure 4. Waist circumference measurements and regression predictions for NHANES, CHMS and CFS, Males



REFERENCES

1. Obesity in Canada: A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. 2011 [Internet]. Available from: http://www.phac-aspc.gc.ca/hp-ps/hl-mvs/oic-oac/assets/pdf/oic-oac-eng.pdf

2. Tremblay MS, Willms JD. Secular trends in the body mass index of Canadian children. Can Med Assoc J. 2000 Nov 28;163(11):1429–33.

3. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013: A systematic analysis. Lancet Lond Engl. 2014 Aug 30;384(9945):766–81.

4. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO consultation on obesity. Geneva: World Health Organization; 2000. Technical Report Series, No. 894:268.

5. World Health Organization. Noncommunicable diseases [Internet]. World Health Organization Health Topics. 2016. Available from: http://www.who.int/topics/noncommunicable_diseases/en/

6. The IDF consensus definition of the metabolic syndrome in children and adolescents. [Internet]. International Diabetes Federation; 2007 p. 1–24. Available from: http://www.idf.org/webdata/docs/Mets_definition_children.pdf

7. Zhu S, Wang Z, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. Am J Clin Nutr. 2002 Oct;76(4):743–9.

8. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. Am J Clin Nutr. 2004;79(3):379–84.

9. Zhang C, Rexrode KM, Dam RM van, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality. Circulation. 2008 Apr 1;117(13):1658–67.

10. Dagenais GR, Yi Q, Mann JFE, Bosch J, Pogue J, Yusuf S. Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. Am Heart J. 2005 Jan;149(1):54–60.

11. Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord. 2000 Nov;24(11):1453–8.

12. The IDF consensus worldwide definition of the metabolic syndrome [Internet]. International Diabetes Federation; 2007 p. 1–24. Available from: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf

13. Ardern CI, Janssen I, Ross R, Katzmarzyk PT. Development of health-related waist circumference thresholds within BMI categories. Obes Res. 2004 Jul;12(7):1094–103.

14. Staiano AE, Bouchard C, Katzmarzyk PT. BMI-specific waist circumference thresholds to discriminate elevated cardiometabolic risk in white and african american adults. Obes Facts. 2013;6(4):317–24.

15. Must A, Anderson S. Pediatratic mini review. Body mass index in children and adolescents: considerations for population-based applications. Int J Obes. 2006;30:590–4.

16. Garn SM, Leonard WR, Hawthorne VM. Three limitations of the body mass index. Am J Clin Nutr. 1986 Dec;44(6):996–7.

17. Pouliot MC, Després JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol. 1994 Mar 1;73(7):460–8.

18. Albanese C, Diessel E, Genant H. Clinical applications of body composition measurements using DXA. J Clin Densitom. 2003;6(2):75–85.

19. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. J Pediatr. 1998 Feb;132(2):204–10.

20. Steinberger J, Jacobs DR, Raatz S, Moran A, Hong C-P, Sinaiko AR. Comparison of body fatness measurements by BMI and skinfolds vs dual energy X-ray absorptiometry and their relation to cardiovascular risk factors in adolescents. Int J Obes. 2005 Nov 1;29(11):1346–52.

21. Bedogni G, Iughetti L, Ferrari M, Malavolti M, Poli M, Bernasconi S, et al. Sensitivity and specificity of body mass index and skinfold thicknesses in detecting excess adiposity in children aged 8-12 years. Ann Hum Biol. 2003 Jan;30(2):132–9.

22. Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. Pediatrics. 2009 Sep 1;124(Supplement 1):S23–34.

23. Neovius MG, Linné YM, Barkeling BS, Rossner SO. Sensitivity and specificity of classification systems for fatness in adolescents. Am J Clin Nutr. 2004 Sep 1;80(3):597–603.

24. Taylor RW, Jones IE, Williams SM, Goulding A. Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3–19 y. Am J Clin Nutr. 2000 Aug 1;72(2):490–5.

25. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11-18y of age. Eur J Clin Nutr. 2004 Jul;58(7):1011–5.

26. Katzmarzyk PT. The Canadian obesity epidemic, 1985–1998. Can Med Assoc J. 2002 Apr 16;166(8):1039–40.

27. Fitness Canada (1983): Fitness and Lifestyle in Canada. Ottawa: Minister of Fitness and Amateur Sport, Government of Canada.

28. Russell SJ, Hyndford C, Beaulieu A. Active Living for Canadian Children and Youth: A Statistical Profile [Internet]. Joint Initiative by the Canadian Fitness and Lifestyle Research Institute and the Active Living Alliance for Children and Youth. 1992 January. Available from: http://schools.ednet.ns.ca/avrsb/994/rfletcher/canadian%20stats.pdf.

29. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1 [Internet]. Statistics Canada; 2014 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.htm

30. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 2 [Internet]. Statistics Canada; 2013 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V2-eng.htm

31. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 3 [Internet]. Statistics Canada; 2014 Sep. Available from: http://www23.statcan.gc.ca:81/imdb/p2SV.pl?Function=getSurvey&SDDS=5071&lang=en&db=imdb&adm=8&dis=2

32. Giroux S. Canadian Health Measures Survey: sampling strategy overview. Health Rep. 2007;18 Suppl:31–6.

33. Centers for Chronic Disease Prevention and Control, U.S. Department of Health & Human Services. NHANES - National Health and Nutrition Examination Survey [Internet]. 2016. Available from: http://www.cdc.gov/nchs/nhanes/

34. Li C, Ford ES, Mokdad AH, Cook S. Recent trends in waist circumference and waist-height ratio among US children and adolescents. Pediatrics. 2006 Nov;118(5):e1390-1398.

35. Fitness Canada (1981). Standardized test of fitness: Operations Manual. 2nd Edition, Ottawa, ON: Ministry of Fitness and Amateur Sport.

36. National Health and Nutrition Examination Survey - Anthropometry Procedures Manual [Internet]. Centers for Disease Control and Prevention; 2000 Dec p. 1–65. Available from: http://www.cdc.gov/nchs/data/nhanes/bm.pdf

37. Canadian Society for Exercise Physiology. 2003. Canadian Physical Activity, Fitness and Lifestyle Approach (CPAFLA). 3rd edition. Ottawa.

38. World Health Organization. Waist circumference and waist–hip ratio: report of a WHO expert consultation. Geneva, Switzerland. December 2008:1-47. [Internet]. Available from: http://apps.who.int/iris/bitstream/10665/44583/1/9789241501491_eng.pdf

39. Patry-Parisien J, Shields M, Bryan S. Comparison of waist circumference using the World Health Organization and National Institutes of Health protocols. Health Rep. 2012 Sep;23(3):56–63.

40. Centers for Disease Control and Prevention, US Department of Health and Human Services. Clinical Growth Charts [Internet]. 2009. Available from: http://www.cdc.gov/growthcharts/clinical_charts.htm

41. World Health Organization. WHO: Global Database on Body Mass Index; The International Classification of adult underweight, overweight and obesity according to BMI [Internet]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

42. Canadian Guidelines for Body Weight Classification in Adults - Health Risk Classification according to Body Mass Index [Internet]. Ottawa, Ontario, Canada: Health Canada; 2003 Mar. (Catalogue H49-179). Available from: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/cg_quick_ref-ldc_rapide_ref-eng.pdf

43. Jabre JF, Pitt MC, Deeb J, Chui KKH. E-norms: a method to extrapolate reference values from a laboratory population. J Clin Neurophysiol Off Publ Am Electroencephalogr Soc. 2015 Jun;32(3):265–70.

44. Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices [Internet]. Joint report by US Department of Health and Human Services, Food and Drug Administration, Center for Devices and Radiological Health, and Center for Biologics Evaluation and Research; 2016 June. Available from:http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm444591.pdf [Internet]. Available from: http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm444591.pdf

45. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. WC percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. J Pediatr. 2004 June;145:439-44.

46. US Department of Health and Human Services, Center for Disease Control and Prevention, National Health Statistics Reports. McDowell MA, Fryar CD, Ogden CL, Flegal KM. Anthropometric Reference Data for Children and Adults: United States, 2003-2006. Oct 2008;10:1-45. http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf [Internet]. Available from: http://www.cdc.gov/nchs/data/nhsr/nhsr010.pdf

47. Cook S, Auinger P, Huang T. Growth curves for cardio-metabolic risk factors in children and adolescents. J Pediatr. 2009 Sep;155(3):15–26.

48. Wang J, Thornton JC, Bari S, Williamson B, Gallagher D, Heymsfield SB, et al. Comparisons of waist circumferences measured at 4 sites. Am J Clin Nutr. 2003 Feb;77(2):379–84.

49. Ekvall SM, Laffert V, Frondorf J, Rittmeyer K, Janecko T, Ekvall V, et al. A waist circumference/growth chart projection for children. J Am Diet Assoc. 1999 Sep 1;99(9):A121.

50. Lau DCW, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. Can Med Assoc J. 2007 Apr 10;176(8):S1–13.

5.3. Cardio-metabolic risk by body mass index, waist circumference, and a combined body mass index-waist circumference indicator, among Canadian children and adolescents

Author references: Miranda MacPherson James (1,2); Margaret de Groh (1); Denis Prud'homme (3); XiaoHong Jiang (1); Lise Dubois (4).

1. Social Determinants and Science Integration Directorate, Public Health Agency of Canada, Ottawa, Ontario, Canada
2. Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
3. Institut de recherche de l'Hôpital Montfort, Ottawa, Ontario, Canada; School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
4. School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

This manuscript will be submitted for publication in a journal regarding pediatric health in January 2017.

ABSTRACT

Introduction: Our objectives were to determine the prevalence of cardiometabolic risk (CMR) factors among Canadian children and adolescents and to quantify the association between CMR and obesity, using three indexes of obesity: body mass index (BMI), waist circumference (WC) and a novel combination of BMI and WC.

Methods: Nationally representative sample of Canadians (6-18 years) based on Canadian Health Measures Survey Cycles 1-3 participants (n=2679). Participants were dichotomized as having 'no CMR factors ' or 'CMR factors', defined as the presence of 1 or more CMRs: fasting triglycerides (≥1.25mmol/L), high-density lipoprotein cholesterol (participants aged 6-15 years and males 16-18 years: <1.03mmol/L and females 16- 18 years <1.3 mmol/L), fasting glucose (≥5.6mmol/L) and/or the presence of diabetes, insulin resistance using the homeostasis model assessment, and elevated blood pressure (6-17 years: age-, sex and height-specific reference data; 18 years: ≥130mm Hg systolic blood pressure and/or a ≥85 mm HG diastolic blood pressure). Statistics Canada derived and classified BMI using the Centers for Disease Control and Prevention's growth charts (6-17 years) and the Canadian Guidelines for Body Weight Classification (18 years). Abdominal obesity was defined as a WC ≥ 90th age- and sex- specific percentile based on data from the 1981 Canada Fitness Survey. Physical activity was measured using Actical activity monitors and assessed against guidelines established by the Canadian Society for Exercise Physiology. Multivariate logistic regression was applied to calculate odds of CMR across age groups, weight status, physical activity and socio-economic profiles.

Results: One quarter (25%) of children and 40% of adolescents were classified as having CMR factors. Among the obesity indexes, in multivariate models adjusting for age, the combined

BMI-WC index 'BMI Obese with Abdominal Obesity' (OR: 8.5) had the highest association with CMR factors followed by BMI Obesity (OR: 7.5) and then abdominal obesity (OR: 4.6), although further testing is required to determine whether these ORs are significant different. Over 95% of participants did not meet the age-appropriate physical activity guidelines, which was a significant predictor for CMR (OR: 5.8) as was an average daily moderate to vigorous physical activity (MVPA) of 29 minutes or less (OR: 2.0), in multivariate models adjusting for age and combined BMI-WC. There was no statistically significantly difference between participants who averaged 30-59 minutes or 60 minutes or more MVPA per day in multivariate models. In univariate models, participants who averaged 30-59 minutes of MVPA/day have a higher association with CMR (OR: 1.7) versus participants who averaged 60 minutes or more MVPA/day.

Conclusions: These findings highlight the importance of measurement and monitoring the CMR factors among children and adolescents, especially those with obesity and abdominal obesity and those identified as having a CMR factor. Policies to facilitate physical activity among Canadian youth may contribute to reduce the incidence of CMR factors.

Keywords: Canada, Child, Adolescent, Obesity, Waist Circumference, Canadian Health Measures Survey, CHMS, Health surveys, Cardio-metabolic risk factors

INTRODUCTION

The presence of cardiometabolic risk factors facilitates early recognition of potential onset of metabolic abnormalities and cardiovascular diseases.(1) These risk factors are both traditional, such as hypertension, smoking, physical inactivity, dyslipidemia, impaired fasting glucose and diabetes, and non-traditional risk factors, such as insulin resistance, genetic predisposition and inflammatory markers, such as high sensitivity c-reactive protein.(1) The cluster of these cardiometabolic risk factors, which increases absolute risk for type 2 diabetes and cardiovascular diseases, is generally attributed to insulin resistance associated with obesity, especially abdominal obesity, underpinned by complex pro-inflammatory and pro-thrombotic mechanisms.(1,2) While coronary heart events are generally experienced in adulthood, atherosclerosis begins during childhood and adolescence and is related to the presence of cardiometabolic risk factors.(3)

Evidence points to a complex association between body fat, abdominal fat and cardiometabolic risk factors among children and youth.(4,5) Children or adolescents with obesity have an elevated risk of presenting one or more cardiometabolic risk factor(s); studies reported a prevalence ranging between 28%-78.5% among youth with overweight or obesity depending on age group, population and indicator of obesity.(6–9) Studies comparing body mass index (BMI) and waist circumference (WC), the key indicators of body composition and abdominal obesity, respectively, for population-level studies, show that even though they are highly correlated they are yet distinct. Studies have shown that WC as an index of adiposity is more predictive of prevalence of cardiometabolic risk factors than BMI among children and adults.(10,11) In 2004, Zhu developed several combined indicators using BMI and WC and

concluded that combining BMI and WC indicator, using existing BMI and WC cut-points had the strongest association with cardiometabolic risk factors than using BMI or WC alone among white men. Inspired by Zhu's (2004) results, we propose a 'Combined BMI-WC Obesity' index to study the association between combinations of BMI and WC measurements with cardiometabolic risk factors. To our knowledge, this proposed approach and application of combining BMI and WC indexes to predict the prevalence of cardiometabolic risk factors in child and adolescent populations is unique. (12)

Health risk behaviours, such has smoking and physical inactivity, are associated with clustering of cardiometabolic risk factors as well as with type 2 diabetes and cardiovascular disease. (3) These behaviours are particularly pronounced among individuals with a low socio-economic status (SES), as measured by household income and education. (13–15) SES is a significant predictor for cardiometabolic risk factors, cardiovascular events, type 2 diabetes and mortality. (12–16) Yet, among children and adolescents, the association between cardiometabolic risk factors and cardiovascular disease and SES status varies between studies and warrants further investigation. (1,16–18)

The objective of this study was first to determine the prevalence of cardio-metabolic risk in a representative sample of Canadian children and adolescents with overweight or obesity by age group, sex and SES. Second, to identify which obesity indicator (BMI versus WC) is the strongest predictor of the prevalence of cardio-metabolic risk in children and adolescents, and to investigate if the generation of a new obesity indicator, a 'Combined BMI-WC' index, is a superior predictor than each traditional obesity index. We hypothesize that the proportion of

respondents with cardiometabolic risk factors will increase with increasing BMI, WC or 'Combined BMI-WC' and that these relationships are associated with demographic, behavioural and social factors (physical activity, age, SES, smoking status and sleep). This study builds on previous national analyses of cardiometabolic risk among Canadian children and adolescents by using three cycles of the Canadian Health Measures Survey (CHMS); by calculating cardio-metabolic risk in a dichotomous form; by using Canadian age- and sex- specific WC reference data to define abdominal obesity; by using a combined BMI-WC obesity index and by examining the association between cardiometabolic risk and measured moderate to vigorous physical activity.(8,9,19)

METHODS

Data Source: The Canadian Health Measures Survey (CHMS) is a comprehensive, nationally-representative survey designed to collect information on the health of Canadians. (20–23) Data from CHMS Cycles 1 (2007-2009), 2 (2009-2011) and 3 (2012-2013) were used in this study.

Study Population: All CHMS respondents aged 6-18 years who provided fasting blood samples were included (n=2679). There were no pregnant participants. Sample weights specific to the fasting subgroup were provided by Statistics Canada to ensure appropriate representativeness at the population level.(20–22) We stratified our analyses by age to examine children (6-11 years) and adolescents (12-18 years) separately. We obtained ethics approval for this project from the University of Ottawa's Research Ethics Board.

Cardio-Metabolic Risk: Participants were dichotomized as having 'no cardio-metabolic risk factors' or 'cardio-metabolic risk factors', defined as the presence of adverse levels of one or more of the following cardiometabolic risk factors: elevated fasting triglycerides (≥1.25mmol/L),

low high-density lipoprotein cholesterol (males and females 6-15 years: <1.03mmol/L; males 16-18 years: <1.03mmol/L; females 16-18 years: <1.3 mmol/L), impaired fasting glucose (≥5.6mmol/L) and/or the presence of diabetes, insulin resistance and elevated blood pressure (BP).(1,3,7,24–27) Insulin Resistance was calculated using the homeostasis model assessment of insulin resistance (fasting insulin concentration (μU/mL) × fasting glucose concentration (mmol/L)/22.5≥3.16).(28) Concerning BP, for participants aged 6-17 years, elevated BP was defined using age-, sex and height-specific reference data by the National High BP Education Program Working Group on High BP for Children and Adolescents; participants with pre-hypertension were included.(24) Elevated BP among participants aged 18 years were defined as systolic BP≥130mm Hg and/or a diastolic BP≥85 mm HG.(29) Participants who reported taking medication for high BP were also classified as having elevated BP.

Behaviours: Physical activity was assessed using Actical activity monitors which participants were requested to wear for a 7 day period.(20–22) Only participants who wore the activity monitors for a minimum of 4 days for at least 10 hours each were included in analyses focused on physical activity (n=2067).(20–22) A participant's average daily moderate-to-vigorous physical activity (MVPA) was derived by Statistics Canada using an intensity cut-point which is equivalent to approximately >3 metabolic equivalents.(20–22) Participants aged 6-17 years were determined to meet the Canadian Physical Activity Guidelines(2003) if they accumulated ≥ 60 minutes of MVPA at least 6 days per week and to meet the Canadian 24 Hour Movement Guidelines if the achieved an average MVPA of ≥ 60 minutes per day, which we termed 'very active'.(31) For comparison purposes, we also established two other activity categories: 'inactive' (0-29 minutes of MVPA/day) and 'active' (30-59 minutes of MVPA/day). Participants

aged 18 years were determined to meet the Canadian Physical Activity Guidelines for Adults if they accumulated ≥ 30 minutes of MVPA at least 5 days a week.(20–22,30,31) Sleep duration per 24 hour period was ascertained by self-report or, for participants aged 6-11 years, by proxy report.(20–22) Consistent with the Canadian 24 Hour Movement Guidelines for Children and Youth and the United States' National Sleep Foundation's Updated Sleep Duration Recommendations, we defined adequate sleep as 9-11 hours for ages 6-13 years, 8-10 hours for ages 14-17 years and 7-9 hours for 18 years.(31, 32) Smoking status was determined using self-reported smoking behaviour, available for participants aged 12-18 years).(20–22) We re-categorized participants into two groups: ever smoked, which included all past and present smokers, and never smoked, which included all participants who had never smoked.

Demographic and Socio-Economic Profile: A participant's demographic and socio-economic profile was assessed by self-report. Parents or guardians responded to questions about their children (6-11 years) by proxy and adolescents (12-17yrs) responded in private, with parental/guardian consent. Participants were identified as having an Aboriginal origin or identity or being an immigrant by self-report or proxy self-report. SES was captured through household educational attainment and household income adequacy variables. Education and income are key determinants of health and the most frequently used indicators of SES.(33–35) Statistics Canada calculated income adequacy by classifying each participant into categories based on total household income from all sources and the number of people living in the household for CHMS Cycles 1-2.(20,21) We applied this approach to generate income adequacy for CHMS Cycle 3. Household educational attainment was derived by Statistics Canada as the highest level of education attained by any member of the household. For participants not living

with parents or guardians (5.1%), their responses pertained to their current household. To allow for greater statistical power and comparability across CHMS Cycles 1-3, we re-classified the household income adequacy and household educational attainment variables. For income adequacy, the categories of 'lowest income' and 'lower middle income' were combined resulting in three categories for income adequacy (lowest and lower middle income, upper middle and highest). For household educational attainment, the categories of 'less than secondary school graduation', 'secondary school graduation' and 'some post-secondary' were combined resulting in two categories (secondary school graduation or less and post-secondary graduation).

