Metabolic Syndrome and Chronic Disease in Canada: The Role of Material, Psychosocial, and Behavioural Factors

by

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Preface

The present thesis was completed in accordance with Canadian Tri-Council Policy on Research Ethics. Ethics approval was obtained for all three papers that are included in this dissertation: from the Ottawa Hospital Research Ethics Board for paper 1, and from the University of Ottawa Research Ethics Board for papers 2 and 3. Access to the Carleton, Ottawa, Outaouais Research Data Centre (COOL-RDC) was obtained for the purpose of analyzing data for papers 2 and 3. Copies of the ethics and RDC approval notices have been included in Appendix A. Paper 1 was a collaborative paper with Dr. Sulan Dai from the Public Health Agency of Canada, who enabled access to the data on site. Papers 2 and 3 were solely academic analyses, and data were accessed at the COOL-RDC.

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This thesis is the work of Deepa Rao under the supervision of Dr. Daniel Krewski and Dr. Heather Orpana. The research questions were a collaborative effort between the candidate and the thesis supervisors. Deepa Rao was involved in data cleaning, coding, statistical analyses, interpretation of the data, and manuscript development. Dr. Daniel Krewski provided guidance on statistical analyses and interpretation of findings. Dr. Heather Orpana provided guidance on statistical analyses, interpretation of data, and revised the entire thesis and associated works extensively.

Abstract

Introduction: Metabolic syndrome (MetS) is a risk condition describing a clustering of traditional cardiovascular risk factors. A number of risk and protective factors have been associated with MetS, and individuals with MetS are at a higher risk for developing chronic diseases such as diabetes, cancer, and cardiovascular disease.

Objective: To contribute to the understanding of MetS in Canada, and to describe how it is a risk state through which material, psychosocial, and behavioural factors associate with chronic diseases. This was examined through three objectives: (i) to describe the prevalence and distribution of MetS; (ii) to examine potential pathways linking income and education with MetS; and (iii) to examine the interplay between non-movement behaviours (NMBs, namely sleep, screen time, and sedentary behaviour) and MetS.

Methods: The Canadian Health Measures Survey (2007-2009, 2009-2011, ages 18 and older) was used for all analyses, which include logistic regression, multinomial regression, and calculation of standardized logit coefficients.

Results: MetS was prevalent among approximately 20% of Canadian adults. It was significantly associated with chronic diseases, such as diabetes (11.2% vs. 3.4% among those with MetS vs. the general population). A social gradient in MetS was identified, and the behavioural risk factors of alcohol use, smoking, physical inactivity, and screen time were suggested to be partial mediators of this pathway. Findings demonstrated that not adhering to physical activity guidelines (150 minutes or more of moderate-to-vigorous physical activity

per week) was associated with increased odds of MetS. A stepwise moderating effect of guideline adherence on screen time and sleep behaviours was demonstrated.

Conclusion**:** MetS is prevalent in Canadian adults, and a high proportion of individuals with MetS have chronic conditions. Addressing the modifiable determinants of physical inactivity, excess screen time, alcohol consumption, and smoking may reduce the social gradient in MetS. Furthermore, adhering to physical activity guidelines may mitigate the associations of NMBs with MetS. The current thesis suggests that healthy behaviours are associated with lower risk for MetS, and therefore, possibly for future chronic disease.

KEY WORDS: metabolic syndrome, cardiometabolic risk, physical activity, sedentary behaviour, non-movement behaviour, physical activity guideline adherence, social gradient

Acknowledgment

I would like to express my sincere gratitude to Dr. Daniel Krewski and Dr. Heather Orpana for giving me the opportunity to work with them. This thesis originated from my personal interest in the social determinants of health and chronic disease. I appreciate their support and guidance on this interdisciplinary topic, which aligns with their respective fields in distinct ways. From Dr. Krewski, I value the opportunity to learn and apply skills in statistical risk assessment. From Dr. Orpana, the introduction to methods in social epidemiology and perspective into the doctoral process was invaluable. Their commitment to support and advise me has been formative, and the lessons will stick with me in my future endeavours.

The ongoing support and encouragement from family, friends, and peers has been tremendous. To my family: thank you for setting the example for the value of commitment and perseverance. To my peers: thank you for fostering our collective development in the field of population health through insightful conversation and debate. To my husband: thank you for your encouragement and counsel through the doctoral process. And finally, a unique acknowledgment of the quote on my thesis notebook that took on new dimensions through my doctoral years and that now best describes the ingenuity and positivity I ascribe to them:

"Creativity is intelligence having fun"- Albert Einstein

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List of Acronyms

11B-HSD1	Beta-hydroxysteroid dehydrogenase type 1
ACR	Albumin: creatinine ratio
ANS	Autonomic nervous system
BMI	Body mass index
BP	Blood pressure
CHD	Coronary heart disease
CHMS	Canadian Health Measures Survey
CI	95% Confidence Interval
CKD	Chronic kidney disease
CMR	Cardiometabolic risk
cpm	Counts per minute
CRH	Corticotropin releasing hormone
CVD	Cardiovascular disease
DBP	Diastolic Blood Pressure
DNA	Deoxyribonucleic acid
DPoRT	Diabetes Population Risk Tool
EGIR	European Group for the study of Insulin Resistance
FFA	Free fatty acids
FPG	Fasting plasma glucose
FRS	Framingham Risk Score
GAS	Generalized Adaptation Syndrome
HDL-C	High density lipoprotein cholesterol
HPA	Hypothalamic pituitary adrenal
HR	Hazard ratio
ICD	International Classification of Diseases
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IL-6	Interleukin-6
IR	Insulin Resistance
LDL-C	Low-density lipoprotein cholesterol
MEC	Mobile examination clinic
METs	Metabolic equivalents
MetS	Metabolic syndrome
MVPA	Moderate-to-vigorous physical activity
NCEP	National Cholesterol Education Program
NHLBI	National Heart, Lung, and Blood Institute
NMB	Non-movement behaviour
OGTT	Oral Glucose Tolerance Test
OR	Odds ratio
PAI-1	Plasminogen activator inhibitor - 1
PCOS	Polycystic ovarian syndrome
rNCEP	Revised National Cholesterol Education Program
RR	Risk ratio or relative risk
SAM	Sympathetic adrenal medullary
SBP	Systolic Blood Pressure
SES	Socioeconomic status
SSB	Sugar sweetened beverages
T2DM	Type 2 diabetes mellitus