Anthropometry: Three indexes of obesity were used in the present population study: BMI, WC, and a 'combined BMI-WC' index. Statistics Canada derived BMI using measured of weight and height (weight (kg)/height (m^2)) and classified BMI using growth charts prepared by the Centers for Disease Control and Prevention for ages 6-17 years and the international body weight classification system recommended by Health Canada and the World Health Organization for ages 18 years.(20–22,36–38) We applied a prediction equation to CHMS Cycles 1 and 2 to the WC data (collected following protocol by the World Health Organization) to align it to the CHMS cycle 3 WC data (collected following protocol from the United States' National Institutes of Health).(39) Abdominal obesity was defined as measured WC ≥ 90^{th} age- and sex- specific percentile for ages 11-18 years based on reference data from the 1981 Canada Fitness Survey.(40) For ages 6-10 years, national reference data from the same time period was unavailable. We generated age- and sex- specific reference points using data from the 1981

Canada Fitness Survey and supplemented with trend lines from the CHMS Cycles 1-3 WC measurements (sex- and age- specific 90th percentile reference points). The methodology for this back-casting approach to generating reference data is elaborated upon in a separate paper.(41) We derived the combined BMI-WC indicator into 4 categories using the following cut-offs: (1) Normal weight (BMI< 85th and WC< 90th); (2) BMI Normal and Abdominal Obesity (BMI< 85th and WC≥ 90th); (3) BMI Overweight and Abdominal Obesity (85th≤ BMI< 95th and WC≥ 90th) and (4) BMI Obese with Abdominal Obesity (BMI> 95th and WC≥ 90th). The CHMS User Guides for Cycles 1, 2, and 3 provide more detailed descriptions of the measurement procedures for all variables in this study.(20–22)

Statistical Methods: The prevalence of cardio-metabolic risk factors, as a dichotomous variable, as well the individual prevalence of each cardiometabolic risk factor was determined and expressed as a percentage with a 95% confidence interval (CI). The associations between cardiometabolic risk and obesity indicators were estimated using X^2 tests, univariate and multivariate regression. Statistical significance was set at a *p* value of less than .05. The analyses were conducted using the bootstrap method with 35 degrees of freedom. (20–22,42) Results with 16.6 < Coefficient of Variation (CV) ≤ 33.3 were published with reservation and results with a frequency of < 10 or a CV ≥ 33.3 were not included and represented with an F. We conducted statistical analyses using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Over 80% of participants were from households with post-secondary educational attainment. The study population's SES and cardiometabolic risk factors profile is presented in Table 1. Approximately 23% of participants reported inadequate sleep with another 2.3% reporting

excessive sleep (data not shown); 93.5% of children and 96.5% of adolescents did not meet Canadian physical activity guidelines; and 10% of adolescents reported some level of past or present smoking. Females were significantly less likely to meet Canadian physical guidelines than males (data not shown). Based on BMI, 14% of children and 16% of adolescents were classified as having overweight and additional 11% of children and 13% of adolescents as having obesity. Based on WC, 26% of children and 40% of adolescents, with a significantly higher prevalence among females (data not shown), were classified as having abdominal obesity. By a combined BMI-WC index, 11% of children and 13% of adolescents were classified as having BMI obesity with abdominal obesity. The most prevalent cardiometabolic risk factors were elevated fasting triglycerides (16%), insulin resistance (16%) and low HDL-C (13%). A quarter (25%) of children and 41% of adolescents were classified as having 'cardio-metabolic risk factor(s)' meaning that they had at least one cardiometabolic risk factor. Females had a significantly higher prevalence of elevated fasting triglycerides, low HDL-C and cardiometabolic risk (data not shown).

For all three indicators of obesity, the weighted prevalence of cardio-metabolic risk increased with increasing in each obesity index and from childhood to adolescence. Table 2 presents the association between cardiometabolic risk factors and indexes of obesity. The weighted prevalence of obese participants with cardiometabolic risk factor(s) progressed from approximately half during childhood to a range of 65-85% for adolescents for all three indexes of obesity.

Tables 3 and 4 present univariate and multivariate associations between cardiometabolic risk factors and obesity index, respectively. The odds of having cardio-metabolic risk factor(s) increased with increased of all three indexes of obesity. For the obesity indexes, the age-adjusted odds for cardiometabolic risk factor(s) was highest for the combined BMI-WC index 'BMI Obese with Abdominal obesity' (OR: 8.5), followed by BMI Obesity (OR: 7.5) and then abdominal obesity (OR: 4.6), though further statistical testing is required to determine if these differences are statistically significant. Physical activity was also a strong predictor for cardiometabolic risk factor(s). In multivariate models adjusted for age and combined BMI-WC, non-adherence to physical activity guidelines was a significant predictor for cardiometabolic risk (OR: 5.8), as was an average daily moderate to vigorous physical activity (MVPA) of 29 minutes or less (OR: 2.0).

In univariate models, the odds of cardiometabolic risk among participants who averaged 30-59 minutes of MVPA/day was significantly higher (OR: 1.7) than those who averaged 60 minutes or more, however, after adjusting for age and weight status, the difference was not statistically significantly different. Age was a significant covariate in all regression models, with adolescents having significantly higher odds of cardiometabolic risk than children. Sex, SES, Aboriginal origin or identity, immigrant status, amount of sleep or smoking status did not significantly affect the association between cardiometabolic risk factor(s), obesity index and physical activity.

DISCUSSION

This study investigated the associations between cardiometabolic risk factors and different obesity indexes among children and adolescents to identify which obesity index is the strongest predictor of the prevalence of cardiometabolic risk factor(s) as well as how other traditional risk factors, such as physical inactivity, contribute to this relationship. The prevalence of cardiometabolic risk factors, defined as having 1 or more risk factors was 25% for children and 40% for adolescents. These findings are staggering given their equivalence to approximately 533,277 and 1,194,454 Canadian children and adolescents have at less one cardiometabolic risk factor, respectively. Two previous studies from Canada studied the prevalence of cardiometabolic risk factors individually without calculating a dichotomous cardiometabolic risk variable, thus not enabling a direct comparison to our study. (8,9) Yet, despite varying methodological approaches, studies found that the prevalence of cardiometabolic risk factors increased with weight status as established by measured BMI category. (6,8,9)

We used three indexes to assess obesity: BMI, WC, and a combined BMI-WC index. We chose to apply multiple indexes of obesity given that they each have their strengths and limitations. BMI is an efficient, cost-effective method to estimate weight status, particularly at the population level given the minimal technique required for measurement and calculation. (43) Studies have shown BMI results to be strongly associated with dual emission x-ray absorptiometry (DXA) results, which is recognized as a highly precise and reproducible measurements method for estimating body fat mass in clinical settings (44), even among children and adolescents. (45,46) A limitation of the BMI index is that it does not precisely differentiate results by the body's overall composition of fat mass and fat free mass. (47)

Conversely, WC index is a good proxy of body fat distribution, especially of abdominal adiposity.(48) Among children and adolescents, evidence indicates that the WC index has high sensitivity and specificity for abdominal fat estimates in comparison with results using DXA. (49) In a consensus statement on WC and cardio-metabolic risk, Shaping America's Health: Association for Weight Management and Obesity Prevention; NAASO, The Obesity Society; and the American Diabetes Association concluded that "*WC provides a unique indicator of body fat distribution, which can identify patients who are at increased risk of obesity-related cardiometabolic diseases, above and beyond the measurement of BMI*".(50) Using a representative sample of adults from United States, Zhu (2004) reported that a combined BMI and WC index, had a stronger association with cardiometabolic risk factors than using BMI or WC index alone for men, with the optimal BMI-WC index composed using the relative weight of 68% BMI and 32% WC.(12) Similarly, Janssen (2005) determined that the combinations of BMI and WC index among 5-18 year olds provided the strongest predictive power for coronary artery disease risk factors.(51)

In our Canadian sample, the prevalence of obesity among children and adolescents, respectively, ranged from 13%-28% and 11%-37%, depending of the obesity index applied. Further, among the three obesity indexes, 'BMI Obese with Abdominal Obesity' defined using the combined BMI-WC index had a significant association with the prevalence of cardiometabolic risk factor(s). These findings support epidemiological approaches in applying the combined BMI-WC index to measure the association between weight status and cardiometabolic diseases. We suggest that further analyses using this combined BMI-WC index be pursued to comprehensively quantify the relationship between this index and

cardiometabolic diseases and other health outcomes. Our results also support the recommendations from the American Society for Clinical Nutrition that, "*the use of BMI-specific WC cut-points may be useful tool to better understanding a patient's health risk and recommend treatment*"(50) as well as the 2006 Canadian Clinical Practice Guidelines on the Management and Prevention of Obesity in Adults and Children that "*Future research should be directed at determining the clinical utility of waist circumference in the identification of health risk among children and youth, independently or in combination with BMI*." (52) Further, as Zhu (2004) noted, calculating combined BMI-WC index requires little additional effort from the clinician once BMI and WC have been measured. (12) Thus, consistent with the aforementioned recommendation, we suggest that both BMI and WC be measured in clinical settings to accurately ascertain a children and adolescent's body weight status and fat distribution (52) and that all patients presenting as BMI overweight or obese or having abdominal obesity should be screened for each cardiometabolic risk factor.

'Metabolically Healthy Obesity' (MHO) is broadly defined as a phenomenon in which a subset of individuals with obesity present at the evaluation with a normal metabolic profile. (53,54) At present, there is ongoing discourse and debate regarding the accuracy and utility of the 'MHO' or 'metabolically normal obese' phenotype and the importance of weight loss to future health outcomes. In a recent study, Fabbrini (2016) found that adults with MHO are resistant to the expected cardiometabolic consequences of excess weight gain. (55) In our study, the prevalence of participants with obesity that did not have cardio-metabolic risk factor vary between 43% to 54% in children and 15% to 35% in adolescents, depending of the obesity index. In a previous study among 8-17 year olds with overweight or obesity (BMI $\geq 85^{th}$) enrolled in a weight

management clinic in Canada, Prince (2014) reported a prevalence of MHO of 21.5% and 31.5%, defining MHO using dichotomous definitions of cardiometabolic risk factors or insulin resistance, respectively.(7) Studies of female adults with obesity have shown that those with MHO have significantly lower levels of abdominal fat, suggesting that the distribution of body fat may influence the overall impact of excess body fat on health.(56,57) Yet, despite reports of the prevalence of MHO and potential explanations, studies regarding the relationship between weight status and the metabolic syndrome among children and adolescents consistently reporting that the prevalence of metabolic syndrome increased significantly with increasing weight status.(27,58) Some researchers posit that the MHO phenotype is a preliminary step towards the inevitable transition to unhealthy obesity during one's lifetime. Following a systemic review of the emerging MHO phenotype and its association with mortality, Robertson (2014) concluded that this phenotype in adults presents a risk for cardiovascular disease that is lower than metabolically unhealthy obesity but greater than the risk for healthy individuals with a normal weight.(59) The results of our study, even if cross-sectional, contribute to this discourse by illustrating a lower prevalence of MHO phenotype in adolescents than in children. These findings are consistent with existing evidence that the effects of excess adiposity on health may simply take years to present.(60,61)

Robertson (2014) posits also that healthy behavioural and lifestyle factors, notably regular physical activity, may help to explain the absence or slower progression of cardiometabolic risk factor(s) among people with obesity.(59) Substantial evidence indicates that regular physical activity and moderate fitness levels are associated with a lower total and abdominal adiposity, independently of BMI.(62,63) Regardless of weight status, physical inactivity and smoking are

well-established risk factors for poor health outcomes, including cardiovascular diseases. (64) Blair and colleagues has repeatedly shown that adults with even moderate levels of cardiorespiratory fitness have a statistically significant lower mortality rate, even in the presence of risk factors for cardiovascular diseases, such as smoking or elevated BP. (65,66) An inverse relationship physical activity, as well as cardiorespiratory fitness, and the presence of cardiometabolic risk factors has been demonstrated among children and adolescent populations. (67,68)

Yet, despite this overwhelming evidence, only 5% of participants in our sample met the Canadian physical activity guidelines and over 10% of adolescents reported some degree of smoking in our study. Non-adherence to the physical activity guidelines was a significant predictor for cardio-metabolic risk. Given the low adherence to the guidelines, we chose to study average daily physical activity as well. We found that participants who were physically active for less than thirty minutes on most days were significantly more likely to have cardio-metabolic risk, as compared to those who were active for thirty minutes to over an hour. Overall, our findings suggest that, though adherence to the physical guidelines would be ideal, even levels that accord with approximately half the recommended level of activity are associated with reduced cardiometabolic risk.

Disadvantaged SES tend to be associated with unhealthy behaviours, such as smoking, and reduced health outcomes. (69) In our study, the household education and income adequacy variables were not significant predictors for the prevalence of cardiometabolic risk factors, although previous studies in Canada and the United States have found varying associations between SES and some individual cardiometabolic risk factors. (6,19) Our approach to apply a

dichotomous cardiometabolic risk factor(s) variable may have impacted the non-significant SES findings due to varying relationships between SES and each cardiometabolic risk factor(s).

Future national studies regarding cardiometabolic risk factor(s) among youth would be well served to pursue more detailed analyses by combining more cycles of the CHMS as the data becomes available. This may allow for more specific disaggregation by age and sex, and a more in-depth analysis of the associations between SES and health behaviours, risks and outcomes. The effect of diet and puberty were not considered for this study due to data limitations but would also be valuable factors to examine. Finally, performing data linkages between national surveys and administrative data would be invaluable towards assessing the health care impacts (e.g. use and cost) relative to the different obesity index.

This study was conducted using government survey data that is of high quality and representative of 96% of Canadians. Abdominal obesity was defined using age- and sex-specific WC cut-offs established from the Canadian population from the time period prior to emerging of a rapid increase in overweight and obesity rates. (40,70) The CHMS is a cross-sectional survey, thus interpretation of results does not allow for causal inference. With an overall response rate between 51-55% per CHMS cycle, the survey results may have some bias due to selective participation by selected respondents even with the use of survey weights. Finally, as the accelerometer is unable capture such as activities as bicycling and swimming, the prevalence of children and adolescents adhering to Canadian physical activity guidelines may be underreported. (71)

CONCLUSIONS

Based on the CHMS, we found that 25% of children and 40% of adolescents have at least one cardiometabolic risk factor, 12% have obesity and over 95% do not achieve the Canadian physical activity guidelines of 60 minutes of moderate-to-vigorous physical activity at least 6 days per week. Our novel Combined BMI-WC index of obesity had a higher association with cardiometabolic risk factors as compared to BMI or WC index measured individually, a finding which warrants further investigation into the epidemiological and clinical utility of this index. Clinical guidelines should be develop to ensure that children and adolescents with BMI or WC index at risk of presenting a cardiometabolic risk factor be properly screened and monitored. Complementary policies to facilitate increased daily physical activity among children and their families would support long-term health outcomes improvement among Canada's youth.

ACKNOWLEDGEMENTS

We are grateful to Statistics Canada for conducting the Canadian Health Measures Survey and to the people of Canada who participated in the study.

There were no competing interests.

We acknowledge the support of the School of Epidemiology, Public Health and Preventive Medicine in the Faculty of Medicine with University of Ottawa and the Public Health Agency of Canada.

Table 1: Study population socio-demographic, weight status and cardio-metabolic profiles, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013)

	Total Sample (n=2679)		Children (6-11 years) (n=1369)		Adolescents (12-18 years) (n=1310)		
Socio-Demographic Profile							
	n	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**p***
Household Income Adequacy							
Lower-Middle	2619	23.7 (20.3-27.1)	1355	25.6 (21.2-30.0)	1264	22.3 (18.6-26.1)	0.21
Upper-Middle		26.4 (23.1-29.7)		27.4 (22.3-32.4)		25.7 (22.675-28.8)	
Highest		49.9 (45.4-54.4)		47.1 (41.6-52.6)		52.0 (47.0-57.0)	
Household Educational Attainment							
Secondary Graduation or Less	2599	17.5 (14.3-20.7)	1333	15.4 (12.3-18.6)	1266	19.0 (14.6-23.5)	<0.05
Post-secondary		82.5 (79.3-85.7)		84.6 (81.4-87.7)		81.0 (76.5-85.4)	
Ethnic Origin							
Aboriginal	2565	4.5 (3.0-6.0)	1321	3.4 (1.9-4.9)[R]	1244	5.4 (3.4-7.3)[R]	0.26
Immigrant	2679	11.9 (8.0-15.9)	1369	10.6 (7.3-13.9)	1310	12.9 (7.6-18.2)[R]	0.28
Weight Status Profile							
	n	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**p**
Body Mass Index (BMI)							
Underweight (BMI<5th)	2679	4.5 (3.1-6.0)	1369	5.6 (3.5-7.8)[R]	1310	3.7 (2.0-5.4)R	<0.05
Normal weight (5th≤BMI<85th)		68.0 (64.7-71.2)		69.9 (66.4-73.5)		66.5 (62.3-70.8)	
Overweight (85th≤BMI<95th)		15.3 (13.0-17.5)		13.7 (10.8-16.5)		16.4 (13.0-19.8)	
Obese (BMI≥95th)		12.3 (10.3-14.3)		10.8 (8.2-13.3)		13.3 (9.7-17.0)	
Waist Circumference (WC)							
No Abdominal Obesity (WC<90th)	2679	65.7 (62.5-69.0)	1369	73.8 (70.0-77.6)	1310	59.8 (55.4-64.3)	<0.0001
Abdominal Obesity (WC≥90th)		34.2 (31.0-37.5)		26.2 (22.4-30.0)		40.0 (35.7-44.6)	
Combined BMI-WC Index							
Normal weight (BMI<85th and WC<90th)	2613	64.9 (61.4-68.3)	1321	72.8 (68.9-76.7	1291	59.3 (54.8-63.8)	<0.0001
BMI Normal with Abdominal Obesity (BMI<85th and WC≥90th)		8.9 (7.6-11.0)		5.7 (4.1-7.2)		11.9 (9.1-14.7)	
BMI Overweight with Abdominal Obesity (85th≤BMI<95th and WC≥90th)		13.4 (11.1-15.7)		10.7 (8.0-13.3		15.3 (11.9-18.8)	
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)		12.4 (10.3-14.5)		10.8 (8.2013.5		13.4 (9.8-17.1)	
Risk Profile							
	n	**% Adverse (95% CI)**	**n**	**% Adverse (95% CI)**	**n**	**% Adverse (95% CI)**	
Canadian Physical Activity Guidelines (2003) < 60 mins MVPA/6 days/week	1919	95.2 (93.4-97.0)	1007	93.5(91.1-96.0)	912	96.5 (94.7-98.2)	<0.05
Canadian 24 Hour Movement Guidelines (2016) <60 mins MVPA/day	1919	60.5 (56.1-64.9)	1007	53.7 (47.6-59.8)	912	66.4 (61.8-71.1)	<0.05
Sleep per 24 hrs (hrs)	2679	24.5 (21.3-27.6)	1369	15.5 (12.1-18.9)	1310	31.0 (26.8-35.3)	<0.0001
Ever Smoked	-----	----------	-------	-------	1292	12.3 (9.4-15.1)	-----
Fasting Triglycerides (mmol/L)	2679	16.2 (13.7-18.7)	1369	12.2 (9.7-14.6)	1310	19.1 (15.3-23.0)	<0.0001
Low HDL-C (mmol/L)	2679	15.8 (14.1-17.6)	1369	8.1 (5.7-10.4)	1310	21.5 (18.8-24.2)	<0.0001
Fasting Glucose (mmol/L)	2679	2.5 (1.6-3.5)[R]	1361	1.6 (0.65-2.5)[R]	1308	3.2 (1.1-4.7)[R]	<0.01
Elevated Blood Pressure (mm Hg)	2679	2.5 (1.8-3.2)	1369	4.1 (2.7-5.5)	1310	1.3 (0.5-2.1)[R]	<0.0001
Insulin resistance	2495	16.3 (13.7-18.9)	1229	9.2 (6.5-11.9)	1266	21.1 (21.116.7-25.6)	<0.0001
Cardio-metabolic risk	2679	34.1 (30.9-37.4)	1369	25.0 (21.4-28.6)	1310	40.9 (36.1-45.7)	<0.0001

Notes:

- Based on weighted data
- *P value denotes the statistical significance between children and adolescents
- R: Published with Reservation due to a 16.6<CV≤33.3, estimate must be interpreted with caution
- Abbreviations: HDL-C, high density lipoprotein cholesterol; WC, waist circumference; TG, triglycerides; BMI, Body Mass Index; CI, Confidence Interval; MVPA, Moderate to Vigorous Physical Activity

Tables 2: Tabular Analysis between Participants with Cardio-Metabolic Risk by Indicator of Obesity and by Adherence to Physical Activity Guidelines, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013)

	Participants with Cardio-Metabolic Risk					
	Total Sample		Children (6-11 years)		Adolescents (12-18 years)	
Proportion with cardio-metabolic risk by Indicators of Obesity						
	% (95% CI)	**P value**	**% (95% CI)**	**P value**	**% (95% CI)**	**P value**
Body Mass Index (BMI)						
Underweight or Normal weight (BMI<85th)	24.1 (20.9-27.3)	<0.0001	17.9 (14.4-21.5)	<.0001	29.0 (24.0-33.9)	<.0001
Overweight (85th≤BMI<95th)	51.5 (43.6-58.7)		41.9 (30.0-53.7)		56.8 (46.2-67.4)	
Obese (BMI≥95th)	72.5 (66.0-78.9)		53.0 (42.3063.7		84.0 (76.4-91.6)	
Waist Circumference (WC)						
No Abdominal Obesity (WC<90th)	22.0 (19.2-24.9)	<0.0001	17.9 (14.6-21.2)	<.0001	25.8 (21.5-30.1)	<.0001
Abdominal Obesity (WC≥90th)	57.4 (52.4-62.4)		45.0 (36.1-54.0)		63.3 (57.1-69.6)	
Combined BMI-WC Index						
Normal weight (BMI<85th and WC<90th)	21.4 (18.1-24.1)	<0.0001	16.3 (12.7-19.9)	<0.0001	25.4 (21.0-29.7)	<0.0001
BMI Normal and Abdominal Obesity (BMI<85th and WC≥90th)	44.9 (32.3-57.5)		38.8 (23.5-54.0)R		46.9 (32.8-61.1)	
BMI Overweight and Abdominal Obesity (85th≤BMI<95th and WC≥90th)	51.5 (42.4-60.7)		39.6 (26.1-53.1)R		57.5 (46.3-68.7)	
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)	73.3 (66.7-80.0)		53.7 (42.6-64.7)		84.5 (76.7-92.3)	
Proportion with cardio-metabolic risk by Physical Activity levels						
	% (95% CI)	**P value**	**% (95% CI)**	**P value**	**% (95% CI)**	**P value**
Adherence to Canadian Physical Activity (PA) Guidelines						
Meet PA Guidelines (6-17 years≥60 min/day; 18 years≥30 mins/day)	11.1 (5.4-16.8)R	<0.0001	6.3 (1.7-10.7)F	<0.0001	17.8 (5.8-30.0)R	<0.0001
Do not meet PA Guidelines (6-17 year<60 min/day; 18 years<30 mins/day)	34.9 (31.6-38.2)		30.0 (21.6-30.3)		41.6 (36.3-46.9)	
Average daily Moderate-to-Vigorous Physical Activity as per Canadian 24 Hour Movement Guidelines						
60 or more minutes/day	24.0	<0.0001	16.6	0.0004	33.0	0.0105
30- 59 minutes/day	34.7		31.2		37.2	
Less than 30mins/day	48.6		32.6		54.1	

Notes:

- Based on weighted data
- R: Published with Reservation due to a 16.6<CV≤33.3, estimate must be interpreted with caution
- F: Estimate is not valid and cannot be published due to CV>33.3 or a cell size<10
- Adherence to Physical Activity Guidelines: Ages 6-17 years ≥60 min/day at least 6 days/week; 18 years≥30 mins/day at least 5 days per week)
- Abbreviations: WC, waist circumference; BMI, Body Mass Index; CI, Confidence Interval; MVPA, Moderate to Vigorous Physical Activity; PA, Physical Activity;

Table 3: Odds Ratio of cardio-metabolic risk based on univariate models of obesity index, physical activity and age

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age						
Children	1.0 (Ref)					
Adolescents	2.1 (1.5-2.9)*					
Body Mass Index (BMI)						
Under or Normal weight (BMI<85th)		1.0 (Ref)				
Overweight (85th≤BMI<95th)		3.9 (2.7-5.5)*				
Obese (BMI≥95th)		7.0 (5.0-10.0)*				
Waist Circumference (WC)						
No Abdominal Obesity (WC<90th)			1.0 (Ref)			
Abdominal Obesity (WC≥90th)			4.6 (3.5-6.0)*			
Combined BMI-WC Index						
Normal weight (BMI<85th and WC<90th)				1.0 (Ref)		
BMI Normal with Abdominal Obesity (BMI<85th and WC≥90th)				2.9 (1.6-5.1)*		
BMI Overweight with Abdominal Obesity (85th≤BMI<95th and C≥90th)				4.6 (3.1-6.7)*		
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)				8.5 (6.1-11.9)*		
Average daily Moderate-to-Vigorous Physical Activity as per Canadian 24 Hour Movement Guidelines						
60 or more minutes/day					1.0 (Ref)	
30- 59 minutes/day					1.7 (1.14-2.50)*	
Less than 30mins/day					3.0 (1.9-4.9)*	
Adherence to Canadian Physical Activity Guidelines						
Meet PA Guidelines						1.0 (Ref)
Do not meet PA Guidelines						4.3 (2.3-8.0)*

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; OR, Odds Ratio; SE, Standard Error; MVPA, Moderate to Vigorous Physical Activity; PA, Physical Activity; Ref, Reference Category; WC, waist circumference;
- * Statistically significant at $p < 0.0001$
- For each model, the reference for the weight status variable was normal weight
- Do not meet Physical Activity Guidelines referred to: 6-17 year<60 min/day; 18 years<30 mins/day)
- The following variables were not significant in any of the regression models: sex, household Income, household education, Aboriginal origin or identity, immigrant status, sleep or smoking (among adolescents only)

Table 4: Odds Ratio of cardio-metabolic risk based on multivariate models of obesity index, physical activity and age

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8	Model 9
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age									
Children	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Adolescents	2.3 (1.7-3.2) [a]	1.9 (1.4-2.7) [a]	2.2 (1.6-3.1) [a]	2.1 (1.5-2.8) [a]	1.7 (1.2-2.4) [b]	2.0 (1.4-2.8) [a]	2.3 (1.7-3.1) [a]	1.9 (1.4-2.6) [a]	2.2 (1.6-3.0) [a]
Body Mass Index (BMI)									
Under or Normal weight (BMI<85th)	1.0 (Ref)			1.0 (Ref)			1.0 (Ref)		
Overweight (85th≤BMI<95th)	4.1 (2.9-5.8) [a]			3.9 (2.9-5.4) [a]			4.3 (3.0-6.0) [a]		
Obese (BMI≥95th)	7.5 (5.0-10.7) [a]			7.1 (4.9-10.2) [a]			8.1 (5.8-11.4) [a]		
Waist Circumference (WC)									
No Abdominal Obesity WC<90th)		1.0 (Ref)			1.0 (Ref)			1.0 (Ref)	
Abdominal Obesity (WC≥90th)		4.6 (3.5-6.0) [a]			4.1 (3.1-5.5) [a]			4.7 (3.5-6.2) [a]	
Combined BMI-WC Index									
Normal weight			1.0 (Ref)			1.0 (Ref)			1.0 (Ref)
BMI Normal with Abdominal Obesity			2.9 (1.6-5.1) [b]			2.2 (1.2-4.1) [b]			2.52 (1.4-4.5) [b]
BMI Overweight with Abdominal Obesity			4.6 (3.2-6.7) [a]			4.3 (3.1-6.1) [a]			4.8 (3.3-7.1) [a]
BMI Obese with Abdominal Obesity			8.5 (6.1-11.9) [a]			8.3 (5.8-11.9) [a]			9.6 (6.9-13.3) [a]
Average daily Moderate-to-Vigorous Physical Activity as per Canadian 24 Hour Movement Guidelines									
60 or more minutes/day				1.0 (Ref)	1.0 (Ref)	1.0 (Ref)			
30-59 minutes/day				1.4 (0.9-2.1)	1.4 (1.0-2.1)	1.3 (0.9-2.0)			
Less than 30mins/day				2.2 (1.3-3.5) [b]	2.0 (1.2-3.4) [b]	2.0 (1.2-3.3) [b]			
Adherence to Canadian Physical Activity Guidelines									
Meet PA Guidelines							1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Do not meet PA Guidelines							6.2 (2.4-16.6) [b]	5.0 (2.2-11.1) [a]	5.8 (2.2-15.2) [b]

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; OR, Odds Ratio; SE, Standard Error; MVPA, Moderate to Vigorous Physical Activity; PA, Physical Activity; Ref, Reference Category; WC, waist circumference;
- [a] Statistically significant at $p < 0.0001$; [b] Statistically significant at $p < 0.05$
- For each model, the reference for the weight status variable was normal weight
- Do not meet Physical Activity Guidelines referred to: 6-17 year<60 min/day; 18 years<30 mins/day)
- Combined BMI-WC Index categories: Normal weight (BMI<85th and WC<90th); BMI Normal with Abdominal Obesity (BMI<85th and WC≥90th); BMI Overweight with Abdominal Obesity (85th≤BMI<95th and WC≥90th); and BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)
- The following variables were not significant in any of the regression models: sex, household Income, household education, Abo riginal origin or identity, immigrant status, sleep or smoking (among adolescents only)

REFERENCES

1. Cardiometabolic Risk Working Group: Executive Committee, Leiter LA, Fitchett DH, Gilbert RE, Gupta M, Mancini GBJ, et al. Cardiometabolic risk in Canada: a detailed analysis and position paper by the cardiometabolic risk working group. Can J Cardiol. 2011 Apr;27(2):e1–33.

2. Deprès J. The Insulin Resistance-Dyslipidemic Syndrome of Visceral Obesity: Effect on Patients' Risk. Obesity. 1998 Apr;6(S1):8S–17S.

3. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report - NHLBI, NIH. Pediatrics. 2011 Dec;128(5):s213-56.

4. Blüher S, Molz E, Wiegand S, Otto K-P, Sergeyev E, Tuschy S, et al. Body mass index, waist wircumference, and waist-to-height ratio as predictors of cardiometabolic risk in childhood obesity depending on pubertal development. J Clin Endocrinol Metab. 2013 Aug;98(8):3384–93.

5. Staiano AE, Gupta AK, Katzmarzyk PT. Cardiometabolic risk factors and fat distribution in children and adolescents. J Pediatr. 2014 Mar;164(3):560–5.

6. Camhi SM, Katzmarzyk PT. Prevalence of cardiometabolic risk factor clustering and body mass index in adolescents. J Pediatr. 2011 Aug;159(2):303–7.

7. Prince RL, Kuk JL, Ambler KA, Dhaliwal J, Ball GDC. Predictors of metabolically healthy obesity in children. Diabetes Care. 2014 May;37(5):1462–8.

8. Maximova K, Kuhle S, Davidson Z, Fung C, Veugelers PJ. Cardiovascular risk-factor profiles of normal and overweight children and adolescents: insights from the Canadian Health Measures Survey. Can J Cardiol. 2013 Aug;29(8):976–82.

9. Lambert M, Delvin EE, Levy E, O'Loughlin J, Paradis G, Barnett T, et al. Prevalence of cardiometabolic risk factors by weight status in a population-based sample of Quebec children and adolescents. Can J Cardiol. 2008 Jul;24(7):575–83.

10. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. Am J Clin Nutr. 2004 Mar 1;79(3):379–84.

11. Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord. 2000 Nov;24(11):1453–8.

12. Zhu S, Heshka S, Wang Z, Shen W, Allison DB, Ross R, et al. Combination of BMI and waist circumference for identifying cardiovascular risk factors in whites. Obes Res. 2004 Apr 1;12(4):633–45.

13. Center for Chronic Disease Prevention and Control, Division of Nutrition, Physical Activity and Obesity, National Center for Chronic Disease Prevention and Promotion. Facts about Physical Activity [Internet]. 2014 [cited 2016 Mar 9]. Available from: http://www.cdc.gov/physicalactivity/data/facts.htm

14. Craig CL, Russell SJ, Cameron C, Bauman A. Twenty-year Trends in Physical Activity Among Canadian Adults. Can J Public Health Rev Can Santee Publique. 2004;95(1):59–63.

15. Physicians for a smoke free Canada. Smoking in Canada [Internet]. 2005 [cited 2016 Mar 9]. Available from: http://www.smoke-free.ca/pdf_1/SmokinginCanada-2005.pdf

16. Ali M, Bullard K, Beckles G, Stevens M, Barker L, Narayan K, et al. Household income and cardiovascular disease risks in U.S. children and young adults: Analyses from NHANES 1999-2008. Diabetes Care. 2011;34(9):1998–2004.

17. Batty GD, Leon DA. Socio-economic position and coronary heart disease risk factors in children and young people. Evidence from UK epidemiological studies. Eur J Public Health. 2002 Dec;12(4):263–72.

18. Loucks EB, Magnusson KT, Cook S, Rehkopf DH, Ford ES, Berkman LF. Socioeconomic Position and the Metabolic Syndrome in Early, Middle, and Late Life: Evidence from NHANES 1999-2002. Ann Epidemiol. 2007;17(10):782–90.

19. Shi Y, de Groh M, Bancej C. Socioeconomic gradients in cardiovascular risk in Canadian children and adolescents. Health Promot Chronic Dis Prev Can. 2016 Feb;36(2).

20. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1 [Internet]. Statistics Canada; 2014 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.htm

21. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 2 [Internet]. Statistics Canada; 2013 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V2-eng.htm

22. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 3 [Internet]. Statistics Canada; 2014 Sep. Available from: http://www23.statcan.gc.ca:81/imdb/p2SV.pl?Function=getSurvey&SDDS=5071&lang=en&db=imdb&adm=8&dis=2

23. Tremblay MS, Gorber SC. Canadian Health Measures Survey: brief overview. Can J Public Heal Can Santee Publique. 2007 Nov;98(6):453–456.

24. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics. 2004 Aug 1;114(Supplement 2):555–76.

25. American Academy of Pediatrics. National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992 Mar;89(3 Pt 2):525–84.

26. Genuth S, Alberti KGMM, Bennett P, Buse J, DeFronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 2003 Nov 1;26(11):3160–8.

27. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med. 2003 Aug;157(8):821–7.

28. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005 Apr 1;115(4):e500–3.

29. Daskalopoulou S, Rabi D, Zarnke K, et al. The 2015 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2015 May;31(5):549–68.

30. Canadian Society for Exercise Physiology. 2003. Canadian Physical Activity, Fitness and Lifestyle Approach (CPAFLA). 3rd edition. Ottawa.

31. Canadian Physical Activity Guidelines for Adults - 18-64 years [Internet]. Canadian Society for Exercise Physiology; 2011 [cited 2016 Nov 6]. Available from: http://csep.ca/CMFiles/Guidelines/CSEP_PAGuidelines_adults_en.pdf

32. Hirshkowitz M, Whiton K, Albert S, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health. 2015 Dec;1(4):233–42.

33. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health - Final Report of the Commission on Social Determinants of Health [Internet]. Geneva, Switzerland.: World Health Organization | Commission on Social Determinants of Health; 2008 [cited 2016 Mar 9]. Available from: http://www.who.int/social_determinants/thecommission/finalreport/en/

34. Winkleby MA, Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. Am J Public Health. 1992 Jun 1;82(6):816–20.

35. Duncan GJ, Daly MC, McDonough P, Williams DR. Optimal Indicators of Socioeconomic Status for Health Research. Am J Public Health. 2002 Jul;92(7):1151–7.

36. Centers for Disease Control and Prevention, US Department of Health and Human Services. Clinical Growth Charts [Internet]. 2009. Available from: http://www.cdc.gov/growthcharts/clinical_charts.htm

37. World Health Organization. WHO: Global Database on Body Mass Index; The International Classification of adult underweight, overweight and obesity according to BMI [Internet]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

38. Canadian Guidelines for Body Weight Classification in Adults [Internet]. [cited 2016 Mar 9]. Available from: http://preventdisease.com/pdf/weight_book-livres_des_poids_e.pdf

39. Patry-Parisien J, Shields M, Bryan S. Comparison of waist circumference using the World Health Organization and National Institutes of Health protocols. Health Rep. 2012 Sep;23(3):56–63.

40. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11-18y of age. Eur J Clin Nutr. 2004 Jul;58(7):1011–5.

41. MacPherson M, de Groh M, Wall R, Prud'Homme D, Jiang X, Dubois L. Establishing waist circumference percentiles for Canadian Children 6-10 years using reference data from the 1981 Canada Fitness Survey, the CHMS Cycles 1-3, and NHANES 1998-1994. [Publication pending].

42. Efron B, Tibshirani R: Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. Statist Sci 1986, 1:54–75. [Internet]. [cited 2016 Mar 9]. Available from: http://matthieuchemin-research.mcgill.ca/ECON742/paper/efron.pdf

43. Must A, Anderson S. Pediatratic mini review. Body mass index in children and adolescents: considerations for population-based applications. Int J Obes. 2006;30:590–4.

44. Albanese C, Diessel E, Genant H. Clinical applications of body composition measurements using DXA. J Clin Densitom. 2003;6(2):75–85.

45. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. J Pediatr. 1998 Feb;132(2):204–10.

46. Steinberger J, Jacobs DR, Raatz S, Moran A, Hong C-P, Sinaiko AR. Comparison of body fatness measurements by BMI and skinfolds vs dual energy X-ray absorptiometry and their relation to cardiovascular risk factors in adolescents. Int J Obes. 2005 Nov 1;29(11):1346–52.

47. Garn SM, Leonard WR, Hawthorne VM. Three limitations of the body mass index. Am J Clin Nutr. 1986 Dec;44(6):996–7.

48. Pouliot MC, Després JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol. 1994 Mar 1;73(7):460–8.

49. Taylor RW, Jones IE, Williams SM, Goulding A. Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3–19 y. Am J Clin Nutr. 2000 Aug 1;72(2):490–5.

50. Klein S, Allison DB, Heymsfield SB, Kelley DE, Leibel RL, Nonas C, et al. Waist Circumference and Cardiometabolic Risk: a Consensus Statement from Shaping America's Health: Association for Weight Management and Obesity Prevention; NAASO, the Obesity Society; the American Society for Nutrition; and the American Diabetes Association. Obes Silver Spring Md. 2007 May;15(5):1061–7.

51. Janssen I, Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, et al. Combined influence of body mass index and waist circumference on Coronary Artery Disease risk factors among children and adolescents. Pediatrics. 2005 Jun 1;115(6):1623–30.

52. Lau DCW, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E, et al. Ths [summary]. Can Med Assoc J. 2007 Apr 10;176(8):S1–13.

53. Blüher M. The distinction of metabolically "healthy" from "unhealthy" obese individuals. Curr Opin Lipidol. 2010 Feb;21(1):38–43.

54. Karelis AD, St-Pierre DH, Conus F, Rabasa-Lhoret R, Poehlman ET. Metabolic and body composition factors in subgroups of obesity: what do we know? J Clin Endocrinol Metab. 2004 Jun;89(6):2569–75.

55. Fabbrini E, Yoshino J, Yoshino M, Magkos F, Tiemann Luecking C, Samovski D, et al. Metabolically normal obese people are protected from adverse effects following weight gain. J Clin Invest. 2015 Feb;125(2):787–95.

56. Karelis AD, Faraj M, Bastard J-P, St-Pierre DH, Brochu M, Prud'homme D, et al. The metabolically healthy but obese individual presents a favorable inflammation profile. J Clin Endocrinol Metab. 2005 Jul;90(7):4145–50.

57. Brochu M, Mathieu ME, Karelis AD, Doucet E, Lavoie ME, Garrel D, et al. Contribution of the lean body mass to insulin resistance in postmenopausal women with visceral obesity: a Monet study. Obesity. 2008;16(5):1085–93.

58. Weiss R, Dziura J, Burgert T, Tamborlane W, Taksali S, Yeckel C, et al. Obesity and the Metabolic Syndrome in Children and Adolescents — NEJM. N Engl J Med. 2004 Jun 3;350:2362–74.

59. Roberson LL, Aneni EC, Maziak W, Agatston A, Feldman T, Rouseff M, et al. Beyond BMI: The "Metabolically healthy obese" phenotype & its association with clinical/subclinical cardiovascular disease and all-cause mortality -- a systematic review. BMC Public Health. 2014;14:14.

60. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies: Healthy obesity and diabetes. Obes Rev. 2014 Jun;15(6):504–15.

61. Appleton SL, Seaborn CJ, Visvanathan R, Hill CL, Gill TK, Taylor AW, et al. Diabetes and Cardiovascular Disease Outcomes in the Metabolically Healthy Obese Phenotype: A cohort study. Diabetes Care. 2013 Aug 1;36(8):2388–94.

62. Janssen I, Katzmarzyk PT, Ross R, Leon AS, Skinner JS, Rao DC, et al. Fitness alters the associations of BMI and waist circumference with total and abdominal fat. Obes Res. 2004 Mar;12(3):525–37.

63. Janiszewski PM, Ross R. Physical activity in the treatment of obesity: beyond body weight reduction. Appl Physiol Nutr Metab Physiol Appliquée Nutr Métabolisme. 2007 Jun;32(3):512–22.

64. World Health Organization. WHO Global Status Report on Non-Communicable Disease. 2014. [Internet]. [cited 2016 Mar 16]. Available from: http://apps.who.int/iris/bitstream/10665/44399/1/9789241599979_eng.pdf

65. Blair SN, Kohl III HW, Paffenbarger R, Clark D, Cooper K, Gibbons L. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA. 1989 Nov 3;262(17):2395–401.

66. Blair SN, Kampert J, Kohl III HW, Barlow C, Macera C, Paffenbarger R, et al. Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. JAMA. 1996 Jul 17;276(3):205–10.

67. Carson V, Janssen I. Volume, patterns, and types of sedentary behavior and cardio-metabolic health in children and adolescents: a cross-sectional study. BMC Public Health. 2011;11:274.

68. Ruiz JR, Ortega FB, Rizzo NS, Villa I, Hurtig-Wennlöf A, Oja L, et al. High cardiovascular fitness is associated with low metabolic risk score in children: the European Youth Heart Study. Pediatr Res. 2007 Mar;61(3):350–5.

69. Pampel FC, Krueger PM, Denney JT. Socioeconomic Disparities in Health Behaviors. Annu Rev Sociol. 2010 Aug;36:349.

70. Tremblay MS, Willms JD. Secular trends in the body mass index of Canadian children. Can Med Assoc J. 2000 Nov 28;163(11):1429–33.

71. Garriguet D, Colley RC. A comparison of self-reported leisuretime physical activity and measured moderate-to-vigorous physical activity in adolescents and adults. Health Rep Stat Can Can Cent Health Inf Rapp Sur Sante Stat Can Cent Can Inf Sur Sante. 2014 Jul 16;25(7):1–11.

5.4. Cardio-metabolic risk, obesity and c-reactive protein among Canadian children and adolescents

Author references: Miranda MacPherson James (1, 2), Margaret de Groh (2), Denis Prud'homme, Lise Dubois (4)

1. Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
2. Social Determinants and Science Integration Directorate, Public Health Agency of Canada, Ottawa, Ontario, Canada
3. Institut de recherche de l'Hôpital Montfort, Ottawa, Ontario, Canada; Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
4. School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

This manuscript will be submitted for publication in January 2017.

ABSTRACT

Introduction: C-reactive protein, a marker of inflammation, is a non-traditional risk factor for cardio-metabolic risk among adults. Our objective was to quantify the association between c-reactive protein and a dichotomous cardio-metabolic risk variable to determine if high CRP was a significant predictor of cardiometabolic risk in a representative sample of Canadian children and adolescents.

Methods: The study population was a nationally representative sample of Canadians (6-18 years) based on Canadian Health Measures Survey Cycles 1 (2007-09), 2 (2009-11) and 3 (2012-13) participants (n=1831). High levels of c-reactive protein were defined as ≥75th age- and sex-specific percentile. Participants were dichotomized as having 'no cardio-metabolic risk' or 'cardio-metabolic risk', defined as the presence of adverse levels of 1 or more risks: fasting triglycerides (≥1.25mmol/L), high-density lipoprotein cholesterol (males and females 6-15 years: <1.03mmol/L; males 16-18 years: <1.03mmol/L; females 16-18 years: <1.3 mmol/L), fasting glucose (≥5.6mmol/L) and/or the presence of diabetes, insulin resistance using the homeostasis model assessment, and elevated blood pressure (6-17 years: age-, sex and height-specific reference data; 18 years: ≥130mm Hg and/or a ≥85 mm HG).

Results: Approximately half of participants with high levels of c-reactive protein, 43.6% of children and 62.0% of adolescents, were classified as having cardio-metabolic risk, significantly higher than those with normal c-reactive protein levels. In univariate models, obesity was a significant predictor for high CRP (Odds Ratio (OR): 2.79-6.65) and high CRP was a significant predictor for cardiometabolic risk (OR: 2.37). In multivariate models adjusting for age and high-CRP, obesity remained a significant predictors for having cardiometabolic risk (OR: 4.27-8.33).

Conclusions: High c-reactive protein concentration, an indicator of inflammation, is a strong, significant predictor for cardiometabolic risk, and significantly associated with obesity among the pediatric population.