TNF- α	Tumour necrosis factor - α
UAER	Urinary albumin excretion rate
VLDL-C	Very low-density lipoprotein cholesterol
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio

CHAPTER 1: Literature Review

1.1 Introduction

1.1.1 Scope

In 2011, almost one in six (15.7%) Canadian adults were living with one or more chronic conditions[1]. These refer to those conditions that last a year or more and require ongoing medical attention and/or limit activities of daily living[2]. Chronic conditions represent the leading causes of death where, in 2011, cancers (29.9%), heart disease (19.7%) and type 2 diabetes mellitus (T2DM or diabetes) (3.0%) accounted for more than half of all mortality in Canada[3]. In the face of an aging population and anticipated associated increases in the prevalence of chronic disease, much focus has been placed on identifying avenues to prevent and control chronic disease[2].

To address the growing burden of chronic disease, prevention strategies aimed at identifying and treating disease in its early, most-treatable stages, have gained momentum. To assist health care professionals with this objective, action at these early stages seek to ease disease progression through prevention efforts rather than depending solely on curative care. This includes screening and treating individuals for distinct chronic disease risk factors, such as with hypertension to prevent possible future heart disease [4].

Metabolic syndrome (MetS), on the other hand, is a syndrome describing the co-expression of several risk factors that increases an individual's risk for a number of chronic diseases, such as cancer[5], T2DM[6] and cardiovascular disease (CVD)[7, 8]. It is an indicator of chronic

disease risk that represents an earlier stage in the etiology of disease. This dissertation explores the potential role of MetS as early indicator of chronic disease in the context of health promotion and chronic disease prevention.

1.1.2 Structure

This thesis is comprised of six chapters: a literature review, three original research papers, and a discussion. This chapter will provide a foundation in the MetS literature. The chronological development of the MetS concept, from its historical beginnings to its consideration in academia as a risk indicator, is first discussed so as to introduce the reader to the global context of this topic. Next, a comprehensive conceptual framework is presented that enables the reader to situate MetS in the natural history of disease[9] alongside concepts of the tiers of prevention and target populations (Figure 2, section 1.2.3). With this framework in mind, a logic model for MetS (Figure 3, section 1.3.1) is then introduced that will help guide the reader through the literature review. This logic model introduces the idea that MetS is associated with risk and protective factors as well as adverse health outcomes.

With this footing on how to conceptualize MetS more globally, the review subsequently examines attributes in detail. This begins with a detailed exploration of MetS in particular. The etiology of MetS, through discussion of contributing proximal and distal physiologic pathways, and the biomedical factors associated with it, are first explored. This is followed by a review of the literature regarding factors associated with MetS more broadly. Upstream determinants of MetS that fall under the psychosocial and behavioural paradigms are detailed, and then discussion focuses on downstream chronic diseases associated with MetS

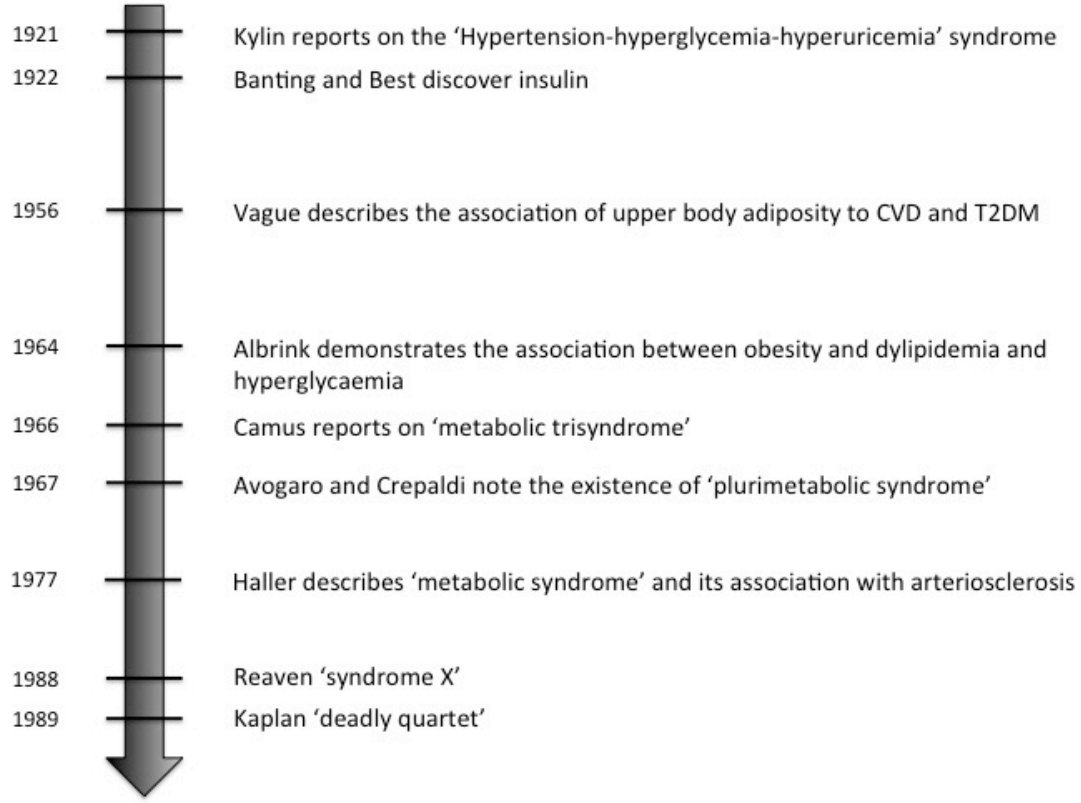
(Figure 3, section 1.3.1). Finally, we come to a fulsome discussion of MetS in the context of public health. This chapter concludes with an exposition of the goals of this thesis.