Keywords: Canada, Child, Adolescent, Obesity, Canadian Health Measures Survey, CHMS, Health surveys, Cardio-metabolic risk factors, c-reactive protein, inflammation

INTRODUCTION

Rationale

Inflammation is now understood as a critical component of the progression of atherosclerosis, the hardening and narrowing of the arteries.(1,2) In conjunction with behavioural, environmental and genetic risk factors, chronic low grade inflammation can lead to an increased absolute risk of cardiovascular diseases.(2,3) Inflammation is also considered a factor in the pathosis of metabolic abnormalities, such as insulin resistance, diabetes and metabolic syndrome.(4,5)

The concept of cardio-metabolic risk facilitates early recognition of predicted risk for cardiovascular diseases and metabolic abnormalities through a comprehensive list of traditional risk factors, such as hypertension, dyslipidemia, glycemia, excess body fat and smoking.(6) The measurement of inflammation, as a complement to these traditional cardio-metabolic risk factors, may provide an enhanced absolute risk and support an earlier diagnosis for cardiovascular diseases.(2,6)

High-sensitivity c-reactive protein (CRP) is an acute phase reactant that is increased in inflammatory states.(2) In a joint scientific statement, the United States' Centers for Disease Control and Prevention and the American Heart Association recommended CRP be applied in clinical practice as the marker for inflammation as a predictor for cardio-metabolic risk for the purposes of risk stratification in the presence of traditional cardiovascular disease risk factors.(2) Population-level studies regarding inflammatory markers and cardio-metabolic risk among adults in Canada and the United States have found that participants with the Metabolic

Syndrome are significantly more likely to have high levels of CRP.(7,8) While considered a non-traditional marker for cardio-metabolic risk, CRP levels are included in some risk prediction models for cardio-metabolic risk for adults.(6)

National studies of Canadian children and adolescents have found that 18% of participants presented with high CRP levels, with significantly higher mean CRP levels among those with a higher weight status, older participants,(9) and adolescent girls (versus adolescent boys).(10) Similar results have been shown in international studies on children and adolescents, with a positively linear relationship between CRP and age (11), weigh status (12–15), and sedentary behaviours.(16)

Objectives

In a recent analysis, we quantified the relationship between cardio-metabolic risk and obesity and found that the odds of having cardio-metabolic risk was 8.3 times higher among participants with obesity,(17) building on previous studies which show a strong association between obesity and cardio-metabolic risk in children and adolescents.(9,18) In the present study, our primary objective is to quantify the associations between CRP, an inflammatory marker, with a dichotomous cardio-metabolic risk variable, in a representative sample of Canadian children and adolescents, to determine if high CRP is a significant predictor for cardiometabolic risk. We hypothesize a significant association between cardio-metabolic risk and high levels of CRP.

METHODS

Data Source

The CHMS is a comprehensive, nationally-representative survey designed to collect information on the health of Canadians.(19–22) The survey is conducted by Statistics Canada in partnership with Health Canada and the Public Health Agency of Canada. The CHMS consists of an in-home interview, a physical assessment conducted at a mobile examination centre and a laboratory analysis of physical specimens. The interview collects demographic, socio-economic, family history and general health information. The physical assessment includes measures of anthropometry, spirometry, blood pressure, fitness, oral health and biological specimens.(19–22)

The laboratory analysis of blood and urine was performed to calculate estimates of disease and markers for disease, nutrition and environmental toxins.(19–21) For the collection of these physical samples, the CHMS team were instructed to follow the detailed protocols for centrifuging, aliquoting, storage and shipping outlined in the Blood/Urine Processing Procedures Manual for protocols regarding.(40) A phlebotomist collected the blood samples following a standardized venipuncture technique.(19-22) The volume of blood collected increased with increasing age as more laboratory analyses were completed for older participants.(19–21) Following collection, the phlebotomist brought the sample to the lab for processing as soon as possible then stored the sample as appropriate.(19-22) The blood specimens dedicated for CRP measurement were shipped weekly to the Health Canada Laboratory, a federal government laboratory that specializes in the analysis of nutrition and chronic disease markers.(40) For quality control purposes, members of the CHMS laboratory

team would visit the Health Canada laboratory to review the laboratory data for errors.(40) The CHMS sampling frame, data collection process and standardized procedures for obtaining and analyzing blood samples have been precisely described in the CHMS User Guides and peer reviewed journals.(19–23,40)

Study Population

All CHMS respondents aged 6-18 years who provided fasting blood samples for CHMS Cycles 1 (2007-2009), 2 (2009-2011) or 3 (2012-2103) were included (n=2679). Due to missing data for CRP (n=848), resulting from the limited blood volume collected for children and adolescents, the final sample was n=1831. There were no pregnant participants. Sample weights specific to the fasting subgroup were provided by Statistics Canada to ensure appropriate representativeness at the population level. We stratified our analyses by age to examine children (6-11 yrs) and adolescents (12-18 years) separately. We obtained ethics approval for this project from the University of Ottawa's Research Ethics Board.

Measures

Cardio-Metabolic Risk and Inflammatory Marker: We dichotomized participants as having 'no cardio-metabolic risk' or 'cardio-metabolic risk', defined as the presence of adverse levels of one or more of the following cardio-metabolic risk factors: elevated fasting triglycerides (≥1.25mmol/L); low high-density lipoprotein cholesterol (males and females 6-15 years: <1.03mmol/L; males 16-18 years: <1.03mmol/L; females 16-18 years: <1.3 mmol/L); impaired fasting glucose (≥5.6mmol/L) and/or the presence of diabetes; insulin resistance and elevated blood pressure (BP).(6,24–30) Insulin resistance was calculated using the homeostasis model assessment of insulin resistance (fasting insulin concentration (μU/mL) × fasting glucose

concentration (mmol/L)/22.5≥3.16).(30) Regarding BP, for participants aged 6-17 years, elevated BP was defined using age-, sex and height-specific reference data by the National High BP Education Program Working Group on High BP for Children and Adolescents; participants with pre-hypertension were included.(25) Elevated BP among participants aged 18 years were defined as systolic BP≥130mm Hg and/or a diastolic BP≥85 mm HG.(31) Participants who reported taking medication for high BP were also classified as having elevated BP.(30) High serum levels of CRP were defined as≥75th (mg/L) age- and sex-specific percentiles calculated using the study population data.(9)

Socio-Demographic Profile: A participant's demographic and socio-economic profile was assessed by self-report. Parents or guardians responded to questions about their children aged 6-11 years (by proxy) and adolescents (12-17yrs) responded in private, with parental/guardian consent. The children and adolescents were identified as having an Aboriginal origin or identity or being an immigrant by self-report or proxy self-report. Socio-economic status was captured through household income adequacy and educational attainment variables. Statistics Canada calculated income adequacy by classifying each participant into categories based on total household income from all sources and the number of people living in the household for CHMS Cycles 1-2.(19,20) We applied this approach to generate income adequacy for CHMS Cycle 3. Household educational attainment was derived by Statistics Canada as the highest level of education attained by any member of the household. For participants not living with parents or guardians (5.0%), their responses pertained to their current household regardless of their age. To allow for greater statistical power and comparability across CHMS Cycles 1-3, we re-classified the household income adequacy and educational attainment variables. For income

adequacy, the categories of 'lowest income' and 'lower middle income' were combined resulting in three categories for income adequacy (lowest and lower middle income, upper middle and highest). For household educational attainment, the categories of 'less than secondary school graduation' and 'secondary school graduation', as well as 'some post-secondary' and 'post-secondary graduation', were combined resulting in two categories (secondary or less and post-secondary).

Anthropometry: Three indicators of obesity were applied to our study population: Body Mass Index (BMI), Abdominal Obesity and a combination of BMI and abdominal obesity titled 'Combined BMI-Abdominal Obesity'. Statistics Canada derived BMI using measured height and weight (weight (kg)/height (m^2)) and classified BMI using growth charts prepared by the Centers for Disease Control and Prevention for ages 6-17 years and the international body weight classification system recommended by Health Canada and the World Health Organization for ages 18 years.(19–21,32–34) We applied a prediction equation to CHMS Cycles 1 and 2 waist circumference (WC) data (collected following protocol by the World Health Organization) to align it to the CHMS cycle 3 WC data (collected following protocol from the United States' National Institutes of Health).(35) Abdominal obesity was defined as measured WC ≥ 90^{th} age- and sex- specific percentile for ages 11-18 years based on reference data from the 1981 Canada Fitness Survey.(36) For ages 6-10 years, national reference data from the same time period was unavailable. We generated age- and sex- specific reference points using data from the 1981 Canada Fitness Survey and supplemented with trend lines from the CHMS Cycles 1-3 WC measurements (sex- and age- specific 90^{th} percentile reference points). The methodology for this approach to generating reference data is elaborated upon in a separate paper.(37) We

derived the combined BMI-Abdominal Obesity indicator into 4 categories using the following cut-offs: (1) Not Obese (BMI<85th and WC<90th); (2) BMI Overweight or Obese (BMI≥85th and WC<90th)); (3) Abdominal Obesity (BMI<85th and WC≥90th); and (4) BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th). The CHMS User Guides for Cycles 1, 2, and 3 provide more detailed descriptions of the measurement procedures for all variables in this study. (19–21)

Statistical Methods: The prevalence of cardio-metabolic risk as a dichotomous variable, the individual risk factors for cardio-metabolic risk and high levels of CRP were estimated and expressed as a percentage with a 95% confidence interval (CI). We calculated weighted means and standard error for CRP. The associations between cardio-metabolic risk and the inflammatory and metabolic markers were estimated using X^2 tests, independent t-tests, univariate and multivariate regression. Pearson correlation coefficients were calculated to examine the relationship between each individual cardio-metabolic risk factor with CRP. Statistical significance was set at a *p*-value of less than .05. The analyses were conducted using the bootstrap method with 35 degrees of freedom. (19–21,38) Results with 16.6<Coefficient of Variation (CV) ≤33.3 were published with reservation and results with a frequency of <10 or a CV≥33.3 were not included and represented with an F. We conducted statistical analyses using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). Sampling weights were applied to produce weighted estimates that are representative of Canadians 6-18 years

RESULTS

Descriptive

The study population's socio-demographic and cardio-metabolic risk profile is presented in Table 1. Mean levels (±Standard Error (SE)) of CRP were 1.29 ± 0.66 mg/L among children and 1.50 ± 0.076 mg/L among adolescents (data not shown).

A tabular analysis between obesity and high CRP (Table 2) shows a significant positive relationship between weight class and high CRP for all three indicators of obesity. Tables 3 and 4 present tabular analyses between the dichotomous cardio-metabolic risk variable and CRP. Participants with high levels of CRP presented with a significantly higher prevalence of cardio-metabolic risk, with 43.6% of children and 62.0% of adolescents with high levels of CRP classified as having cardio-metabolic risk (Table 3). Mean concentration levels of CRP were significantly higher among participants classified as having cardio-metabolic risk versus participants without cardio-metabolic risk for both children and adolescents (Table 4). Significant correlations were observed between CRP and age, elevated fasting triglycerides, low HDL-C, elevated fasting insulin, presence of insulin resistance, presence of cardio-metabolic risk, obesity (defined by either BMI, waist circumference, or a combination of both measures) (Table 5).

Regression

Logistic regression was applied to verify associations between obesity, CRP and cardio-metabolic risk (Tables 6 and 7). Table 6 presents the univariate associations between high levels of CRP and obesity. The odds of high CRP were significantly greater among participants with obesity for all three indicators of obesity: BMI Obesity (Odds Ratio (OR): 5.77), Abdominal

Obesity (OR: 2.79), and a BMI Obese with Abdominal obesity (OR: 6.65). Table 7 presents the univariate associations between cardiometabolic risk and high CRP. The odds of cardiometabolic risk were significantly greater among participants with high levels of CRP (OR: 2.37)

Table 8 shows the multivariate associations between cardio-metabolic risk, high CRP, obesity and age. In a multivariate models, we found that the age and high-CRP adjusted-odds of having cardio-metabolic risk was significant for all indicators of obesity (BMI Obese OR: 6.70; Abdominal obesity OR: 3.87; and BMI Obese with Abdominal obesity OR: 8.33). Sex and other socio-demographic factors did not significantly affect the association between high CRP, age, obesity and cardio-metabolic risk.

DISCUSSION

Key Findings

Our primary objective was to quantify the association between cardio-metabolic risk, as a dichotomous variable, and CRP, an inflammation marker, in a nationally representative sample of Canadian children and adolescents.

Inspired by Maximova (2011), we similarly chose to define high CRP using ≥75th age- and sex-specific cut-offs establishing using our study population given the absence of established reference data for children and adolescents.(9) Some studies examining high CRP in child populations have also defined high CRP using adult criteria; however evidence suggests that CRP concentrations increase with age.(9,11) Ford and Giles (2003) examined the mean CRP distribution for children and adolescents in United States and found a gradual increase by age, with females 16-19 years having significantly higher mean levels than their males

counterparts.(11) Overall, the authors concluded that the mean CRP levels in pediatric populations are lower than adult populations. In our study, we found that children had significantly lower mean CRP levels than adolescents, with female adolescents having significantly higher mean levels than male adolescents. For females aged 17 and 18 the cut-off for high CRP was 3.000mg/L which correspondents to the adult cut-off.(2)

As expected, participants with high levels of CRP presented with a significantly higher prevalence of cardio-metabolic risk. The age-adjusted odds of having cardio-metabolic risk were 2.37 times higher for participants with high CRP levels. Previous national studies have shown a significant, positive relationship between the number of metabolic syndrome components and CRP for adults in Canada and the United States.(8,7) Notably, the prevalence of participants with high CRP and cardio-metabolic risk was higher among adolescents (62%) than among children (43%). These findings may point to the potentially negative impacts of low-grade inflammation on health over time, although a causal relationship cannot be inferred given the cross-sectional nature of the CHMS data. Yet, these findings are consistent with evidence indicating that precursors for cardio-metabolic diseases, including low-grade inflammation, may begin developing in childhood.(39)

Consistent with previous national and international findings, we found mean CRP levels were significantly higher in overweight or obese participants versus those at a normal body weight.(9,13,14) Further, the individual associations between obesity and cardio-metabolic risk, as well as CRP and cardio-metabolic risk, are both reduced when examined together in multivariate models. Concisely, it is theorized that fat tissue produces cytokines which, in turn,

leads to liver to manufacture CRP.(6) Roh (2007) identified a significant association between high CRP and early subclinical stage atherosclerosis in adolescents with obesity.(14)

The alarming levels of both obesity and high CRP indicate that Canadian children and adolescents are at risk for developing cardio-metabolic disease in their future. From a policy perspective, strategies and interventions to promote and maintain healthy weights are important towards reducing risk for metabolic and cardiovascular diseases. From a clinical perspective, we suggest that CRP adds value in predicting cardio-metabolic risk in conjunction with traditional cardio-metabolic risk factors for pediatric populations. Roh (2007) concluded that serum CRP provides a cost-effective, relative to ultrasound technology, estimate of atherosclerosis.(14) Further, measurement, monitoring and treatment for both traditional and non-traditional risk factors, such as inflammation, are critically important towards addressing and treating cardio-metabolic health. These recommendations are consistent with the recommendations from the Cardiometabolic Risk Working Group in Canada and a joint position statement from the Centers for Disease Control and Prevention (CDC) and the American Heart Association (AHA) that measurement of CRP can contribute to overall cardio-metabolic risk prediction for adults and that pharmacological treatment for high levels of CRP should be initiate to reduce cardio-metabolic risk.(2,6)

Strengths and Limitations

Our study was performed using the Government of Canada's CHMS data, which is of high quality and representative of 96% of Canadians. Our sample population of fasting 6-18 years was missing n=788 data reference points for the CRP variable. This resulted from the limited blood drawn from younger participants (the blood volume drawn increased with increasing

age) and the correspondingly lower blood analyses performed for children and adolescents.(19–21) Using survey weights, 1831 participants is equivalent to 3,568,140 Canadians. Three cycles of CHMS data were also not available for inflammatory markers fibrinogen and homocysteine, although a joint scientific statement from the CDC and AHA recommended CRP as the best marker for inflammation against a number of criteria.(2) It is important to note that elevated levels of inflammation can also be indicative of acute medical issues, such as infections, thus not all elevated CRP scores may be attributable to atherosclerosis.(2) Consequently, the CDC and AHA also recommended that two measures of CRP be taken at least 2 weeks apart to procure more accurate estimations of actual CRP.(2) Given the cross-sectional nature of this survey, the results cannot be interpreted as causal inference.

Future Research

Future studies may build on this work by continuing to establish age-and sex-specific cut-offs for defining high CRP. Prospective studies that measure the implications for low-grade inflammation and weight status in childhood and adolescents on cardio-metabolic risk over a long-term period would be helpful.

CONCLUSIONS

In conclusion, this study presented novel findings regarding the relationships between obesity, low grade inflammation and cardio-metabolic risk in children and adolescents. Overall, we found CRP to be a significant predictor for cardio-metabolic risk for children and adolescents and suggest that CRP is a useful indicator for cardiometabolic risk for the pediatric population.

ACKNOWLEDGEMENTS

We are grateful to Statistics Canada for conducting the Canadian Health Measures Survey and to the people of Canada who participated in the study. There were no competing interests.

We acknowledge the support of the School of Epidemiology, Public Health and Preventive Medicine in the Faculty of Medicine with University of Ottawa and the Public Health Agency of Canada.

TABLES

Table 1: Description of study population – socio-demographic and risk profile, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013)

	Total Sample (n=1831)		Children (6-11 years) (n=863)		Adolescents (12-18 years) (n=968)		
Socio-Demographic Profile							
	n	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	***p****
Household Income Adequacy							
Lower-Middle	1787	23.8 (20.20-27.4)	856	26.7 (21.5-32.0)	931	22.0 (18.3-25.6)	0.12
Upper-Middle		26.0 (22.5-29.5)		25.7 (20.4-30.9)		26.2 (22.5-30.0)	
Highest		50.2 (45.9-54.5)		47.6 (42.2-53.0)		51.8 (46.9-56.7)	
Household Education							
Secondary or Less	1772	17.8 (14.6-21.0)	838	16.9 (13.2-20.66)	934	18.3 (13.8-22.9)	0.58
Post-secondary		82.2 (79.0-85.4)		83.1 (79.4-86.7)		81.7 (77.1-86.3)	
Ethnic Origin							
Aboriginal	1753	5.1 (3.2-7.0)[R]	834	4.0-1.9-6.0)[R]	919	5.8 (3.5-8.1)	0.56
Immigrant	1831	12.7 (8.4-17.0)[R]	863	12.6 (8.4-16.9)[R]	968	12.8 (7.5-18.1)	0.24
Risk Profile							
	n	**% Adverse (95% CI)**	**n**	**% Adverse (95% CI)**	**n**	**% Adverse (95% CI)**	***p****
Obesity indicators							
BMI Obese (BMI≥95th)	1831	15.4 (12.9-17.8)	863	14.1 (10.1-18.0)	968	16.2 (10.0-20.3)	<0.05
Abdominal Obesity (WC≥90th)		41.7 (38.1-45.3		33.1 (27.7-38.4)		46.9 (42.1-51.8)	<0.0001
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)		15.5 (12.9-18.1)		14.3 (10.1-18.3		16.2 (12.1-20.4)	<0.0001
Cardio-metabolic Risk Factors							
Fasting Triglycerides (mmol/L)	1831	18.7 (15.3)	863	15.1 (11.8-18.4)	968	21.0 (16.1-25.8)	0.0095
Low HDL-C (mmol/L)	1831	14.8 (12.6-17.0)	863	11.2 (7.8-14.6)	968	17.0 (14.1-19.7)	<0.0001
Fasting Glucose (mmol/L)	1826	2.5 (1.3-3.7)[R]	860	F	966	2.9 (1.9-4.6)[R]	---------
Elevated Blood Pressure (mm Hg)	1831	2.6 (1.8-3.5)	863	4.8 (3.1-6.5)[R]	968	F	---------
Insulin resistance	1729	19.4 (16.1-22.7)	795	11.8 (8.4-15.1)	934	23.9 (18.7-29.1)	<0.0001
Cardio-metabolic risk	1831	39.2 (34.8-43.7)	863	30.7 (26.0-35.4)	968	44.4 (38.2-50.7)	<0.0001

Notes:

- Based on weighted data
- R: Published with Reservation due to a 16.6<CV≤33.3, estimate must be interpreted with caution
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; HDL-C, high density lipoprotein cholesterol
- **p*-value denotes the statistical significance between children and adolescents

Table 2: Tabular analysis between obesity and high levels of c-reactive protein, Canadian Health Measures Survey Cycles 1 (2007-2009), 2 (2010-2011) and 3 (2012-2013)

	Participants with high CRP		
Indicators of Obesity	**Total % (95% CI) (SE)**	**Children % (95% CI) (SE)**	**Adolescents % (95% CI) (SE)**
BMI			
Underweight or Normal weight (BMI<85th)	18.4 (15.3-21.4) (1.5)	18.4 (14.1-22.7) (2.1)	18.3 (14.0-22.7) (2.1)
Overweight (85th≤BMI<95th)	20.6 (14.5-26.7) (3.0)	28.1 (17.5-38.6) (5.2)^{R}	16.2 (10.4-21.9) (2.8)^{R}
Obese (BMI≥95th)	56.4 (48.6-64.4) (3.9)	48.2 (34.4-62.0) (6.8)	60.9 (51.1-79.7) (4.8)
*p**	<0.0001	<0.0001	<0.0001
Abdominal Obesity			
Normal (WC<90th)	16.6 (13.5-19.8) (1.5)	17.1 (12.9-21.3) (2.1)	16.3 (11.5-21.1) (2.4)
Abdominal Obesity (WC≥90th)	35.6 (29.2-42.3) (3.2)	39.0 (29.3-48.6) (4.8)	34.4 (26.7-42.1) (3.8)
*p**	<0.0001	<0.0001	0.0004
Combined BMI-Abdominal Obesity			
Normal weight (BMI<85th and WC<90th)	16.5 (13.1-19.8) (1.6)	17.4 (13.0-21.8) (2.2)	15.8 (10.8-20.8) (2.5)
BMI Normal and Abdominal Obesity (BMI<85th and WC≥90th)	28.2 (15.8-40.5) (6.1)^{R}	28.1 (13.6-42.6) (7.1)^{R}	28.2 (12.3-44.0) (7.8)^{R}
BMI Overweight and Abdominal Obesity (85th≤BMI<95th and WC≥90th)	21.0 (14.4-27.7) (3.3)^{R}	33.8 (20.0-47.7) (6.9)^{R}	15.1 (9.4-20.9) (2.8)^{R}
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)	56.8 (48.6-64.9) (4.0)	49.2 (35.1-63.3) (7.0)	60.6 (50.8-70.5) (4.9)
*p**	<0.0001	<0.0001	<0.0001