1.2 Conceptualizing Metabolic Syndrome

1.2.1 Importance of a Name

As far back as the 1920's, scientists were beginning to report on the abnormal clustering of cardiovascular risk factors. The Swedish physician Kylin reported the unusual co-occurrence of hypertension, hyperglycemia and gout[10, 11]. Following their discovery of insulin, Banting and Best [12] sparked expanded investigation into the mechanisms of insulin resistance (IR) [13, 14]. Later, Vague reported the association of upper body adiposity, versus lower body obesity, with factors linked to CVD and T2DM[15]. Soon, obesity was also suggested to relate with dyslipidemia and hyperglycaemia[16]. As more scientists began to note the clustering of risk states, various names for MetS started to appear. For example, in 1966, Camus reported on 'metabolic trisyndrome', consisting of diabetes, hyperlipidemia, and gout[17]. Next, in 1967, Avogaro and Crepaldi observed the co-presentation of obesity, hyperlipidemia, and diabetes, and sometimes coronary artery disease and hypertension, and named this 'plurimetabolic syndrome'[11]. Once the combination of cardiovascular risk factors and insulin were collectively seen to have a directing influence on the development of arteriosclerosis, Haller introduced the concept of what he termed MetS in 1977 (Figure 1)[18].

Figure 1. Timeline of development of the metabolic syndrome concept



With his Banting lecture in 1988, Gerald Reaven systematized the concept of a risk factor syndrome, Syndrome X, which described the clustering of hypertension, dyslipidemia, IR and glucose intolerance. He envisioned Syndrome X as a theoretical construct useful in describing the causes of disordered metabolism[19, 20]. Whereas Reaven did not necessitate obesity in his construct of MetS, but hypothesized its role as a risk factor for the development of the syndrome, Kaplan was soon describing the 'deadly quartet' condition relating upper-body obesity to hypertension, diabetes, and hypertriglyceridiemia via

hyperinsulinemia[21]. Once the World Health Organization (WHO) operationalized a clinical definition for what they termed as MetS in 1998, an alternate perspective of this syndrome as one warranting clinical diagnosis started to gain momentum and foster debate[22]. This definition, and the ones that follow, are summarized in Table 1.

In response to the WHO definition, the European Group for the study of Insulin Resistance (EGIR) proposed the inclusion of different indicators, such as the use of waist circumference in place of waist-to-hip ratio (WHR) or body mass index (BMI), and the exclusion of others, for example the removal of microalbuminuria as a criterion, so as to create a simpler definition. Their definition also excluded individuals with T2DM, whereas the WHO definition did not use diabetes status as an exclusion criterion. Finally, the EGIR also believed that IR Syndrome was a more appropriate name for the condition described by MetS.[23] It is noteworthy that both organizations agreed that IR or glucose intolerance was a central component to the identification of MetS.

Next, in 2001, the National Cholesterol Education Program (NCEP) released their definition for MetS. With their new definition, they switched emphasis to abdominal obesity as a surrogate for IR. Their definition was also more streamlined than those of the WHO and EGIR, such that once an individual met three of the five risk marker criteria, they would be classified as having the syndrome[24]. Revised again in 2004, their definition (revised NCEP or rNCEP) was easy-to-use and aimed to identify people at higher long-term risk of atherosclerotic cardiovascular disease[25]. Around this point in time, research and debate regarding MetS was starting to cast doubt on its utility due to the imprecise definition of the syndrome, the lack of certainty regarding its pathogenesis, and the absence of ethnicity

specific considerations[26, 27]. On this basis then, the WHO reversed their position on the utility of MetS, and instead conceded that while it offered an easily understood public health message, it had limited practical utility as a diagnostic or management tool[26].

Nevertheless, given the mounting interest into the syndrome, the International Diabetes Federation (IDF) released their definition for MetS in 2005. Their criteria were more inclusive due to a lowered glucose threshold and the fact that people who were previously excluded, i.e. those currently undergoing treatment for high glucose, triglycerides or high-density lipoprotein cholesterol (HDL-C) abnormalities, could now be included. Furthermore, in recognition of evidence that relate the degree of obesity associated with increased chronic disease risk differed by population subgroups, the IDF used ethnic-specific waist circumference thresholds in their definition[28]. For example, given the same level of excess abdominal fat, T2DM is consistently more prevalent among Asians than Europids[28, 29].

By 2009, there was no consensus on the most appropriate definition to use for MetS. The rNCEP definition was widely used, but because of the range of definitions being used, prevalences from various studies and within different populations were not easily compared. This was by way of, for example, that only some definitions included treatment as a criterion or that only some used ethnic-specific waist circumference cut-offs, leading to different prevalence estimates depending on the definition used[30]. For example, in a comparison between definitions of MetS applied to the same study population, Carlsson et al. found that 23.5% were considered to have MetS using the EGIR definition, 38.4% using the IDF definition, and 31.8% using the NCEP definition[31]. Another weakness was the fact that some

commonly used definitions for MetS may underestimate the true prevalence based on ethnic background[32].

Growing concerns ultimately led to a discussion between the IDF and NHLBI-American Heart Association to create a practical definition for MetS that could be used worldwide. Their collaboration resulted in the definition now referred to as the 'Harmonized' definition. The Harmonized definition was created in hopes of addressing such issues, but the transition to using this definition is still underway. It is noteworthy that Alberti et al. make mention of the IDF ethnic specific waist-circumference cut-offs for their Harmonized definition, but do not clearly designate whether or not that is the preferred method for identifying central obesity in their definition[33] (Table 1).

Table 1. Definitions for metabolic syndrome

	WHO [22] 1998	**EGIR** [23] 1999	**rNCEP** [25] 2004	**IDF** [28] 2005	**Harmonized** [33] 2009
Criteria for identification	IR (T2DM, IFG, IGT) and ≥ 2 risk markers	IR or IGT and ≥ 2 risk markers	≥ 3 risk markers	Central Obesity and ≥2 of the risk markers	≥ 3 of the risk markers
Central Obesity	BMI ≥ 30kg/m^2 and/or WHR >0.90 (M) WHR >0.85 (F)	WC ≥ 94 cm (M) WC ≥ 80 cm (F)	WC ≥ 102 cm (M) WC ≥ 88 cm (F)	Europids WC ≥ 94 cm (M) South Asians, Chinese, Japanese, Ethnic &Central South Americans WC ≥ 90 cm (M) Japanese WC ≥85cm(M) All ethnic groups: WC ≥ 80cm (F)	Europids WC ≥ 94 cm (M) South Asians, Chinese, Japanese, Ethnic &Central South Americans WC ≥ 90 cm (M) Japanese WC ≥85cm(M) All ethnic groups: WC ≥ 80cm (F)
Triglycerides	≥ 1.7 mmol/L	≥ 2.0 mmol/L or treatment	≥ 1.7 mmol/L	≥ 1.7 mmol/L or Treatment	≥ 1.7 mmol/L or Treatment
HDL - C	< 0.9 mmol/L (M) < 1.0 mmol/L (F)	< 1.0 mmol/L or treatment	< 1.0 mmol/L (M) < 1.3 mmol/L (F)	< 1.0 mmol/L (M) < 1.3 mmol/L (F) or Treatment	< 1.0 mmol/L (M) < 1.3 mmol/L (F) or Treatment
Blood pressure (BP)	SBP ≥140 mmHg or DBP ≥ 90 mmHg or treatment	SBP ≥140 mmHg or DBP ≥ 90 mmHg	SBP ≥130 mmHg or DBP ≥ 85 mmHg	SBP ≥130 mmHg or DBP ≥ 85 mmHg or Treatment	SBP ≥130 mmHg or DBP ≥ 85 mmHg or Treatment
Glucose	IR (T2DM, IFG or IGT) or FPG ≥ 6.1 mmol/L	FPG ≥ 6.1 mmol/L	FPG ≥ 5.6 mmol/L	FPG ≥ 5.6 mmol/L or diagnosis with T2DM	FPG ≥ 5.6 mmol/L or Treatment
Additional criteria	Microalbuminuria UAER ≥ 20g/min or ACR ≥ 30mg/g	-	-	-	-
Inclusion of patients with T2DM	Yes	No	Yes	Yes	Yes

* (M) – Males, (F) – Females, WHR – waist to hip ratio, BMI – Body mass index, WC – waist circumference, OGTT – Oral Glucose Tolerance Test, IFG- impaired fasting glucose, IGT – impaired glucose tolerance, FPG – Fasting plasma glucose, UAER – Urinary albumin excretion rate, ACR – albumin:creatinine ratio

1.2.2 Shifting focus and measuring risk

Considerations of a dysmetabolic state began with an academic appreciation of the atherogenic and diabetogenic pathophysiologic states described in section 1.2.1 that describe cardiometabolic risk (CMR). CMR is a broad term used to describe an array of abnormal physiologic states such as inflammation, elevated blood pressure, and dyslipidemia that is diverse and not systematized. Within the constellation of factors captured under the term CMR, one finds the distinct diagnosable clinical entity of MetS, which is identified on the basis of having 3 or more of 5 CMR risk markers present, and as such, gives equal importance to each of the component risk markers[34].MetS is a simple screening tool used to identify individuals who might be at a greater risk for associated chronic disease[35]. The equal weighting of the five component factors presumes that the subgroups of combinations that may be formed are physiologically similar with regard to clinical prognosis, whereas more recent research is suggestive of the different associations on the basis of risk marker combinations[36]. Nevertheless, it is worth noting that MetS is a screening tool to identify risk using a limited subset of parameters that more globally describe CMR. While it is true that MetS restricts discussion of CMR to a few of many important characteristics of chronic disease risk, it provides a standard definition for a dysmetabolic state that may be used to study associations across the natural history of disease[9].

In Canada, a study by Riediger et al. identified that the prevalence of MetS among Canadian adults was 19.1% using the Harmonized definition[37]. In a time trend analysis of MetS between 2003 and 2012 using the NCEP definition, Aguilar et al. demonstrate how the overall prevalence of MetS in the United States was 33% (32.5%-33.5%), and increased

from 32.9% (31.6%-34.2%) in 2003-2004 to 34.7% (33.5%-36.0%) in 2011-2012. Overall rates, however, have remained stable between 2007 and 2012[38].