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; SE, Standard Error
- **p*-value denotes the statistical significance between the weight status categories for each of the obesity indicators

Table 3: Tabular analysis between cardio-metabolic risk and c-reactive protein

	Total sample with Cardio-metabolic Risk		Children with Cardio-metabolic Risk		Adolescents with Cardio-metabolic Risk	
	% (95% CI)	*p**	% (95% CI)	*p**	% (95% CI)	*p**
C-reactive protein (mg/L)						
· Normal	34.1 (28.8-39.3)1	<0.0001	26.6 (20.5-32.8)	0.0105	38.7 (31.8-45.5)	0.0003
· High	55.1 (47.4-62.7)		43.4 (33.6-58.2)		62.0 (51.6-72.5)	

Notes:

· Based on weighted data

· Abbreviations: CI, Confidence Interval

· *p** denotes the statistical significance between normal and high levels of c-reactive protein among participants with cardio-metabolic risk

Table 4: Tabular analysis between cardio-metabolic risk and mean levels of c-reactive protein

	Total sample			Children			Adolescents		
	Normal	**Risk**	***p****	**Normal**	**Risk**	***p****	**Normal**	**Risk**	***p****
C-reactive protein (mg/L) Mean ± SE	1.07 ± 0.05	1.97 ± 0.10	<0.0001	1.08 ± 0.08	1.75 ± 0.14	<0.0001	1.05± 0.08	2.11 ± 0.14	<0.0001

Notes:

· Abbreviations: SE, Standard Error; Risk, Cardio-metabolic risk

· *p** denotes the statistical significance of mean c-reactive levels between participants dichotomized as 'normal' or having 'cardio-metabolic risk'

Table 5: Correlations between individual cardio-metabolic risk factors and c-reactive protein

Demography and Cardio-metabolic Risk Factors	Inflammatory Marker	
	n	c-reactive protein (mg/L)
		r
Sex	1831	0.0335
Age	1831	0.0808*
Elevated Blood Pressure	1831	0.0192
Elevated Fasting Triglycerides	1831	0.1417*
Low HDL-C	1831	-0.1207*
Elevated Fasting Glucose	1826	-0.0019
Elevated Fasting Insulin	1733	0.2509*
Insulin Resistance	1733	0.2307*
Cardio-metabolic Risk	1831	0.2013*
BMI Obese	1831	0.2302*
Abdominal Obesity	1831	0.1898*
BMI Obese with Abdominal Obesity	1381	0.2678*

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; HDL-C, high density lipoprotein cholesterol; r, correlation coefficient
- *Significant at $p<0.0001$

Table 6: Odds Ratio of high c-reactive protein based on univariate models of age, sex and obesity, using three indexes of obesity

	Model 1	Model 2	Model 3	Model 4	Model 5
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age					
Children	1.0 (Ref)				
Adolescents	1.03 (0.73-1.44)				
Sex					
Male		1.0 (Ref)			
Female		1.05 (0.76-1.45)			
Body Mass Index (BMI)					
Under or Normal weight (BMI<85th)			1.0 (Ref)		
Overweight (85th≤BMI<95th)			1.16 (0.77-1.73)		
Obese (BMI≥95th)			5.77[a] (9.98-8.38)		
Waist Circumference (WC)					
No Abdominal Obesity (WC<90th)				1.0 (Ref)	
Abdominal Obesity (WC≥90th)				2.79[a] (1.91-4.08)	
Combined BMI-WC Index					
Normal weight (BMI<85th and WC<90th)					1.0 (Ref)
BMI Normal with Abdominal Obesity (BMI<85th and WC≥90th)					1.99 (0.98-4.02)
BMI Overweight with Abdominal Obesity (85th≤BMI<95th and C≥90th)					1.35 (0.82-2.22)
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)					6.65[a] (4.33-10.22)

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; CRP, c-reactive protein (mg/L); OR, Odds Ratio
- [a] Statistically significant at $p < 0.0001$; [b] Statistically significant at $p < 0.05$

Table 7. Odds Ratio of cardiometabolic risk based on univariate models of age and c-reactive protein

	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age			
Children	1.0 (Ref)		
Adolescents	1.81[a] (1.33-2.46)		
Sex			
Male		1.0 (Ref)	
Female		0.92 (0.66-1.22)	
C-reactive protein			
Normal			1.0 (Ref)
High			2.37[a] (1.64-3.43)

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; CRP, c-reactive protein (mg/L); OR, Odds Ratio
- For each model, the reference for the weight status variable was normal weight
- [a] Statistically significant at $p < 0.0001$; [b] Statistically significant at $p < 0.05$

Table 8: Odds Ratios of cardiometabolic risk based on multivariate models of age, c-reactive protein and obesity

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age							
Children	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (ref)
Adolescents	1.84[a] (1.35-2.50)	1.88[a] (1.37-2.56)	1.90[a] (1.38-2.59)	1.56[b] (1.15-2.12)	1.59[b] (1.19-2.17)	1.80[b] (1.30-2.48)	1.83[b] (1.32-2.53)
C-reactive protein							
Normal CRP	1.0 (Ref)		1.0 (Ref)		1.0 (Ref)		1.0 (Ref)
Adverse CRP	2.40[a] (1.67-3.46)		1.68[b] (1.8-2.39)		1.83[b] (1.25-2.69)		1.56[b] (1.07-2.27)
Body Mass Index (BMI)							
Under or Normal weight (BMI<85th)		1.0 (Ref)	1.0 (Ref)				
Overweight (85th≤BMI<95th)		3.11[a] (2.34-4.14)	3.11[a] (2.32-4.17)				
Obese (BMI≥95th)		7.92[a] (5.17-12.14)	6.70[a] (4.35-10.30)				
Waist Circumference (WC)							
No Abdominal Obesity (WC<90th)				1.0 (Ref)	1.0 (Ref)		
Abdominal Obesity (WC≥90th)				4.27[a] (3.41-5.33)	3.87[a] (3.04-4.93)		
Combined BMI-WC Index							
Normal weight (BMI<85th and WC<90th)						1.0 (Ref)	1.0 (Ref)
BMI Normal with Abdominal Obesity (BMI<85th and WC≥90th)						2.44[b] (1.40-4.25)	2.32[b] (1.34-4.02)
BMI Overweight with Abdominal Obesity (85th≤BMI<95th and C≥90th)						3.63[a] (2.63-5.01)	3.58[a] (2.57-5.00)
BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th)						9.74[a] (6.49-14.62)	8.33[a] (5.52-12.58)

Notes:

- Based on weighted data
- Abbreviations: BMI, Body Mass Index; CI, Confidence Interval; CRP, c-reactive protein (mg/L); OR, Odds Ratio
- For each model, the reference for the weight status variable was normal weight
- [a] Statistically significant at $p < 0.0001$; [b] Statistically significant at $p < 0.05$

REFERENCES

1. Wong B, Meredith A, Lin D, McManus B. The Biological Role of Inflammation in Atherosclerosis - Canadian Journal of Cardiology. Can J Cardiol. 2012 Dec;28(6):631–41.

2. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M, et al. Markers of Inflammation and Cardiovascular Disease Application to Clinical and Public Health Practice: A Statement for Healthcare Professionals From the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003 Jan 28;107(3):499–511.

3. Lusis AJ. Atherosclerosis. Nature. 2000 Sep 14;407(6801):233–41.

4. Badawi A, Klip A, Haddad P, Cole DE, Bailo BG, El-Sohemy A, et al. Type 2 diabetes mellitus and inflammation: Prospects for biomarkers of risk and nutritional intervention. Diabetes Metab Syndr Obes Targets Ther. 2010 May 26;3:173–86.

5. Festa A, D'Agostino R, Howard G, Mykkanen L, Tracy RP, Haffner SM. Chronic Subclinical Inflammation as Part of the Insulin Resistance Syndrome : The Insulin Resistance Atherosclerosis Study (IRAS). Circulation. 2000 Jul 4;102(1):42–7.

6. Cardiometabolic Risk Working Group: Executive Committee, Leiter LA, Fitchett DH, Gilbert RE, Gupta M, Mancini GBJ, et al. Cardiometabolic risk in Canada: a detailed analysis and position paper by the cardiometabolic risk working group. Can J Cardiol. 2011 Apr;27(2):e1–33.

7. Ford ES. The metabolic syndrome and C-reactive protein, fibrinogen, and leukocyte count: findings from the Third National Health and Nutrition Examination Survey. Atherosclerosis. 2003 Jun;168(2):351–8.

8. Brenner D, Arora P, Garcia-Bailo B, Morrison H, El-Sohemy A, Karmali M, et al. The Relationship between Metabolic Syndrome and Markers of Cardiometabolic Disease among Canadian Adults. J Diabetes Metab. 2011 Dec;s2.

9. Maximova K, Kuhle S, Davidson Z, Fung C, Veugelers PJ. Cardiovascular risk-factor profiles of normal and overweight children and adolescents: insights from the Canadian Health Measures Survey. Can J Cardiol. 2013 Aug;29(8):976–82.

10. Shi Y, de Groh M, Bancej C. Socioeconomic gradients in cardiovascular risk in Canadian children and adolescents - Health Promotion and Chronic Disease Prevention in Canada: Research, Policy and Practice - Public Health Agency of Canada. Health Promot Chronic Dis Prev Can [Internet]. 2016 Feb;36(2). Available from: http://www.phac-aspc.gc.ca/publicat/hpcdp-pspmc/36-2/ar-02-eng.php

11. Ford ES, Giles WH, Myers GL, Rifai N, Ridker PM, Mannino DM. C-reactive protein concentration distribution among US children and young adults: findings from the National Health and Nutrition Examination Survey, 1999-2000. Clin Chem. 2003 Aug;49(8):1353–7.

12. Soriano-Guillén L, Hernandez-Garcia B, Pita J, Dominguez-Garrido N, Del Rio-Camacho D, Rovira A. High-sensitivity C-reactive protein is a good marker of cardiovascular risk in obese children and adolescents. - PubMed - NCBI. Eur J Endocrinol. 2008 Jul 1;159(1):R1-4.

13. CorvalÃ¡n C, Uauy R, Kain J, Martorell R. Obesity indicators and cardiometabolic status in 4-y-old children. Am J Clin Nutr. 2010;91(1):166.

14. Roh EJ, Lim JW, Ko KO, Cheon EJ. A Useful Predictor of Early Atherosclerosis in Obese Children: Serum High-sensitivity C-reactive Protein. J Korean Med Sci. 2007 Apr;22(2):192–7.

15. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB. Low-grade systemic inflammation in overweight children. Pediatrics. 2001 Jan;107(1):E13.

16. Carson V, Janssen I. Volume, patterns, and types of sedentary behavior and cardio-metabolic health in children and adolescents: a cross-sectional study. BMC Public Health. 2011;11(Journal Article):274.

17. MacPherson M, de Groh M, Prud'homme D, Jiang X, Dubois L.Cardio-metabolic risk by Body Mass Index, Waist Circumference, and a combined Body Mass Index-Waist Circumference indicator, among Canadian children and adolescents.(Publication pending).

18. Lambert M, Delvin EE, Levy E, O'Loughlin J, Paradis G, Barnett T, et al. Prevalence of cardiometabolic risk factors by weight status in a population-based sample of Quebec children and adolescents. Can J Cardiol. 2008 Jul;24(7):575–83.

19. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1 [Internet]. Statistics Canada; 2014 Apr [cited 2016 Mar 9]. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.htm

20. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 2 [Internet]. Statistics Canada; 2013 Apr [cited 2016 Mar 9]. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V2-eng.htm

21. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 3 [Internet]. Statistics Canada; 2014 Sep [cited 2016 Mar 9]. Available from: http://www23.statcan.gc.ca:81/imdb/p2SV.pl?Function=getSurvey&SDDS=5071&lang=en&db=imdb&adm=8&dis=2

22. Tremblay MS, Gorber SC. Canadian health measures survey: brief overview. Can J Public Heal Can Santee Publique. 2007 Nov;98(6):453–456.

23. Giroux S. Canadian Health Measures Survey: sampling strategy overview. Health Rep. 2007;18 Suppl:31–6.

24. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report - NHLBI, NIH. Pediatrics. 2011 Dec;128(5):s213-56.

25. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics. 2004 Aug 1;114(Supplement 2):555–76.

26. American Academy of Pediatrics. National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992 Mar;89(3 Pt 2):525–84.

27. Genuth S, Alberti KGMM, Bennett P, Buse J, DeFronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 2003 Nov 1;26(11):3160–8.

28. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med. 2003 Aug;157(8):821–7.

29. Prince RL, Kuk JL, Ambler KA, Dhaliwal J, Ball GDC. Predictors of metabolically healthy obesity in children. Diabetes Care. 2014 May;37(5):1462–8.

30. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis Model Assessment Is More Reliable Than the Fasting Glucose/Insulin Ratio and Quantitative Insulin Sensitivity Check Index for Assessing Insulin Resistance Among Obese Children and Adolescents. Pediatrics. 2005 Apr 1;115(4):e500–3.

31. Daskalopoulou S, Rabi D, Zarnke K, et al. The 2015 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2015 May;31(5):549–68.

32. Centers for Disease Control and Prevention. Clinical Growth Charts [Internet]. 2009 [cited 2016 Mar 9]. Available from: http://www.cdc.gov/growthcharts/clinical_charts.htm

33. World Health Organization. WHO : Global Database on Body Mass Index; The International Classification of adult underweight, overweight and obesity according to BMI [Internet]. [cited 2016 Mar 9]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

34. Canadian Guidelines for Body Weight Classification in Adults - Health Risk Classification according to Body Mass Index [Internet]. Ottawa, Ontario, Canada: Health Canada; 2003

Mar. (Catalogue H49-179). Available from: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/cg_quick_ref-ldc_rapide_ref-eng.pdf

35. Patry-Parisien J, Shields M, Bryan S. Comparison of waist circumference using the World Health Organization and National Institutes of Health protocols. Health Rep. 2012 Sep;23(3):56–63.

36. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11-18y of age. Eur J Clin Nutr. 2004 Jul;58(7):1011–5.

37. MacPherson M, de Groh M, Wall R, Prud'Homme D, Jiang X, Dubois L. Estimating waist circumference percentiles for Canadian Children 6-10 years using reference data from the 1981 Canada Fitness Survey, the CHMS Cycles 1-3, and NHANES 1998-1994. [Publication pending].

38. Efron B, Tibshirani R: Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. Statist Sci 1986, 1:54–75. [Internet]. [cited 2016 Mar 9]. Available from: http://matthieuchemin-research.mcgill.ca/ECON742/paper/efron.pdf

39. Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA. Association between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults. N Engl J Med. 1998 Jun 4;338(23):1650–6.

40. Bryan S, St-Denis M, Wojtas D. Canadian Health Measures Survey: Clinic operations and logistics. Statistics Canada Health Reports Catalogue no. 82-003-S. 2007 Dec. http://www.statcan.gc.ca/pub/82-003-s/2007000/article/10366-eng.pdf

6. DISCUSSION

The overarching objective of this research endeavour was to contribute towards an improved understanding of the current state of health and risk for onset of cardio-metabolic diseases in Canadian children and adolescents. Through a series of four research projects, I have estimated the prevalence of traditional and emerging risk factors for cardio-metabolic diseases; quantified the associations between these risk factors and several anthropometric, behavioural, demographic and socio-economic factors; and proposed novel indicators and reference data for measuring obesity and inflammation in the pediatric population.

6.1. Discussion of Key Findings

6.1.1. Key Findings per Hypothesis

Paper 1 Metabolic Syndrome*: The prevalence of MetS will be approximately 4% with a significantly higher prevalence among female, Aboriginal and older participants, as well as those with obesity and/or a lower socio-economic status.*

- Only 2.1% of Canadians aged 10-18 years were classified as having the Mets using the International Diabetes Federation consensus definition for children and adolescents (10-15 years) and worldwide adult definition (≥ 16 years). Participants from households with the highest income adequacy and educational attainment levels had the lowest prevalence of one or more MetS risk factors, abdominal obesity and low HDL-C. Due to the low prevalence of MetS, disaggregation by sex, age, Aboriginal status or SES was not statistically possible.

Paper 2 Waist Circumference Cut-Offs*: Regression of linear, logarithmic and quadratic functions will generate sound reference data that is consistent with trends observed from the Canadian Health Measures Survey and National Health and Nutrition Examination Survey. As compared to linear and quadratic functions, the logarithmic function will generate reference data with the smallest degree of error and highest degree of sensitivity and specificity.*

- The logarithmic function had the strongest predictive power as its extrapolated values had the smallest degree of error, particularly for the NHANES and CHMS, as compared to the linear and quadratic functions.

Paper 3 Cardio-Metabolic Risk*: The prevalence of cardio-metabolic risk among children and adolescents will be approximately 30% with a significantly higher prevalence among adolescents and smokers, as well as those with obesity, low levels of physical activity, insufficient sleep and with low socio-economic status. All three obesity indicators (BMI, WC, Combined BMI-WC) will be positively associated with cardio-metabolic with the 'combined BMI-WC' being the strongest predictor for cardio-metabolic risk.*

- The prevalence of cardio-metabolic risk was 35% with significantly higher levels among those classified as having obesity and those who did not achieve physical activity targets established by the Canadian Society for Exercise Physiology. Sleep, SES and smoking status (available for adolescents only) were not significant predictors for cardio-metabolic risk. The 'Combined BMI-WC' had the strongest association with cardio-metabolic among the three indicators of obesity, although BMI and WC both had strong, significant associations with cardio-metabolic risk.

Paper 4 Inflammation Marker*: High levels of CRP, a blood marker for inflammation, will be a significant predictor for cardio-metabolic risk.*

- The relationship between cardio-metabolic risk and *high* levels of CRP was significant with 43.6% of children and 62.0% of adolescents with *high* levels of CRP classified as having cardio-metabolic risk.

6.1.2. Key Findings Overall

Overwhelming, Canadian children and adolescents presented with good health overall. Less than 3.0% of participants had MetS, diabetes, impaired fasting glucoses, or hypertension. Further, perhaps contrary to the significant societal discourse regarding childhood obesity, between 65%-72% of participants were classified as under or normal weight.

Yet, the substantial prevalence of multiple risk factors which predict premature onset of chronic disease foreshadows potential years of morbidity in adulthood. Notably, the percentage of children (6.5%) and adolescents (3.5%) that achieve the physical activity guidelines was astonishingly low, while over 12.0% of adolescents reported some degree of smoking behaviour. Approximately 20% of participants live in households with low income or low parental education levels.

Depending on the obesity indicator applied (BMI, WC or Combined BMI-WC), between 12%-35% of participants were classified as having obesity. Regarding the three indicators of obesity, both BMI and WC performed well as predictors for cardio-metabolic risk which is consistent with previous studies. However, the Combined BMI-WC had the strongest associations signaling

the potential value of collective consideration of both overall body fat, as well as type of body fat, in assess cardio-metabolic risk.

Non-attainment of the recommended levels of physical activity was significantly associated with weight status and a significant predictor for cardio-metabolic risk regardless of weight status.

Although only 2.1% of participants were defined as having MetS, 25% of children and 40% of adolescents have at least one risk factor for cardio-metabolic diseases. These figures are particularly striking when the evidenced propensity for these cardio-metabolic risks to increase with age and with increasing weight status is taken into account. (145,147,148) Disconcertingly, the presence of MetS indicates a twofold increased risk for cardiovascular disease and a fivefold increased risk for type 2 diabetes. (85,101,149,150) Thus, considered together, the prevalent risks of obesity, smoking, insufficient physical activity and traditional and emerging risk factors for cardio-metabolic diseases point to substantial risk for future onset of chronic diseases for this generation's child and adolescent population.

6.2. Interpretation of Findings and Policy Implications

6.2.1. Metabolic Syndrome and Cardio-Metabolic Risk

- **Which concept is more suitable for estimating the future chronic disease risks of youth?**

The evolution of focus from Mets to cardio-metabolic risk was predicated on two factors:

(1) Cardio-metabolic risk offers a broader assessment of the known risk factors

Cardio-metabolic risk offers a more inclusive approach to assessing future risk for cardiovascular and metabolic diseases than does MetS. The risk factors included in the diagnosis of cardio-metabolic risk can include both traditional risk factors, such as hypertension, smoking, physical inactivity, dislipidemia (low-density lipoprotein cholesterol, HDL-C, triglycerides, apolipoprotein B), glycaemia (diabetes and impaired fasting glucose), as well as emerging risk factors, such as insulin resistance, genetic predisposition, inflammation (CRP, fibrinogen), homocysteine and prothrombic profile.(104,151,152) Conversely, MetS is limited to five risk factors and only diagnosed with the presence of 3 or more risk factors(89,143), despite evidence that having even one of these risk factors elevates ones relative risk for cardiovascular disease and diabetes.(104) Thus, the benefit of the cardio-metabolic concept approach, over MetS, is that it facilitates a more comprehensive assessment of cardio-metabolic risk.(104) Furthermore, cardio-metabolic risk allows for statistically rich analyses to examine the associations between cardio-metabolic risk and obesity. This is important as, though evidence generally identifies a positive relationship between cardio-metabolic risk and obesity (124,145,153,154), not all those with obesity are classified as having cardio-metabolic risk.(155–157) Studying the relationship between MetS and obesity is less

meaningful as abdominal obesity is one of the five risk factors that constitute a diagnosis for MetS, and in some cases, must be present for a MetS diagnosis. (89,143)

(2) CRM allows for greater statistical power

Furthermore, until data from additional CHMS data collection cycles becomes available, there are an insufficient number of Canadian children and adolescents with the MetS to achieve the statistical power necessary to reliably assess the associations between MetS and other health, behavioural and socio-economic factors. With data from three CHMS cycles, there were only 21 participants with MetS. Conversely, cardio-metabolic risk, particularly as a dichotomous variable, offers a larger sample from which to study this phenomenon.