1.2.3 Identifying and Understanding Risk

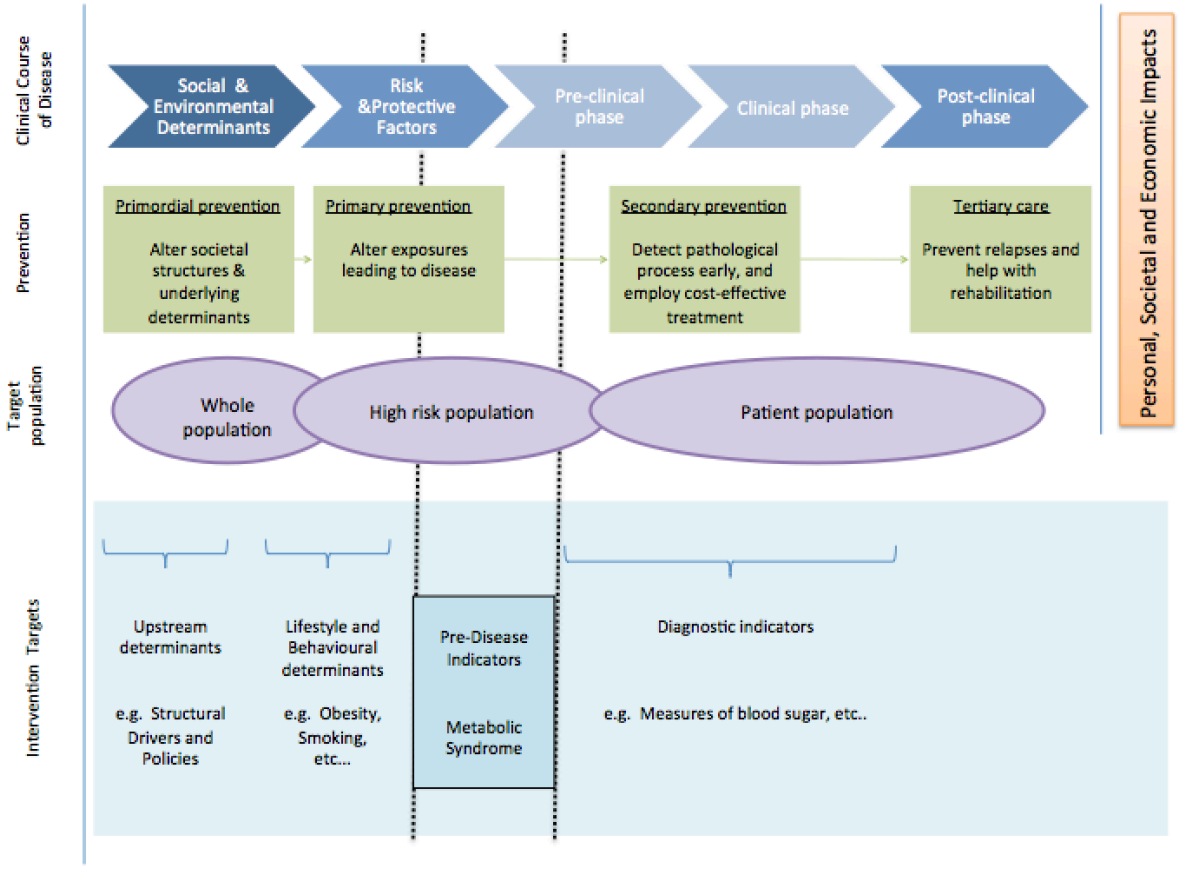
The utility of MetS has also been called into question with respect to its effectiveness to predict future chronic disease. Studies have demonstrated a gradient in risk as the number of MetS risk factors increase[27, 39-42]. For example, in an examination of current blood pressure control in patients with multiple atherosclerotic risk factors in the U.S. and Canada, authors noted that as the number of concomitant CVD risk factors increased (including factors such as smoking, obesity, diabetes, dyslipidemia and chronic kidney disease (CKD)), the prevalence of hypertension increased as did the proportion of individuals who had their hypertension controlled. It is noteworthy that hypertensives exhibited similar risk factor profiles to those with uncontrolled blood pressure, and overall CVD risk as calculated using Framingham scores were substantially higher among individuals who achieved guideline-recommended hypertension targets as compared with normotensive individuals[4]. So, while there have been notable reductions in the rates of hypertension in particular, the consistently high prevalence of additional CVD risk factors could blunt the potential magnitude of reductions in CVD morbidity and mortality that would have been expected[4, 43]. This study highlights a limitation with treatment aimed at attainment of target levels for individual risk factors, and suggests the utility of considering all atherosclerotic risk factors.[44]

In addition to risk factor patterning, research on MetS has demonstrated its association with increased relative risk of future disease. In a meta-analysis of prospective studies examining

its associated risk with CVD, individuals with MetS had increased mortality from all causes (RR 1.35, 1.17-1.56) and CVD (RR 1.74, 1.29-2.35). Increased incidence of CVD (RR 1.53, 1.26-1.87), coronary heart disease (RR 1.52, 1.37-1.69), and stroke (RR 1.76, 1.37-2.25) were also identified[7]. Similarly, the fixed-effects summary relative risk for incident diabetes was identified as 5.16 (4.43, 6.00)[45]. Though the concept of MetS grew out of the recognition that risk factors clustered together greater than predicted by chance, there has been speculation as to whether the predictive value of the syndrome is better than that of the individual risk factors that comprise it. This question has been examined, and while some studies have hinted that 'the sum is greater than the parts'[46, 47], as in the syndrome addressing the risk markers collectively is more informative than treating risk markers independently, many instead suggest the opposite[27, 40, 48-50].

Such population findings are thus suggestive of MetS as an early indicator of chronic disease. It is worthwhile then to conceptualize MetS in the context of prevention targets. Unlike more upstream risk factors such as obesity and smoking habits, which are common targets for population based primary prevention strategies, MetS is further downstream in the course of disease development. On the other end of the natural history of disease spectrum, MetS is not as developed an intervention target as those proposed for secondary prevention efforts, such as screening targets like elevated low-density-lipoprotein cholesterol levels which identify individuals as being at high risk for CVD. MetS criteria are more lenient than those used in screening guidelines, and serves to include a larger subset of the population as being at risk. Therefore, it might be worthwhile to situate MetS as an intermediary risk indicator situated between targets for primary and secondary prevention (Figure 2).

Figure 2. Metabolic Syndrome and Health



As a natural consequence of research suggestive of MetS as an early indicator of chronic disease, scientists have looked into the predictive power of MetS relative to other tools for determining risk of adverse events. One common comparison is to the Framingham Risk Score (FRS), which is a widely recommended predictive risk tool that identifies individuals at high risk of a CVD event. In comparison to this tool, the predictive power of MetS for CVD appears to be weaker (area under the receiver operator curves for 10-year risk of Coronary Heart Disease was 0.63 using MetS vs. 0.73 using FRS)[51]. These critiques fail to appreciate the key differences between these predictive tools. For example, the FRS is meant to assist with the identification of individuals at immediate or short-term risk for a CVD event (usually within a 10-year period), while MetS is meant to gauge future longer-term

risks. For instance, there is little predictive power gained by adding abdominal obesity, triglycerides or fasting glucose to the FRS tool, since they come into play in the longer term[52]. The former converts a risk score to an estimate of absolute risk based on measures such as LDL-C levels and family history alongside risk probability derived from prospective data. The latter is a measure of relative risk that uses commonly captured lab test measures[29]. The benefit of the latter is further evidenced by the broad-ranging criteria for the inclusion of individuals as having MetS. They allow for a larger population subset to be considered as having MetS and at risk for its associated adverse health outcomes. With a wider population identified, it's no surprise that the relative risk and specificity of disease associated with MetS versus FRS is lower. But, the advantage MetS has by virtue of it including a larger population subset is that it identifies individuals earlier on in the development of illness in such a manner that these individuals could benefit greatly from less invasive interventions to prevent future chronic disease, such as through lifestyle modification and other preventive interventions.[42]

1.3 Determinants of Metabolic Syndrome

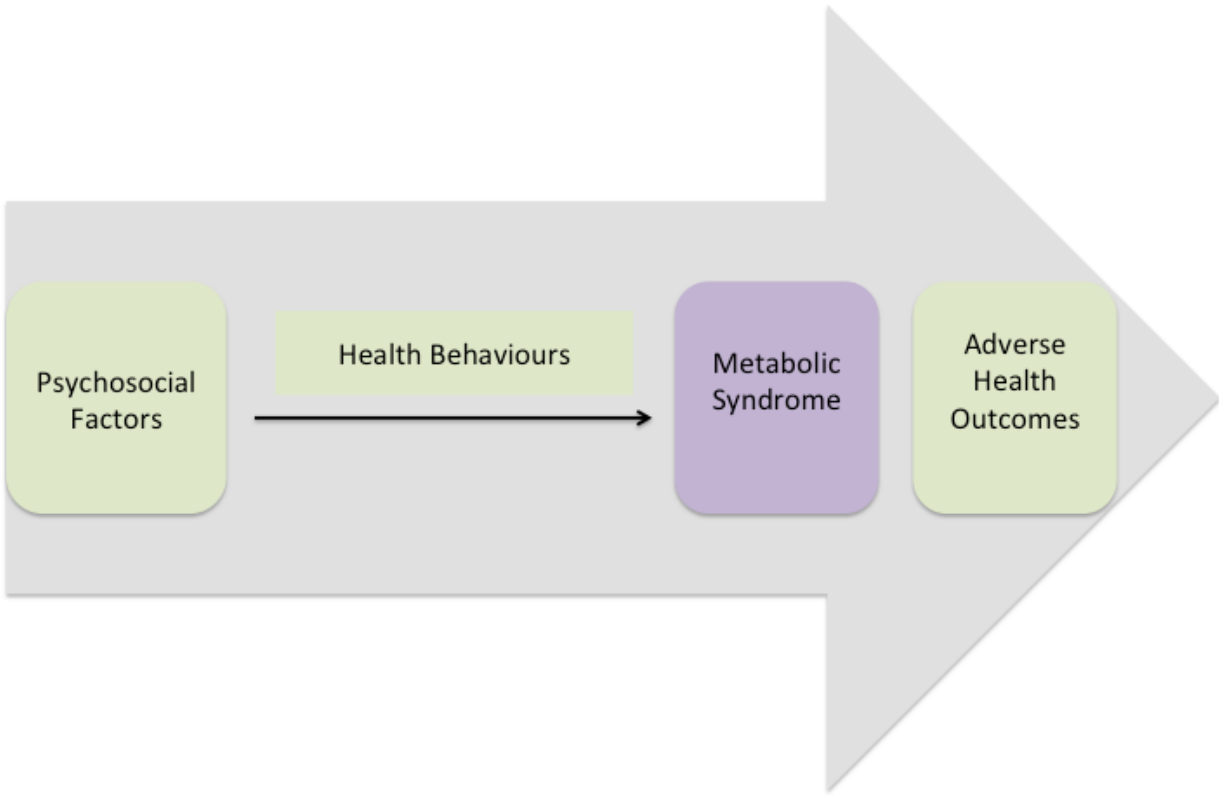
1.3.1 Factors influencing Metabolic Syndrome

Advances in medical innovation and treatment have assisted with the transition of populations away from mortality due to infectious diseases. In its place, we now have increasing rates of non-communicable and degenerative diseases.[53, 54] The evolution from being hunter gatherers, to a society plagued by infectious diseases, to our most recent status where CVD and diabetes are prevalent chronic conditions has been described by the four stages of the epidemiologic transition.[54] It has been proposed that we now find ourselves in the fifth phase, an age of obesity and physical inactivity.[55] Increased caloric intake, reduced

physical activity and the increased consumption of refined carbohydrates have all contributed to a surge in obesity, now at approximately 24% in Canada and 34% in the United States.[53] In the context of the fifth stage of the epidemiologic transition, addressing adverse health will require understanding that a range of personal, cultural, social, economic and environmental factors interact to affect variations in health outcomes. This interplay of determinants is well described by Etches' Conceptual Framework of Population Health [56].