For these two overarching reasons, studying cardio-metabolic risk is a more appropriate measure at the national level to estimate risk for cardiovascular disease and diabetes.

- **What information does a diagnosis of 'having cardio-metabolic risk' provide?**

It is understood that the presence of cardio-metabolic risk factors increases one's relative risk for cardiovascular and metabolic diseases. However, more evidence is required to compare the relative risks associated with each cardio-metabolic risk and risk factor clusters to determine their distinct predictive strengths for the various health outcomes. (104) For adults, several risk assessment tools, such as the Framingham Risk Assessment Tool, are available to calculate absolute risk for cardiovascular diseases based on select demographic information and select risk factors for cardiovascular disease. (104,158) Valid risk assessment calculations to determine absolute cardio-metabolic disease risk for pediatric populations are unavailable. (104,159) In time, more evidence regarding the relative risks associated with each pattern of cardio-vascular

risk factors could contribute towards further strengthening the predictive capabilities of existing risk assessment tools.(104)

Yet, even for children and adolescents, the concept of cardio-metabolic risk offers much value. From a clinical perspective, identification of any cardio-metabolic risk factor should initiate lifestyle, medical and, potentially, pharmaceutical interventions to treat the risk factor, screen for the presence of other risk factors, and initiate prevention efforts to deter other risk factors from presenting.(151,160)

From a research perspective, measuring cardio-metabolic risk facilitates an improved understanding of the complex etiology of cardio-metabolic disease which should support policy, behavioural, medical and pharmaceutical progress over time. Recently, Huang (2015) studied evidence regarding the pathways through which cardio-metabolic risks persist from childhood to adulthood, informed by the Developmental Origins for Health and Disease theory.(160) She concluded that *"cardio-metabolic risk can be both an outcome and also a mediator towards ultimate cardiovascular diseases".*(160)

<u>How does inflammation contribute to pediatric cardio-metabolic risk assessment?</u>

Cardio-metabolic risk factors may present uniquely although they tend to cluster as their pathologies are intertwined. In 2008, the American Diabetes Association and American College of Cardiology Foundation released a consensus conference report which included visual presentation of the heterogeneous pathways through which cardio-metabolic risk factors present (Figure 1).(141) It is theorized, with some supporting evidence, that insulin resistance, obesity, atherosclerosis, and inflammation, phenomena that are related yet distinct, are the key features that drive cardio-metabolic risk factor clustering.(104)

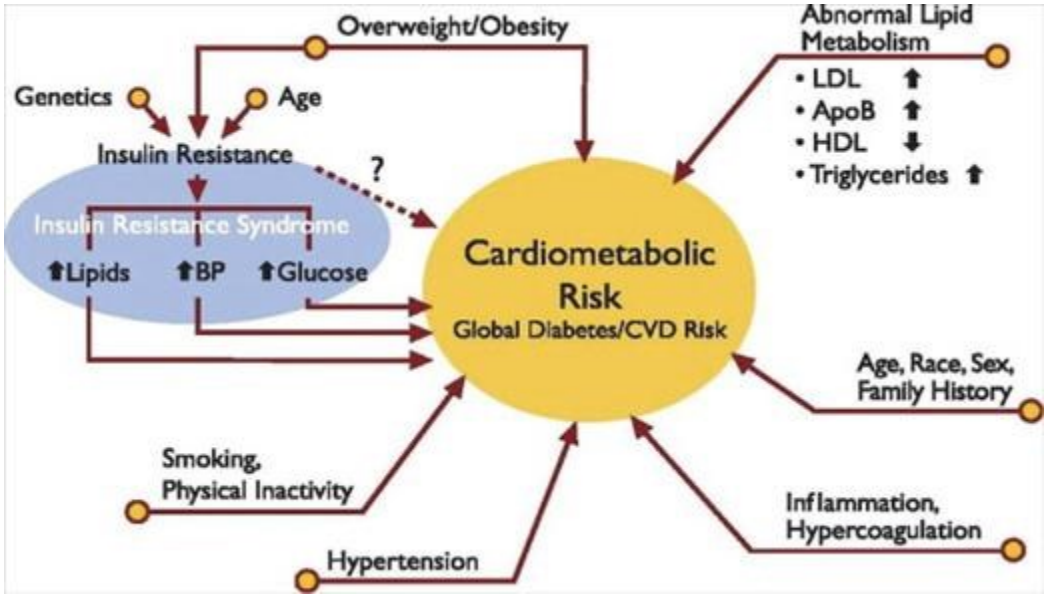


Figure 2. Factors contributing to cardio-metabolic risk (151)
Reprinted and included with permission from Elsevier (Licence: 3916580434773)

Evidence indicates that the presence of high levels of CRP, the most suitable blood marker for measuring systemic low grade inflammation, is associated with the presence of atherosclerosis and cardio-metabolic risk among children.(154,161,162) It is theorized that the presence of excess body fat produces elevated levels of cytokines which can contribute to insulin resistance and cardiovascular diseases.(104) Although classified as an emerging risk factor but not commonly included in risk assessment tools, the presence of high levels of CRP may increase relative risk and treatment is recommended to reduce CRM risk. Age-, sex- and ethnically-specific cut-offs for high levels of CRP are needed to precisely measure associations between low grade inflammation and cardio-metabolic risk. The findings from the fourth paper, Inflammation Marker, aim to contribute towards this need and suggest that CRP is a meaningful risk factor for cardio-metabolic risk for pediatric populations.

6.2.2. Obesity

- **Indicators of obesity: Does the 'Combined BMI-WC' indicator add value?**

In the third and fourth papers, Cardio-Metabolic Risk and Inflammation Marker, respectively, three indicators of obesity were applied to compare the strength of the associations between cardio-metabolic risk, inflammation and obesity. As discussed in the Literature Review chapter, though estimates of body fatness by BMI and WC are both highly correlated with estimates using DXA (56,71,74), each indicator has distinct strengths and weaknesses. BMI is a fast and simple indicator of weight class and, although it is a not direct measure of fat, it is strongly associated with adverse health status.(163) WC is a direct measure of abdominal obesity which, some evidence suggests, is more strongly associated with diabetes, cardiovascular disease and mortality than BMI (43,45,164,165), and a key risk factors for the MetS.(89,143) I sought to compare the associations between these indicators and to understand if a combined measure of BMI and WC would have a stronger association with cardio-metabolic risk. I concluded that obesity defined using the 'Combined BMI-WC' indicator was more strongly associated with cardio-metabolic risk as compared to BMI or WC alone.

Should the 'Combined BMI-WC' be adopted for widespread clinical or epidemiological use?

Not necessarily. First and foremost, BMI performed very well as an indicator of obesity; after adjusting for age and physical activity levels, the odds of having cardio-metabolic risk was 8.13 times higher among those with BMI-obesity (versus 9.58 higher times for those with obesity defined using the 'combined BM-WC' indicator). Clearly, those presenting with obesity have a much elevated risk for cardio-metabolic risk regardless of their WC. Therefore, given BMI's ease

of use and speed of calculation, the indicator may be sufficient for estimating body fatness for many circumstances.

Secondly, accurately estimating abdominal obesity using measured WC is more technical and prone to error than using BMI. There are multiple protocols for measuring WC, varying by the exact location(s) of measurement of the abdomen, with the WHO measurement protocol and the National institutes of Health method to measure WC being the most prominent. (60,166) A recent literature review spanning 1975-2011 regarding measurement error of WC estimated that errors varied between 0.7 cm and 15 cm among measurements.(167) Similarly, a review of anthropometric measure error found that WC measurements are more prone to error, relative to height and weight measurements, even among the same technician following the same protocol.(168) The authors suggested this challenge may weaken associations between WC and health outcomes presented in scientific studies and recommended technicians adopt a common protocol and undergo substantial training.(168) Further, particularly for the pediatric population, age-, sex- and ethnically- specific reference data is required to determine the appropriate WC cut-offs for establishing abdominal obesity. My second paper, Waist Circumference Cut-offs, aimed to contribute towards addressing this challenge by generating age- and sex-specific WC cut offs for ages 6-10 years generated using pre-obesity epidemic population.

Finally, more analysis is required to reach consensus regarding the ideal 'Combined BMI-WC' indicator that is most predictive of cardio-metabolic and chronic disease risk. For the third paper, Cardio-Metabolic Risk, I applied an indicator that represented a progressive increase of both BMI and WC: (1) Normal weight (BMI<85^{th} and WC<90^{th}); (2) BMI Normal and Abdominal

Obesity (BMI<85th and WC≥90th); (3) BMI Overweight and Abdominal Obesity (85th≤BMI<95th and WC≥90th); and (4) BMI Obese with Abdominal Obesity (BMI≥95th and WC≥90th). Prior to this, I had tried a Combined BMI-WC indicator which aimed to differentiate between obesity by BMI versus by WC: (1) Normal weight (BMI<85th and WC<90th); (2) BMI Overweight or Obese only (BMI≥85th and WC<90th)); (3) Abdominal obesity only (BMI<85th and WC≥90th); and (4) BMI Overweight-Obese with Abdominal Obesity (BMI≥85th and WC≥90th). We found this indicator to be a less effective combined BMI-WC indicator because the sample of respondents in category 2 "BMI overweight or obese only" were too small to conduct meaningful analysis plus the association between this indicator of obesity and cardio-metabolic was not as strong (data not shown).

Zhu (2004) derived combinations of BMI and WC to determine the equation most predictive for cardiovascular disease risk, concluding that 68% BMI and 32% WC constituted the optimal combined indicator for predicting risk among adult white males.(169) In a study comparing the associations of BMI, WC and combination of BMI and WC with risk factors for coronary artery disease among children and adolescents, Janssen (2005) chose to examine the combination of BMI and WC by including them both in the models as continuous variables. He concluded that the combination of BMI and WC provided the strongest predictive power for the risk factors.(170)

Other studies purport that WC is best suited to differentiate relative risk for cardiovascular disease within BMI categories. In a study of adult participants using data from the Third NHANES (1988-1994) in the United Sates, Sahakyan (2015) reported a higher mortality rate

among adults with normal BMI and abdominal obesity versus those classified as normal weight, for example.(165) Guidelines from Health Canada for weight classification among adults state that while WC is useful for understanding health risks for those classified as under, normal, overweight or obese class I, WC is *"not useful for obese class II or III in distinguishing relative level of risk"*(38). Thus, more research is needed, including longitudinal studies or data linkage studies between epidemiological and hospital administrative databases, to make a final conclusion regarding the utility and ideal design of a combined BMI-WC measure for children and adolescents.

6.2.3. Socio-Economic Status

- **Why were the associations between socio-economic status and health not more substantial given the existing evidence?**

Our estimates indicate that slightly less than one quarter of Canadian children or adolescents live in households classified as having low SES by either low-middle household income or educational attainment. As discussed in the Introduction and Literature Review chapters, substantial evidence suggests that those having lower SES are more likely to experience ill health resulting from constrained access to social, economic and physical environments that are conductive to good health and health promoting behaviours.

Yet, our findings regarding the associations between SES and cardio-metabolic risk factors were not as substantial as I had expected. In the first paper, Metabolic Syndrome, a significant inverse association between one or more MetS risk factors, abdominal obesity and low HDL-C and SES, both by household income and educational, was observed.

In the third and fourth papers, Cardio-Metabolic Risk and Inflammation Marker, respectively, I endeavored to build on these findings by using regression to identify the predictive power of SES for cardio-metabolic risk as a dichotomous variable. However, household income and educational attainment were not significant in any of the regression models. Comparably, Shi (2016) examined the social gradient for cardio-metabolic risk factors individually using regression among children and adolescents using the CHMS. (13) She reported distinct socio-demographic patterns for blood pressure, HDL-C and obesity. (13) By using a dichotomous cardio-metabolic risk variable, my intention was to generate more powerful, compelling results regarding the socio-economic groups most vulnerable for cardio-metabolic diseases in their future. Unfortunately, it is likely the dichotomous cardio-metabolic risk variable diluted, rather than strengthened, the distinct associations between cardio-metabolic risk factors and SES.

6.2.4. Policy Implications

- **How should cardio-metabolic risk be addressed at the policy level?**

Canadians should find it disconcerting that 25% of children and 40% of adolescents have at least one risk factor for cardio-metabolic diseases at such an early stage in their life course. Although clinical assessment and treatment are critical to preventing and managing cardio-metabolic risk, policies are also essential in order to meaningfully address these issues at the macro-level. In their 2008 conference consensus report, the American Diabetes Association and the American College of Cardiology Foundation advocated for, "*A concerted, multifaceted, public health effort, focused on lifestyle modifications, to reduce mean population levels of atherogenic lipoproteins to values well below current ones*" as key to addressing cardio-metabolic risk across all segments of society. (151) Similarly, the Cardiometabolic Risk Working

Group stated that, *"Health behaviour interventions (weight loss, physical activity, diet, smoking cessation) in people identified at high cardio-metabolic risk are of critical importance given the emerging crisis of obesity and the consequent epidemic of type 2 diabetes"*. (104) Furthermore, the group specifically listed restriction of sugar sweetened beverages and moderate to vigorous activity as important elements to reducing abdominal obesity and cardio-metabolic risk.(104) Thus, support for broad, multi-disciplinary approaches for preventing and managing cardio-metabolic exists, with a focus on preventing and managing obesity, increasing physical activity, as well as other risk factors. The specific suggested policy approaches for obesity and physical activity will be discussed in a subsequent section.

<u>Critical that policies reduce, not exacerbate, health disparities</u>

The compelling body of evidence for the associations between socio-economic and cardio-metabolic signal the critical importance of policies designed to reduce health disparities across socio-economic groups.(171) A position statement by the Cardiometabolic Risk Working Group (2011) called for "*more research on the social determinants of health specifically in the area of cardiometabolic diseases, (to) help clarify therapeutic strategies and the health policies needed to minimize risk in this population*".(104) Shi (2016) research signals the importance of intervening during childhood when the risks for cardiovascular diseases begin to present. (13) Policies designed to reach vulnerable children and their families through increased social benefits, parent support and targeted education may provide the early intervention to prevent these risk factors from presenting in childhood and persisting in adulthood.

- **How should obesity be address at the policy level?**

Given the prevalence of obesity among children and adolescents, as well as the clear association between excess body fat and health, policy efforts towards this significant health problem are important. But what should be done?

Pursuing a comprehensive, multi-pronged approach

Among those who study obesity within a community, national or socio-environmental context, there is a general consensus that, given the complexity of factors that are driving this issue, a substantial, multi-pronged approach is required in order to meaningful address this issue. Canada's Standing Senate Committee on Social Affairs, Science and Technology recently released a report describing the measures needed to address obesity using a whole-of-society approach.(79) These measures include: improved nutrition labeling, elimination of food and beverage marketing aimed at children, taxation of certain processed food items, improved Canada Food Guide, increased access and affordability of nutritious foods and normalizing healthy foods in such environments as schools, sports arenas and hospitals, and health promotion and public awareness and education to support a healthy diet and physical activity.(79) Similarly, the final report of the United Kingdom's Foresight programme 'Tackling Obesities: Future Choices" called for a multi-factorial approach for obesity with many recommendations that overlap with the Senate's report.(47) The Foresight programme also developed a series of models to test and project the potential outcomes of various policies and concluded that the following policy responses would generate the most significant impacts towards preventing and reducing obesity:

- "Increasing walkability/cyclability of the build environment;

- Targeting health interventions for those at increased risk;
- Controlling the availability of/exposure to obesogenic foods and drinks;
- Increasing the responsibility of organizations for the health of their employees; and
- Early life interventions at birth or in infancy" (47)

The *'Obesity in Canada'* report, a joint report released by the Canadian Institute for Health Information and the Public Health Agency of Canada (2011), describes Canada's extensive suite of social and health policies and programs designed to support Canadians in maintaining and improving their health and well-being. Briefly, these programs include: universal health care; public primary and secondary education; subsidy programs to support healthy eating among vulnerable and remote populations; some food labeling; Canada's Food Guide; structured voluntary initiative regarding food marketing to children; and financial tax credits to promote physical activity.(117) The economic analyses included in the report indicate that the estimated annual costs related to obesity increased by 20% between 2000 and 2008 ($ 3.9 billion in 2000 and $4.6 billion in 2008).(117) Clearly, despite the existing initiatives in place, the increasing rates and increases costs of obesity command even more attention and resources.

A parallel can be drawn between smoking prevention efforts over the last 40 years and the similar urgency for whole-of-society approaches to societal food consumption and physical activity patterns. Although the percentage of daily smokers has decreased over the past 40 years, young adults (20-34 years) report the highest prevalence of smoking behaviours among all age groups.(172) That smoking behaviours persists despite significant efforts to deter smoking including front-of-package labeling, public health campaigns, taxation, restrictions on

tobacco purchasing, and legislated smoking bans in many public places, should give some insight into the magnitude and breadth of policy and societal initiatives required to meaningfully prevent and curb obesity.

Reducing weight bias and discrimination

In her research work, Dr. Puhl of the Rudd Center for Food Policy & Obesity at the University of Connecticut, has repeatedly demonstrated the high degree to which individuals with obesity experience discrimination in their everyday lives and in medical settings(173,174), and that these experiences are actually associated with worsened health outcomes.(175,176) Thus, it is important that measures to access obesity serve to reduce, not exacerbate, weight bias in society.(177) Dr. Puhl has proposed several policy measures to reduce weight bias and discrimination including: dedicated weight bias training for clinicians, anti-bullying campaigns, and legislation against weight-based discrimination.(176,178)

Recognizing that obesity is a 'sometimes' modifiable risk factor

There is substantial evidence indicating that maintaining significant weight loss is challenging with minimal to moderate success over the long term, attributed to both recidivism to unhealthy diet and behaviours and complex physiological adaptations following weight loss.(179,180) Yet, weight loss is regularly listed as a modifiable risk factor in clinical guidelines and scientific articles regarding associations between obesity and health outcomes.(151) However, taking into account the evidence regarding weight regain, the importance and urgency of preventing obesity is clear, particularly among pediatric populations who have a lower prevalence of overweight and obesity than adults.

Promoting physical activity as a key element towards obesity prevention

In the third paper, Cardio-Metabolic Risk, I reported that over 95% of participants did not meet the physical activity guidelines established by the Canadian Society of Exercise Physiology, with adolescents and females significantly less likely than children and males to achieve the guidelines. Further, a lack of physical activity was a significant predictor for cardio-metabolic risk and was significantly associated with weight class. Overall, it is well-documented that regular physical activity is an important element towards maintaining a healthy body weight and further, regardless of weight, an important factor towards reduced cardio-metabolic risk. Policy efforts to promote and support physical activity among children and adolescents are important to maintaining their current health as well as encouraging them to adopt this health promoting habit into their adult years. Beyond recess and gym class, which is generally offered well-below suggested guideline, there are minimal publically funded opportunities in the school system to participate in physical activity.(181) Furthermore, the emphases of physical activity are largely geared towards the athletic-inclined children and towards competitive sports. More emphasis on educating children and adolescents the importance of physical activity, on the range of options available to be active, as well as more support for time spent being active, would serve to positively encourage greater physical activity levels among youth. (181)

6.3. Strengths and Limitations

6.3.1. Strengths

This doctoral research project addresses important and relevant population health concerns faced by Canadians, such as obesity, risk for chronic disease and health disparities. Research endeavours that are focused on understanding obesity and chronic diseases, particularly regarding children who are at a developmentally vulnerable period of life and require age- and sex- specific measurements, are critical for addressing the growing prevalence of chronic diseases in Canada and globally.

A key strength of this research work was the data set, the CHMS, a nationally representative survey of over 96% of Canadians. The progressive application of three data collection cycles of the CHMS (2007-2009; 2009-2011; and 2012-13) for papers 3 and four, Cardio-Metabolic Risk and Inflammation Marker, respectively, generated a large study sample which allowed for greater statistical power. Further, this study relied on anthropometric and clinical data that was collected using direct measures which are more accurate than data collected by self-report. Evidence from a study using nationally representative data for Canadians 12 years and older showed that direct measurement of height and weight resulted in a prevalence of obesity that was 6.0-9.0% greater than self-reported measurements.(182) Similarly, for children aged 6-11 years, weight and weight estimates obtained by proxy self-report resulted in significant misclassifications of weight categories.(183) Finally, physical measures of health status allows for successful identification of undiagnosed diabetes and hypertension, which were important risk factors for this work.

6.3.2. Limitations

Several limitations are present in this doctoral research endeavour. Most notably, the study data is cross-sectional thus interpretation of causation is not possible. The research projects were consistently limited by their sample size which was particularly challenged by the limited age range and inclusion of fasting participants only. Unfortunately, comparison across CHMS cycles was not always possible due to changes in the collection methods and priorities of each collection cycle, which further limited sample size and analytical opportunities. For example, this challenge precluded our ability to meaningfully study nutrition as key factor in these health issues. Moreover, the low prevalence of MetS among children and adolescents and certain socio-demographic groups limited the statistical power with which accurate, disaggregated estimates could be calculated. Regarding the blood measures, the inclusion of CRP further reduced our study sample (by n=848). Understandably, Statistics Canada limits the blood drawn for younger CHMS participants thus a limited range of blood tests are available for those ages. In addition, as CRP values are also influenced by infections and other issues, it is recommended that blood measures be collected twice, at least two weeks apart, to obtain accurate results.(104)

As mentioned in Chapter 4 Methodology, the overall response rate for each CHMS cycle is slightly more than 50%, thus biases may exist for those who selected to participate or declined participation the CHMS, though through the use of oversampling and sample weights, Statistics Canada aims to correct for these biases. Overall, although the CHMS is representative of more than 96% of Canadians, the exclusions of individual living on First nations and reserves and

those in federal prisons, both known for worse health outcomes, these results are not truly reflective of the health of the entire Canadian population.