These same determinants, both the upstream (e.g. social and economic) and downstream (e.g. gender and age) determinants, have a directing role in MetS status and chronic disease risk. The explanatory determinants contributing to MetS status that we propose to examine are depicted in Figure 3, and can be broadly grouped as being biomedical, psychosocial, and behavioural factors. The sections that follow will discuss these same groupings of risk factors in the same order.

Figure 3. Explanatory Model for metabolic syndrome



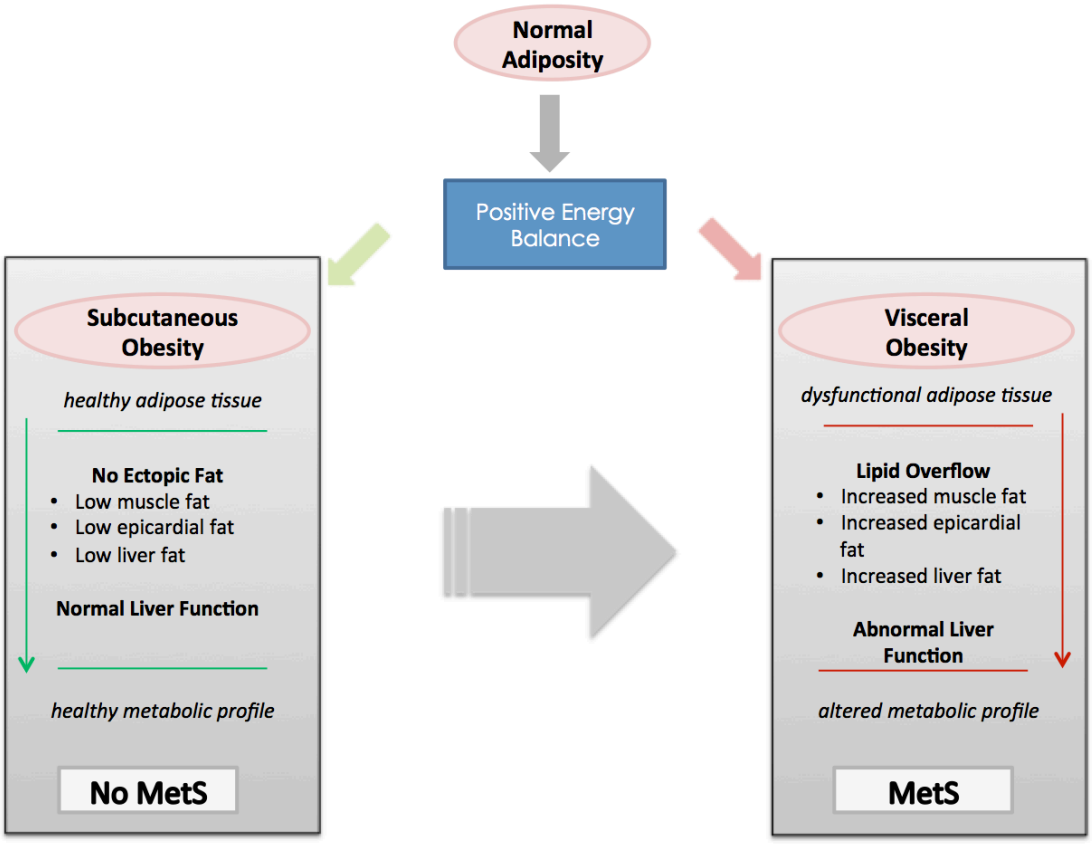
1.3.2 Etiology

1.3.2.1 Proximal Pathways to MetS

From a biomedical standpoint, two components stand out as part of the etiologic construct for the pathogenesis of MetS: positive energy balance (i.e. obesity) and IR. Both these components are interrelated and are also mediated by the effects of immunologic, hepatic or vascular factors.[25, 57] In describing the etiologic construct for MetS, we also demonstrate how each of the risk markers that constitute MetS develops.

Obesity is a well-established risk factor for chronic disease, and often precedes the hyperinsulinemic state of MetS.[35, 58, 59] The NCEP and the IDF have both taken the position that obesity is a key trait that influences MetS risk marker aggregation.[24, 28, 59] When caloric intake exceeds caloric expenditure, the ensuing positive energy balance can result in obesity.[35] This excess energy may be stored in healthy subcutaneous adipose tissue, or alternatively, in dysfunctional visceral adipose tissue or ectopic sites (Figure 4). Healthy subcutaneous adipose tissue acts as a metabolic sink, and provides for a normal metabolic profile and a reduced likelihood of MetS. When subcutaneous adipose tissue becomes dysfunctional, or can no longer serve as a fat storage location, adipose tissue becomes visceral fat[35]. In this form, adipose tissue begins to accumulate in ectopic sites and the abdominal viscera (overflow hypothesis)[35, 60] Visceral fat deposits on ectopic sites, such as the epicardium, muscle, and the liver. This type of fat appears to be more metabolically active than the subcutaneous type, and will often empty directly into the hepatic portal circulation, yielding elevated levels of circulating plasma free fatty acid (FFA, mechanism 1) on the liver, and thereby impacting cholesterol metabolism. Taken together, this pathway started by visceral adiposity is associated with abnormal metabolic profiles and MetS (Figure 4).