There are several limitations associated with combination of multiple cycles of a cross-sectional dataset, such as the CHMS. Primarily, this combined or 'pooled' dataset does not represent an actual population from a specific point in time, thus there is the potential for statistical differences between the findings from each individual cycle and the combined dataset. (184) Furthermore, due to the potential of procedural variations between each cycle introduced by changes to the data collection team, collection instruments or other shifts related to the passage of time, there is a possibility that some variables may be different from one cycle to the next, even if the overall collection protocol for the variable was identical in description.(184)

Longitudinal analyses that compare the performance of the WHO, CDC and IOTF body weight classification systems among children and adolescents from a health-outcomes perspective are essential towards reaching global consensus on the optimal classification system. Though this will take many years, it would eventually enable richer international comparisons.

6.4. Innovation and Knowledge Contribution

This doctoral research endeavours makes several contributions of original knowledge to the field of population health. From a methodological perspective, the regression of multiple of statistical functions to estimate values for a children based on measured values established on an adolescent population was novel to population health. This approach had been demonstrated in select clinical neurological studies but has the potential for broader application to measured health indicators. Furthermore, this WC Cut-Offs paper filled a critical knowledge gap by proposing age- and sex- specific cut-offs from which to establish abdominal obesity in 6 to 10 years that was established using a measured, national, pre-obesity epidemic population. Prior to this paper, investigators seeking to estimate abdominal obesity among 6 to 10 years old in Canada would have had to rely on cut-offs established using a sub-sample of the Canadian population, a study from the United States using the NHANES data or a more recent national, measured dataset, such as the CHMS, would be skewed by our current obesity epidemic. The examination of BMI and WC as a combined measure of obesity also offered a novel methodological contribution to population health. While further research would be required to precisely determine the ideal combined BMI-WC, this methodological approach offers the potential to capitalize of the strengths of each measure.

The exploration of inflammation, using CRP, as an emerging cardio-metabolic risk factor for the pediatric population provided evidence of a strong, significant relationship between inflammation and cardio-metabolic risk. This study also contributed towards the discourse of defining high levels of CRP is an important element of measuring and quantifying cardio-metabolic risk factors.

6.5. Future Research

In their 2008 conference consensus report, the American Diabetes Association and the American College of Cardiology Foundation postulated that, "*the initial presentation of cardiovascular diseases in up to one-third of patients is sudden death*".(141) One can extrapolate from that quote the significance of research work that improves our understanding, ability for early identification and treatment of all risk factors for cardiovascular diseases. Thus, given the importance and timeliness of the issues of cardio-metabolic risk and obesity, more research is needed to improve our understanding of these issues, and, in particular, focused on pediatric populations. I suggest two complementary research foci for future research endeavours to study these phenomena:

(1) CHMS: (i) The continued analysis of the CHMS as the sample size grows through each additional CHMS cycle will enable more powerful statistical analysis with which to analyse the child and adolescent populations to better measure the implications of SES on cardio-metabolic risk factors, with more detailed focus on diabetes, hypertension, MetS, physical activity and smoking; (ii) The inclusion of technical measures of atherosclerosis, intima media thickness or arterial stiffness, as means to calculate the associations between cardio-metabolic risk factors and physical measure that predict cardiovascular risk (160); and (iii) The linkage between CHMS data and hospital administrative databases that would allow, over time, rich analyses between measured health status and future health outcomes.

(2) Prospective longitudinal studies: Measuring the associations between individual cardio-metabolic risk factors, as continuous variables, as well as the patterns of risk factor clustering, and health outcomes over the lifecourse would help to determine the precise

age- and sex- specific cut offs for each cardio-metabolic risk factor that "predict future disease risk"(160)

6.6. Conclusions

With this doctoral thesis, I endeavoured to contribute to population health by developing new knowledge regarding current health status and onset risk for cardio-metabolic disease among Canadian children and adolescents. These detailed analyses of risk factors for cardio-metabolic diseases and their associations with weight status, physical activity and inflammation foster a better understanding of the precursors for ill health for pediatric populations. I strived to advance the study of obesity in Canada by establishing criteria to define abdominal obesity in children ages 6-10 years based on national, pre-obesogenic reference data. Further, these projects should serve to inspire future research by proposing a novel indicator of obesity as well as risk cut points for inflammation and abdominal obesity for children.

Through a population health perspective, I aimed to foster further understanding of the social inequities that lead to disparities in health and to propose policy responses that would reduce, not exacerbate health inequalities. Recognizing that Canadians classified as obese are a heterogeneous group, a multi-faceted, whole-of-society approach is required to meaningfully address the physical, environmental and social factors that are driving increasing rates of obesity and chronic diseases.

While this thesis represents a contribution towards better understand and ultimately improving health in Canada, much more research, policy, clinical and societal effort will be needed to turn the tide towards lifelong health and wellbeing for our millennial generation.

APPENDIX A: CHMS Raw and Derived variables

- Aboriginal origin or identity (D)
- BMI classifications respondents ≥18 years (measured) (WHO) (D)
- BMI Classification respondents <18 years (measured) (CDC) (D)
- Bootstrap weights
- Clinic identifier
- Clinic age
- Cycle
- Diabetes - has diabetes
- Diabetes - insulin dependant
- Diabetes - non-insulin dependant
- Fasting sample weight
- Fasting Status
- Final prevalence average diastolic blood pressure (mmHg) (D)
- Final prevalence average systolic blood pressure (mmHg) (D)
- Full sample weight
- Glucose (Fasting)
- Has High Blood Pressure
- High Density Lipoprotein Cholesterol (mmol/L)
- High-sensitivity c-reactive protein (mg/L)
- Household educational attainment (4 categories) (D)
- Household income adequacy (4 categories) (D)
- Immigrant (D)
- Insulin (Fasting)
- Measured BMI (D)
- Medication high blood pressure – past month
- Number of hours sleeping per 24 hours
- Pregnant
- Probability of accumulating at least 30 minutes of moderate-to-vigorous physical activity on at least 5 days of the week for adults (18-79 years) (D)
- Probability of meeting Canadian Physical Activity Guidelines for children (5-17 years) (D)
- Sex
- Triglycerides (Fasting) (mmol/L)
- Type of smoker (D)
- Waist circumference (cm) (Cycles 2-3) (National Institutes of Health protocol)
- Waist circumference (cm) (Cycles 1-2) (WHO protocol)

(D) Denotes that the variable was derived by Statist Canada

APPENDIX B: Project Derived Variables

Computed Colum	Description
Abdominal obesity Linear	Using age- and sex- specific cut-offs Cut-offs for ages 6-10 years developed by regression of a linear function 0: Normal 1: Abdominal obesity
Abdominal obesity Ln	Using age- and sex- specific cut-offs Cut-offs for ages 6-10 years developed by regression of a logarithmic function 0: Normal 1: Abdominal obesity
Abdominal Obesity Quadratic	Using age- and sex- specific cut-offs Cut-offs for ages 6-10 years developed by regression of a quadratic function 0: Normal 1: Abdominal obesity
High c-reactive protein (mg/L)	Using age- and sex- specific cut-offs 0: Normal 1: High
Age group	Paper 2 1: Children (6-10 years) 2:Adolescent (11-18 years) Papers 3 and 4 1: Children (6-11 years) 2: Adolescent (12-18 years)
BMI3	3 categories ages 6-18 years 1: Under or normal weight 3: Overweight 4: Obese

BMI4	4 categories ages 6-18 years 1: Underweight 2: Normal weight 3: Overweight 4: Obese
BMI OBESE	0: Not obese 1: Obese
Cardio-metabolic risk factor score	Number of cardio-metabolic risk factors
Cardio-metabolic risk	0: No 1: Cardio-metabolic risk (presence of 1 or more cardio-metabolic risk factors)
Combined BMI-WC Indicator of Obesity	1: Normal: BMI<85th and WC<90th 2: BMI Normal with Abdominal Obesity: BMI<85th and WC≥90th 3: BMI Overweight with Abdominal Obesity: BMI≥85th and WC≥90th 4: BMI Obese with Abdominal Obesity: BMI≥95th and WC≥90th
Elevated blood pressure risk	Using age-, sex- and height- specific cut-offs 0: No risk 1: Elevated Risk or Pre/Hypertension
Elevated fasting triglycerides	0: No risk 1: Elevated
Elevated fasting blood glucose	0: No risk 1: Elevated
Elevated high density lipoprotein cholesterol	Using age- and sex- specific cut-offs 0: No risk 1: Elevated
Household educational attainment	Collapsed 4 categories into 2 categories 1: Secondary school graduation or less 2: Some post-secondary or post-secondary graduation)
Household educational attainment	Collapsed 4 categories into 3 categories 1: Secondary school graduation or less 2: Some post-secondary 3: Post-secondary graduation

Household Income Adequacy	Collapsed 4 categories into 3 categories 1: Lowest and lower middle 2: Upper middle 3: Highest
Insulin Resistance	0: No 1: Insulin resistance
Meet physical activity guidelines	Using age- and sex- specific cut-offs 0: Meet guidelines 1: Do not meet guidelines
Metabolic syndrome	0: No 1: Metabolic syndrome
Metabolic syndrome score	Number of metabolic syndrome components
Smoker	0: Never smoked 1: Ever smoked
Sleep risk	Using age-specific cut-offs 0: Sufficient sleep 1: Insufficient sleep
Waist circumference	Cycles 1-3 Applied a prediction equation to align the waist circumference variables in Cycles 1-2 (obtained using the WHO protocol) with Cycle 3 variables (obtained using the NIH protocol))

REFERENCES

1. Universal Declaration of Human Rights - 1948 [Internet]. United Nations; 1948 Dec. Available from: http://www.un.org/en/udhrbook/pdf/udhr_booklet_en_web.pdf

2. Closing the Gap in a Generation: Health Equity through Action on the Social Determinants of Health - Final Report of the Commission on Social Determinants of Health [Internet]. Geneva, Switzerland: World Health Organization | Commission on Social Determinants of Health; 2008 p. 1–256. Available from: http://apps.who.int/iris/bitstream/10665/43943/1/9789241563703_eng.pdf

3. Barker DJP. Developmental origins of chronic disease. Public Health.2012 March;126(3):185-9.

4. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. N Engl J Med. 2008 Jul 3;359(1):61.

5. Global Status Report on noncommunicable diseases 2014 [Internet]. Geneva, Switzerland: World Health Organization; 2014 p. 1–298. Available from: http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf

6. Diabetes: Canada at the Tipping Point - Charting a New Path [Internet]. Joint publication by Canadian Diabetes Association and Diabetes Quebec; 2008 p. 1–30. Available from: https://www.diabetes.ca/CDA/media/documents/publications-and-newsletters/advocacy-reports/canada-at-the-tipping-point-english.pdf

7. Chronic Disease and Injury Indicator Framework: Quick Stats, 2015 Edition. Ottawa (ON): Public Health Agency of Canada Center for Chronic Disease Prevention and Control; 2015. [Internet]. [cited 2016 Jul 7]. Available from: http://www.phac-aspc.gc.ca/publicat/hpcdp-pspmc/35-10/assets/pdf/ar-03-eng.pdf

8. Popkin BM. Global changes in diet and activity patterns as drivers of the nutrition transition. In 'Emerging Societies – Coexistence of Childhood Malnutrition and Obesity by Kalhan, S.C., Prentice, A.M. & Yajnik, C.S. Karger: Switzerland. 2009.

9. Reducing Gaps in Health: A Focus on Socio-Economic Status in Urban Canada. [Internet]. Canadian Population Health Initiative; [cited 2016 Jul 19]. Available from: https://secure.cihi.ca/free_products/Reducing_Gaps_in_Health_Summary_Report_EN_080816.pdf

10. Galobardes B, Smith GD, Lynch JW. Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. Ann Epidemiol. 2006 Feb;16(2):91–104.

11. Oliver L, Hayes M. Neighbourhood socio-economic status and the prevalence of overweight Canadian children and youth. Can J Public Health. 2005 Dec;96(6):415–20.

12. To T, Dell S, Tassoudji M, Wang C. Health outcomes in low-income children with current asthma in Canada. Chronic Dis Can. 2009;28(2):49–55.

13. Shi Y, de Groh M, Bancej C. Socioeconomic gradients in cardiovascular risk in Canadian children and adolescents. Health Promot Chronic Dis Prev Can. 2016 Feb;36(2).

14. World Health Organization. Health and human rights - Fact sheet No 323 [Internet]. World Health Organization. 2015. Available from: http://www.who.int/mediacentre/factsheets/fs323/en/

15. Public Health Agency of Canada. What is the Population Health Approach? [Internet]. 2013. Available from: http://www.phac-aspc.gc.ca/ph-sp/approach-approche/appr-eng.php

16. A healthy, productive Canada: A determinants of health approach. Ottawa, Ontario, Canada: The Standing Senate Committee on Social Affairs, Science and Technology; 2009 Jun. (Final Report of Senate Subcommittee on Population Health).

17. World Health Organization. The determinants of health [Internet]. World Health Organization. 2016. Available from: http://www.who.int/hia/evidence/doh/en/

18. Solar O, Irwin A. A conceptual framework for action on the social determinants of health. Social Determinants of Health Discussion Paper 2 (Policy and Practice). [Internet]. Geneva, Switzerland: World Health Organization; 2010. Available from: http://www.who.int/sdhconference/resources/ConceptualframeworkforactiononSDH_eng.pdf

19. Marmot M. The Status Syndrome: How Social Standing Affects Our Health and Longevity. New York, New York: Holt Paperbacks.; 2005.

20. Persons in low income after tax (In percent, 2007 to 2011) CANSIM table 202-0802 and Catalogue no. 75-202-X. Statistics Canada; 2013 Jun.

21. Child Poverty [Internet]. The Conference Board of Canada; 2013 Jan [cited 2016 Jun 29]. Available from: http://www.conferenceboard.ca/hcp/details/society/child-poverty.aspx

22. Macdonald D, Wilson D. Shameful Neglect: Indigenous Child Poverty in Canada. [Internet]. Canadian Centre for Policy Alternatives; 2016 May [cited 2016 Jul 19]. Available from: https://www.policyalternatives.ca/sites/default/files/uploads/publications/National%20Office/2016/05/Indigenous_Child%20_Poverty.pdf

23. The Chief Public Health Officer's Report on The State of Public Health in Canada 2008 [Internet]. Ottawa, Ontario, Canada: Public Health Agency of Canada; 2008 Jun. Available from: http://www.phac-aspc.gc.ca/cphorsphc-respcacsp/2008/fr-rc/index-eng.php

24. Dubois L, Farmer A, Girard M, Porcherie M (2006). Family food insufficiency is related to overweight among preschoolers. Soc Sci Med. 63(6): 1503-16.

25. Evans T, Whitehead M, Diderichsen F, Bhuiya A, Wirth M. Challenging Inequities in Health [Internet]. Oxford University Press; 2001. Available from: http://www.oxfordscholarship.com/view/10.1093/acprof:oso/9780195137408.001.0001/acprof-9780195137408

26. World Health Organization. Noncommunicable diseases [Internet]. World Health Organization Health Topics. 2016. Available from: http://www.who.int/topics/noncommunicable_diseases/en/

27. Chronic Disease Facts and Figures - Chronic Disease and Injury Indicator Framework [Internet]. Ottawa: Centre for Chronic Disease Prevention, Public Health Agency of Canada; 2016 Jun. Available from: http://www.phac-aspc.gc.ca/cd-mc/facts_figures-faits_chiffres-eng.php

28. Blouin C, Chopra M, van der Hoeven R. Trade and social determinants of health. Lancet. 2009 Jan;373(9662):502-7.

29. Hawkes C. Uneven dietary development: linking the policies and processes of globalization with the nutrition transition, obesity and diet-related chronic diseases. Global Health. 2006 Mar;2:4.

30. Healthy People Healthy Places: Current smoking [Internet]. Statistics Canada; 2015 Nov. (Health Reports). Report No.: 82–229–X. Available from: http://www.statcan.gc.ca/pub/82-229-x/2009001/deter/cos-eng.htm

31. Colley RC, Garriguet D, Janssen I, Craig CL, Clarke J, Tremblay MS. Physical activity of Canadian children and youth: Accelerometer results from the 2007 to 2009 Canadian Health Measures Survey. Statistics Canada; 2011 Jan p. 1–10. (Health Reports). Report No.: 82–003–X.

32. Healthy People Healthy Places: Fruit and vegetable consumption [Internet]. Statistics Canada; 2015 Nov. (Health Reports). Report No.: 82–229–X. Available from: http://www.statcan.gc.ca/pub/82-229-x/2009001/deter/fvc-eng.htm

33. Am B, De W, F P. Population patterns of chronic health conditions, co-morbidity and healthcare use in Canada: implications for policy and practice. Healthc Q Tor Ont. 2007 Dec;11(3):70–6.

34. Manuel DG, Leung M, Nguyen K, Tanuseputro P, Johansen H. Burden of cardiovascular disease in Canada. Can J Cardiol 2003;19(9):997-1004. [Internet]. [cited 2016 Jul 7]. Available from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.492.6462&rep=rep1&type=pdf

35. Heart and Stroke Foundation. Heart disease and stroke statistics [Internet]. Heart and Stroke Foundation. 2016. Available from: http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3483991/k.34A8/Statistics.htm#References

36. Leading causes of death, by sex, 2012 (Both sexes) [Internet]. Statistics Canada; 2015 Dec [cited 2016 Jul 7]. Report No.: CANSIM table 102-0561. Available from: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/hlth36a-eng.htm

37. WHO | Obesity and overweight [Internet]. WHO. Available from: http://www.who.int/mediacentre/factsheets/fs311/en/

38. Canadian Guidelines for Body Weight Classification in Adults - Health Risk Classification according to Body Mass Index [Internet]. Ottawa, Ontario, Canada: Health Canada; 2003 Mar. (Catalogue H49-179). Available from: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/cg_quick_ref-ldc_rapide_ref-eng.pdf

39. Gaggini M, Saponaro C, Gastaldelli A. Not all fats are created equal: adipose vs. ectopic fat, implication in cardiometabolic diseases. Horm Mol Biol Clin Investig. 2015 Apr;22(1):7–18.

40. Neeland IJ, Turer AT, Ayers CR, Powell-Wiley TM, Vega GL, Farzaneh-Far R, et al. Dysfunctional Adiposity and the Risk of Prediabetes and Type 2 Diabetes in Obese Adults. JAMA. 2012 Sep 19;308(11):1150–9.

41. Smith U. Abdominal obesity: a marker of ectopic fat accumulation. J Clin Invest. 2015 May;125(5):1790–2.

42. Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord. 2000 Nov;24(11):1453–8.

43. Zhang C, Rexrode KM, Dam RM van, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality. Circulation. 2008 Apr 1;117(13):1658–67.

44. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. Am J Clin Nutr. 2004 Mar 1;79(3):379–84.

45. Dagenais GR, Yi Q, Mann JFE, Bosch J, Pogue J, Yusuf S. Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. Am Heart J. 2005 Jan;149(1):54–60.

46. Katzmarzyk PT. The Canadian obesity epidemic, 1985–1998. Can Med Assoc J. 2002 Apr 16;166(8):1039–40.

47. Foresight - Tackling obesities: future choices - project report (2nd edition). [Internet]. United Kingdom Government Office for Science; 2008 p. 1–164. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/287937/07-1184x-tackling-obesities-future-choices-report.pdf

48. Rippe J, Crossley S, Ringer R. Obesity as a chronic disease: modern medical and lifestyle management. J Am Diet Assoc. 1998 Oct;98(10 Suppl 2):S9-15.

49. Canadian Medical Association. CMA recognizes obesity as a disease [Internet]. 2015. Available from: https://www.cma.ca/En/Pages/cma-recognizes-obesity-as-a-disease.aspx

50. American Medical Association. AMA Adopts New Policies on Second Day of Voting at Annual Meeting [Internet]. 2013. Available from: http://www.ama-assn.org/ama/pub/news/news/2013/2013-06-18-new-ama-policies-annual-meeting.page

51. Tjepkema M. Adult obesity in Canada: Measured height and weight [Internet]. Statistics Canada; 2008 Nov. Report No.: 82-620-MWE. Available from: http://www.statcan.gc.ca/pub/82-620-m/2005001/pdf/4224906-eng.pdf.

52. Jokovia A, Frood J, Leeb K. Bariatric surgery in Canada. [cited 2016 Jul 20]; Available from: http://www.ncbi.nlm.nih.gov/pubmed/19305656

53. US Department of Health & Human Services, National Institutes of Health: Gastrointestinal Surgery for Severe Obesity. Consensus Development Conference Statement. NIH Consensus Development Program; 1991 March.

54. Sjöström L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C. Lifestyle, Diabetes, and Cardiovascular Risk Factors 10 Years after Bariatric Surgery. N Engl J Med. 351:2683–93.

55. Wells JCK. Measuring body composition. Arch Dis Child. 2005 Jun 14;91(7):612–7.

56. Steinberger J, Jacobs DR, Raatz S, Moran A, Hong C-P, Sinaiko AR. Comparison of body fatness measurements by BMI and skinfolds vs dual energy X-ray absorptiometry and their relation to cardiovascular risk factors in adolescents. Int J Obes. 2005 Nov 1;29(11):1346–52.

57. Fields DA, Goran MI, McCrory MA. Body-composition assessment via air-displacement plethysmography in adults and children: a review. Am J Clin Nutr. 2002 Mar 1;75(3):453–67.

58. Nicholson JC, McDuffie JR, Bonat SH, Russell DL, Boyce KA, McCann S, et al. Estimation of Body Fatness by Air Displacement Plethysmography in African American and White Children. Pediatr Res. 2001 Oct;50(4):467–73.

59. Dewit O, Fuller N, Fewtrell M, Elia M, Wells J. Whole body air displacement plethysmography compared with hydrodensitometry for body composition analysis. Arch Dis Child. 2000 Feb;82(2):159.

60. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO consultation on obesity. Geneva: World Health Organization; 2000. Technical Report Series, No. 894:268.

61. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. Geneva, World Health Organization; 1995. Technical Report Series, No. 854:329. [Internet]. [cited 2016 Jul 29]. Available from: http://apps.who.int/iris/bitstream/10665/37003/1/WHO_TRS_854.pdf

62. Centers for Disease Control and Prevention. About Child & Teen BMI [Internet]. 2015. Available from: http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html

63. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Geneva, Switzerland: World Health Organization; 2007 Sep p. 660–7. (Bulletin of the World Health Organization). Report No.: 85(9).

64. Kuczmarski RJ, Ogden CL, Guo SS, et al. CDC Growth Charts for the United States: methods and development. Vital Health Stat. 2002 Nov:1–190.

65. Flegal KM, Ogden CL. Childhood obesity: Are we all speaking the same language? Adv Nutr Int Rev J. 2011 Mar 1;2(2):159S–166S.

66. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000 May;320(7244): 1240-3.

67. Reilly JJ, Kelly J, Wilson DC. Accuracy of simple clinical and epidemiological definitions of childhood obesity: systematic review and evidence appraisal. Obes Rev. 2010 Sep;11(9): 645-55.

68. Roberts KC, Shields M, de Groh M, Aziz A, Gilbert J. Overweight and obesity in children and adolescents: Results from the 2009 to 2011 Canadian Health Measures Survey. Stat Can Health Rep. 2012 Aug;Catalogue no. 82-003-X.

69. Lemelin L, Haggerty J, Gallagher F. Comparaison de trois systèmes de classification du poids de l'enfant d'âge préscolaire d'une région québécoise. Santé Publique Vandoeuvre-Lès-Nancy Fr. 2013 Oct;25(5):571–8.

70. Gonzalez-Casanova I, Sarmiento OL, Gazmararian JA, Cunningham SA, Martorell R, Pratt M, et al. Comparing three body mass index classification systems to assess overweight and obesity in children and adolescents. Rev Panam Salud Pública Pan Am J Public Health. 2013 May;33(5):349–55.

71. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. J Pediatr. 1998 Feb;132(2):204–10.

72. Garn SM, Leonard WR, Hawthorne VM. Three limitations of the body mass index. Am J Clin Nutr. 1986 Dec;44(6):996–7.

73. Pouliot MC, Després JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol. 1994 Mar 1;73(7):460–8.

74. Taylor RW, Jones IE, Williams SM, Goulding A. Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3–19 y. Am J Clin Nutr. 2000 Aug 1;72(2):490–5.

75. Kelishadi R, Mirmoghtadaee, P, Najafi, H, keikha, M. Systematic review on the association of abdominal obesity in children and adolescents with cardio-metabolic risk factors. J Res Med Sci. 2015 Mar;20(3):294–307.

76. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11-18y of age. Eur J Clin Nutr. 2004 Jul;58(7):1011–5.

77. Measured adult body mass index, by age group and sex, household population aged 18 and over excluding pregnant females, Canada (excluding territories) [Internet]. Statistics Canada; 2009 Jun. Report No.: CANSIM Table 105-0507. Available from: http://www5.statcan.gc.ca/cansim/a26?lang=eng&id=1050507

78. Body mass index of children and youth, 2012 to 2013 [Internet]. Statistics Canada; 2014 Oct [cited 2016 Jul 15]. (Health Reports). Report No.: 82–625–X. Available from: http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14105-eng.htm

79. Obesity in Canada: A Whole-of-Society Approach for a Healthier Canada. Report of the Standing Senate Committee on Social Affairs, Science and Technology. March 2016 [Internet]. [cited 2016 Jul 15]. Available from: http://www.parl.gc.ca/content/sen/committee/421/SOCI/Reports/2016-02-25_Revised_report_Obesity_in_Canada_e.pdf

80. Nilsson S. Research contributions of Eskil Kylin. Sven Med Tidskr. 2000;5(1),15-28.

81. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;365(9468):1415–28.

82. Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence worldwide populations. Endocrinolology Metabolism Clinics of North America. 2000;33(2):351-75.

83. Cook S, Auinger P, Li C, Ford ES. Metabolic syndrome rates in United States adolescents, from the National Health and Nutrition Examination Survey, 1999-2002. J Pediatr. 2008;152(2).

84. Huang TTK, Ball GDC, Franks PW. Metabolic syndrome in youth: Current issues and challenges. Appl Physiol Nutr Metab. 2007;32(1):13–22.

85. Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome - A new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med. 2006;23(5):469–80.

86. National Heart, Lung, and Blood Institute, National Institutes of Health. National Cholesterol Education Program ATP III Guidelines [Internet]. 2001 May p. 1–6. Report No.: NIH Publication No. 01-3305. Available from: http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf

87. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998 Jul; 15(7):539–53.

88. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung and Blood Institute scientific statement. Circulation. 2006 Jan ;21(2):1-6.

89. The IDF consensus definition of the metabolic syndrome in children and adolescents. [Internet]. International Diabetes Federation; 2007 p. 1–24. Available from: http://www.idf.org/webdata/docs/Mets_definition_children.pdf

90. Silveira L, Buonani C, Monteiro P, Antunes B, Freitas Junior I. Metabolic Syndrome: Criteria for diagnosing in children and adolescents. Encodrinol Metab Synd. 2013 Oct;2(3):1–6.

91. Huang, T. (2007). Metabolic syndrome in youth: current issues and challenges. Applied Physiology, Nutrition, and Metabolism, 32, 13–22.

92. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, Galluzzo A. Visceral Adiposity Index: A reliable indicator of visceral fat function associated with cardio-metabolic Risk. Diabetes Care. 2010;33(4):920-2.

93. Reaven GE, Abbasi F, McLaughlin T. Obesity, insulin resistance, and cardiovascular disease. Recent Progress in Hormone Research. 2004 Jan 1;59:207-24.

94. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: Findings from the Third National Health and Nutrition Examination Survey. J Am Med Assoc. 2002;287(3):356–9.

95. Ruderman, N., Chishold, D., Pi-Sunyer, X., & Schneider, S. (1998). The metabolically obese, normal-weight individual revisited. Diabetes, 47, 699-713.

96. Riediger ND, Clara I. Prevalence of metabolic syndrome in the Canadian adult population. CMAJ. 2011 Oct 18;183(15):e1127.

97. Setayeshgar S, Whiting SJ, Vatanparast H. Metabolic syndrome in Canadian adults and adolescents: prevalence and associated dietary intake. ISRN Obesity. 2012;2012:1-8.

98. Ardern CI, Katzmarzyk PT. Geographic and demographic variation in the prevalence of the metabolic syndrome in Canada. Can J Diabetes. 2007;31(1):34–46.

99. Kranz, S., Mahood, L.J., & Wagstaff, D.(2007). Diagnostic criteria patterns of U.S. children with Metabolic Syndrome: NHANES 1999–2002. Nutrition Journal, 6, 38-40.

100. van den Hooven, C., Ploemacher, J. & Godwin, M. (2006). Metabolic syndrome in a family practice population: Prevalence and clinical characteristics. Canadian Family Physician, 52(8), 983.

101. Isomaa, B., Almgren, P. Tuomik, T., et al. (2001). Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care, 24, 683-689.

102. Bayturan O, Tuzcu EM, Lavoie A, Hu T, Wolski K, Schoenhagen P, et al. The metabolic syndrome, its component risk factors, and progression of coronary atherosclerosis. Arch Intern Med. 2010;170(5):478–84.

103. Reilly MP, Rader DJ. The Metabolic Syndrome. Circulation. 2003 Sep 30;108(13):1546–51.

104. Cardiometabolic Risk Working Group: Executive Committee, Leiter LA, Fitchett DH, Gilbert RE, Gupta M, Mancini GBJ, et al. Cardiometabolic risk in Canada: a detailed analysis and position paper by the cardiometabolic risk working group. Can J Cardiol. 2011 Apr;27(2):e1–33.

105. Marmot M. Income inequality, social environment, and inequalities in health. J Policy Anal Manage. 2001 Feb;20(1):156–9.

106. Winkleby MA, Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. Am J Public Health. 1992 Jun 1;82(6):816–20.

107. Liberatos P, Link B, Kelsey J. The measurement of social class in epidemiology. Epidemiol Rev. 1988;10:87–121.

108. Duncan GJ, Daly MC, McDonough P, Williams DR. Optimal Indicators of Socioeconomic Status for Health Research. Am J Public Health. 2002 Jul;92(7):1151–7.

109. Krieger N, Williams DR, Moss NE. Measuring Social Class in US Public Health Research: Concepts, Methodologies, and Guidelines. Annu Rev Public Health. 1997 May;18(1):341–78.

110. Messer LC, Laraia BA, Kaufman JS, Eyster J, Holzman C, Culhane J, et al. The development of a standardized neighborhood deprivation index. J Urban Health Bull N Y Acad Med. 2006 Nov;83(6):1041.

111. Lynch JW, Kaplan GA, Salonen JT. Why do poor people behave poorly? Variation in adult health behaviours and psychosocial characteristics by stages of the socioeconomic lifecourse. Soc Sci Med. 1997 Mar 1;44(6):809–19.

112. Organisation for Economic Co-operation and Development. (2008). Growing Unequal: Income Distribution and Poverty in OECD Nations. Paris: OECD.

113. Average total income of the population 15 years and over by highest certificate, diploma or degree, by province and territory (2006 Census) (Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick) [Internet]. Ottawa, Ontario, Canada: Statistics Canada; 2009 Oct [cited 2016 Jul 19]. Available from: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/labor50a-eng.htm

114. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation. 1993 Oct 1;88(4):1973–98.

115. 2011 Census of Population, Statistics Canada Catalogue no. 98-311-XCB2011022. Statistics Canada; 2012 May.

116. Marmot M. Social determinants of health inequalities. Lancet. 2005 Mar;365(9464):1099–114.

117. Obesity in Canada: A joint report from the Public Health Agency of Canada and the Canadian Institute for Health Information. 2011 [Internet]. [cited 2016 Jul 7]. Available from: http://www.phac-aspc.gc.ca/hp-ps/hl-mvs/oic-oac/assets/pdf/oic-oac-eng.pdf

118. Reading, C.L. & Wien, F. (2009). Health Inequalities and Social Determinants of Aboriginal Peoples' Health. Prince George, BC: National Collaborating Centre for Aboriginal Health. [Internet]. [cited 2016 Jul 7]. Available from: http://www.sac-conference.ca/wp-content/uploads/2016/04/Fred-Wien-Social-Determinants-of-Health-Among-Aboriginal-Populations-in-Canada-Handout-21.pdf

119. Kaler SN, Ralph-Campbell K, Pohar S, King M, Laboucan CR, Toth EL. High rates of the metabolic syndrome in a First Nations Community in western Canada: prevalence and determinants in adults and children. Int J Circumpolar Health. 2006;65(5):389–402.

120. Raitakari OT, Juonala M, Kähönen M, Taittonen L, Laitinen T, Mäki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. JAMA. 2003 Nov 5;290(17):2277–83.

121. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. J Epidemiol Community Health. 2003 Oct;57(10):778–83.

122. Freedman DS, Kettel L, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. Pediatrics2005;115:22–27.

123. Spalding KL, Arner E, Westermark PO, Bernard S, Buchholz BA, Bergmann O, et al. Dynamics of fat cell turnover in humans. Nature. 2008 Jun 5;453(7196):783–7.

124. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report - NHLBI, NIH. Pediatrics. 2011 Dec;128(5):s213-56.

125. Tremblay MS, Gorber SC. Canadian Health Measures Survey: brief overview. Can J Public Heal Can Santee Publique. 2007 Nov;98(6):453–456.

126 .Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1 [Internet]. Statistics Canada; 2014 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V1-eng.htm

127 .Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 2 [Internet]. Statistics Canada; 2013 Apr. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D2_T1_V2-eng.htm

128 .Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 3 [Internet]. Statistics Canada; 2014 Sep. Available from: http://www23.statcan.gc.ca:81/imdb/p2SV.pl?Function=getSurvey&SDDS=5071&lang=en&db=imdb&adm=8&dis=2

129. Giroux S. Canadian Health Measures Survey: sampling strategy overview. Health Rep. 2007;18 Suppl:31–6.

130. Duncan GJ, Daly MC, McDonough P, Williams DR. Optimal Indicators of Socioeconomic Status for Health Research. Am J Public Health. 2002 Jul;92(7):1151.

131. Centers for Disease Control and Prevention, US Department of Health and Human Services. Clinical Growth Charts [Internet]. 2009. Available from: http://www.cdc.gov/growthcharts/clinical_charts.htm

132. World Health Organization. WHO: Global Database on Body Mass Index; The International Classification of adult underweight, overweight and obesity according to BMI [Internet]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html

133 .Canadian Guidelines for Body Weight Classification in Adults [Internet]. Ottawa, Ontario, Canada: Health Canada; 2003 [cited 2016 Mar 9] p. 1–41. Available from: http://preventdisease.com/pdf/weight_book-livres_des_poids_e.pdf

134. Patry-Parisien J, Shields M, Bryan S. Comparison of waist circumference using the World Health Organization and National Institutes of Health protocols. Health Rep. 2012 Sep;23(3):56–63.

135. MacPherson M, de Groh M, Wall R, Prud'Homme D, Jiang X, Dubois L. Establishing waist circumference percentiles for Canadian Children 6-10 years using reference data from the 1981 Canada Fitness Survey, the CHMS Cycles 1-3, and NHANES 1998-1994. [Publication pending].

136. Canadian Physical Activity Guidelines – Canadian Sedentary Behaviour Guidelines [Internet]. Canadian Society for Exercise Physiology; 2012 [cited 2016 Mar 9]. Available from: http://www.csep.ca/CMFiles/Guidelines/CSEP_Guidelines_Handbook.pdf

137. Hirshkowitz M, Whiton K, Albert S, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health. 2015 Dec;1(4):233–42.

138. American Academy of Pediatrics. National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992 Mar;89(3 Pt 2):525–84.

139. Genuth S, Alberti KGMM, Bennett P, Buse J, DeFronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care. 2003 Nov 1;26(11):3160–8.

140. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005 Apr 1;115(4):e500–3.

141. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics. 2004 Aug 1;114(Supplement 2):555–76.

142. Daskalopoulou S, Rabi D, Zarnke K, et al. The 2015 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol. 2015 May;31(5):549–68.

143. The IDF consensus worldwide definition of the metabolic syndrome [Internet]. International Diabetes Federation; 2007 p. 1–24. Available from: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf

144. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M, et al. Markers of inflammation and cardiovascular disease application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003 Jan 28;107(3):499–511.

145. Maximova K, Kuhle S, Davidson Z, Fung C, Veugelers PJ. Cardiovascular risk-factor profiles of normal and overweight children and adolescents: insights from the Canadian Health Measures Survey. Can J Cardiol. 2013 Aug;29(8):976–82.

146. Efron B, Tibshirani R. Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. Stat Sci. 1986 Feb;1(1):54–75.

147. Lambert M, Delvin EE, Levy E, O'Loughlin J, Paradis G, Barnett T, et al. Prevalence of cardiometabolic risk factors by weight status in a population-based sample of Quebec children and adolescents. Can J Cardiol. 2008 Jul;24(7):575–83.

148. Statistics Canada. Health Fact Sheets - Metabolic syndrome in Canada: 2009-2011. Ottawa (ON): Statistics Canada; 2012 [Statistics Canada, Catalogue No.: 82-625-X].

149. Haffner SM, Valdex RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin resistance syndrome (Syndrome X). Diabetes. 1992;41(6): 715-22.

150. McNeill AM, Rosamond WD, Girman CJ, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities study. Diabetes Care. 2005;28(2)385-90.

151. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, et al. Lipoprotein management in patients with cardiometabolic risk. J Am Coll Cardiol. 2008 Apr;51(15):1512–24.

152. Debra L. Parker P, Mary Ann Tucker P, Teresa K. Hoffmann P. Emerging risk factors and risk markers for cardiovascular disease: Looking beyond NCEP ATP III. Formulary [Internet]. 2009 Aug 1 [cited 2016 Jul 26]; Available from: http://formularyjournal.modernmedicine.com/formulary-journal/news/clinical/clinical-pharmacology/emerging-risk-factors-and-risk-markers-cardiov

153. Camhi SM, Katzmarzyk PT. Prevalence of cardiometabolic risk factor clustering and body mass index in adolescents. J Pediatr. 2011 Aug;159(2):303–7.

154. Lambert M, Delvin EE, Paradis G, O'Loughlin J, Hanley JA, Levy E. C-Reactive protein and features of the metabolic syndrome in a population-based sample of children and adolescents. Clin Chem. 2004;50(10):1762–8.

155. Prince RL, Kuk JL, Ambler KA, Dhaliwal J, Ball GDC. Predictors of metabolically healthy obesity in children. Diabetes Care. 2014 May;37(5):1462–8.

156. Fabbrini E, Yoshino J, Yoshino M, Magkos F, Tiemann Luecking C, Samovski D, et al. Metabolically normal obese people are protected from adverse effects following weight gain. J Clin Invest. 2015 Feb;125(2):787–95.

157. Karelis AD, Faraj M, Bastard J-P, St-Pierre DH, Brochu M, Prud'homme D, et al. The metabolically healthy but obese individual presents a favorable inflammation profile. J Clin Endocrinol Metab. 2005 Jul;90(7):4145–50.

158. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The framingham heart study. Circulation. 2008 Feb 12;117(6):743–53.

159. Daskalopoulou SS, Athyros VG, Kolovou GD, Anagnostopoulou KK, Mikhailidis DP. Definitions of metabolic syndrome: Where are we now? Curr Vasc Pharmacol. 2006 Jul;4(3):185–97.

160. Huang R-C, Prescott SL, Godfrey KM, Davis EA. Assessment of cardiometabolic risk in children in population studies: underpinning developmental origins of health and disease mother–offspring cohort studies. J Nutr Sci [Internet]. 2015 Apr 10 [cited 2016 Jul 26];4(e12). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4463019/

161. Roh EJ, Lim JW, Ko KO, Cheon EJ. A Useful Predictor of Early Atherosclerosis in Obese Children: Serum High-sensitivity C-reactive Protein. J Korean Med Sci. 2007 Apr;22(2):192–7.

162. Huang R-C, Mori TA, Burke V, Newnham J, Stanley FJ, Landau LI, et al. Synergy between adiposity, insulin resistance, metabolic risk factors, and inflammation in adolescents. Diabetes Care. 2009 Apr;32(4):695–701.

163. Must A, Anderson S. Pediatratic mini review. Body mass index in children and adolescents: considerations for population-based applications. Int J Obes. 2006;30:590–4.

164. Balkau B, Deanfield JE, Després J-P, Bassand J-P, Fox KAA, Smith SC, et al. International Day for the Evaluation of Abdominal Obesity: a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. Circulation. 2007 Oct 23;116(17):1942–51.

165. Sahakyan KR, Somers VK, Rodriguez-Escudero JP, Hodge DO, Carter RE, Sochor O, et al. Normal-Weight Central Obesity: Implications for Total and Cardiovascular Mortality. Ann Intern Med. 2015 Dec 1;163(11):827.

166. National Institutes of Health. The practical guide to the identification, evaluation and treatment of overweight and obesity in adults. Bethesda, Maryland: National Institutes of Health, 2000.

167. Verweij LM, Terwee CB, Proper KI, Hulshof CTJ, van Mechelen W. Measurement error of waist circumference: gaps in knowledge. Public Health Nutr. 2013 Feb;16(2):281–8.

168. Ulijaszek SJ, Kerr DA. Anthropometric measurement error and the assessment of nutritional status. Br J Nutr 1999;82(3):165-177.

169. Zhu S, Heshka S, Wang Z, Shen W, Allison DB, Ross R, et al. Combination of BMI and waist circumference for identifying cardiovascular risk factors in whites. Obes Res. 2004 Apr 1;12(4):633–45.

170. Janssen I, Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, et al. Combined influence of body mass index and waist circumference on Coronary Artery Disease risk factors among children and adolescents. Pediatrics. 2005 Jun 1;115(6):1623–30.

171. Ali M, Bullard K, Beckles G, Stevens M, Barker L, Narayan K, et al. Household income and cardiovascular disease risks in U.S. children and young adults: Analyses from NHANES 1999-2008. Diabetes Care. 2011;34(9):1998–2004.

172. Reid JL, Hammond D, Rynard VL, Burkhalter R. Tobacco Use in Canada: Patterns and Trends, 2014 Edition. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo.

173. Peterson JL, Puhl RM, Luedicke J. An experimental assessment of physical educators' expectations and attitudes: The importance of student weight and gender. J Sch Health. 2012 Sep;82(9):432–40.

174. Schvey NA, Puhl RM, Levandoski KA, Brownell KD. The influence of a defendant's body weight on perceptions of guilt. Int J Obes. 2013 Jan;1:1–7.

175. Schvey, NA, Puhl, RM, Brownell, KD. The stress of stigma: Exploring the effects of weight stigma on cortisol reactivity. Psychosom Med. 2014 Jan;76:1–7.

176. Puhl RM, Heuer CA. Obesity stigma: Important considerations for public health. Am J Public Health. 2010 Jun;100(6):1019–28.

177. Puhl RM, Peterson JL, Luedicke J. Fighting obesity or obese persons? Public perceptions of obesity-related health messages. Int J Obes. 2012 Sep;1–9.

178. Puhl RM. Weight stigmatization toward youth: A significant problem in need of societal solutions. Child Obes. 2011 Oct;7(2):1–15.

179. Wing RR, Phelan S. Long-term weight loss maintenance. Am J Clin Nutr. 2005 Jul 1;82(1):222S–225S.

180. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. Am J Clin Nutr. 2001 Nov 1;74(5):579–84.

181. Pate RR, Davis MG, Robinson TN, Stone EJ, McKenzie TL, Young JC. Promoting physical activity in children and youth: A leadership role for schools: A scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism (Physical Activity Committee) in collaboration with the Councils on Cardiovascular Disease in the Young and Cardiovascular Nursing. Circulation. 2006 Aug 28;114(11):1214–24.

182. Shields M, Connor Gorber S, Tremblay M. Estimates of obesity based on self-report versus direct measures article. Statistics Canada; 2009 Jun p. 1–17. (Health Reports, Vol. 19, No. 2). Report No.: 82-003.

183. Shields M, Connor Gorber S, Janssen I, Tremblay MS. Obesity estimates for children based on parent-reported versus direct measures. Statistics Canada; 2011 Sep. (Health Reports, Vol. 22, no. 3). Report No.: 82–003–XPE.

184. Thomas S, Wannell B. Combining cycles of the Canadian Community Health Survey – Methodological insights. Health Rep Stat Can Cat No 82-003-XPE. 2009 Mar;20(1):55–60.