Figure 4. Obesity and the Lipid Overflow Hypothesis



- adapted from Despres et al. [35]

The onslaught of FFA brought on by visceral adiposity results in elevated very low-density lipoprotein cholesterol (VLDL-C) secretion, reduced insulin clearance, hypertriglyceridemia, and dysregulation of gluconeogenesis[19, 61, 62]. In the presence of this elevated FFA state, there is a decrease in the cholesterol content of HDL-C, leading to an increased clearance of HDL-C from the circulation, and an ensuing increase in circulating LDL-C. Elevated plasma FFA also work to inhibit insulin's anti-lipolytic action, which then further increases the rate of FFA release into the circulation.[63] Circulating FFAs also inhibit insulin-mediated glucose

uptake by reducing the insulin sensitivity of muscle, which then provokes insulin secretion from the pancreas and results in hyperinsulinemia (decreased insulin clearance).[30] Further outcomes include glucose intolerance through increased hepatic glucose production, and hypertriglyceridemia.[34]

Since adipocytes function as an endocrine organ (mechanism 2), the adipokines they release trigger additional physiologic processes associated with MetS, such as via the release of interleukin-6 (IL-6), and tumour necrosis factor-α (TNF-α), which both stimulate inflammatory processes, and plasminogen activator inhibitor-1 (PAI-1), which inhibits fibrinolysis and thereby promotes clotting[64, 65]. This endocrine functions of adipose tissue thus contributes to an altered metabolic profile demarcated by IR, and proinflammatory, prothrombotic and prohypertensive states[34].

A final route associating adipocytes to associated dysmetabolism is through lipodystrophy (mechanism 3). Individuals with positive energy balance may be unable to store excess fat as subcutaneous adipose tissue because of its inability to expand, or because adipose tissues have hypertrophied, become dysfunctional, or insulin resistant. It is thought that these three mechanisms - through excess FFA, endocrine effects, and lipodystrophy- all work in combination to instigate dysmetabolism[34].

Exploring the association of obesity with MetS has served to explain the association of some of its component risk markers, such as hyperinsulinemia, elevated waist circumference, reduced HDL-C, and hypertriglyceridemia. Hypertension, the fifth risk marker identifying MetS, is also associated through a variety of mechanisms. FFAs (mechanism 1) mediate

vasoconstriction by inducing oxidative stress and creating a proinflammatory environment. Their action can also result in sympathetic hyperfunctioning through their effects on factors such as insulin, leptin, and nitric oxide. Because adipocytes can release increased levels of angiotensinogen (mechanism 2), which influences the renin-angiotensin system, they can increase sodium resorption and thus elevate blood pressure[66, 67]. IR also causes increased sodium resorption in the kidney and elevated blood pressure[68]. In this manner, the increased levels of circulating FFAs and their adipokines result in obesity induced IR and its secondary effects[62].

Some suggest that IR might trigger many of the processes described above. The hyperinsulinemic state induced by IR can in turn result in obesity, to which it is closely associated, but also result in pancreatic beta cell exhaustion and atherogenic dyslipidemia due to high FFA flux[19, 30, 57]. Insulin connects with more indirect pathways leading to MetS. More specifically, insulin is known to stimulate the uptake and metabolism of glucose. Its uptake in the ventromedial nucleus of the hypothalamus suppresses an inhibitory pathway between regulatory cells and the brain stem. Thereby, tonically active sympathetic regulatory centres in the brain are disinhibited, and sympathetic activity increases. This leads us into a discussion of distal contributors to the development of MetS[69].

1.3.2.2 Distal Pathways to Metabolic Syndrome

Beyond the factors more directly implicated in the etiology of MetS, there are a number of distal biological processes that influence its development. Broadly speaking, these feed into how the determinants described in section 1.3.1 might associate with MetS status[56]. The

autonomic nervous system (ANS), for example, has been implicated in the progression of MetS by virtue of its role in maintaining hemostasis. The ANS is comprised of two systems, the sympathetic "fight or flight" system and the parasympathetic "rest and digest" system. Their actions work both centrally and peripherally to produce a variety of responses. When an individual experiences threats to homeostasis, or allostasis (defined more specifically in the context of stress in section 1.3.4.2), this triggers an allostatic response aimed to maintain physiologic stability by changing parameters in the internal milieu in relation to environmental demands. Real or interpreted threats initiate the sympathetic-adrenal-medullary (SAM) axis to release catecholamines and the hypothalamic-pituitary-adrenal (HPA) axis to secrete glucocorticoids. Both these hormones mobilize the 'flight-or-fight' stress response so as to change physiological parameters to meet environmental demands [70]. While these allow for acute adaptation to stress, a chronic over-activation of these pathways[71] induces a chronic response. This has been described by McEwen as the allostatic load model of chronic stress, which postulates a sequential chain of deregulation of multiple systemic mediators, such as through the prolonged actions of cortisol and epinephrine or suppressed cellular immunity[70, 72].

Selye's model for Generalized Adaptation Syndrome (GAS) presents a biological explanation for the chronological development of the response to stressors when their presence is prolonged[73]. It consists of three stages. First there is the alarm stage, which is the initial reaction to a stressor that immediately triggers the fight or flight response as described in the previous paragraph. Through the activation of the SAM and HPA-axes, stress hormones such as adrenaline, norepinephrine and cortisol are released. Next, after the body has responded to the stressor, there is the resistance stage where the stressor is either

eradicated or reduced. The body is weaker and allocates energy to repair damaged muscle tissue from the effects of the first stage. The body is still on guard, and may still be producing a response to the stressor, although one that is more adapted and not as strong as the initial response. The final stage, the exhaustion phase, is when the stress has persisted for a longer period of time. In this chronic state of stress, the body loses its ability to combat stressors since its adaptive energy has burned out[73, 74]. This final stage is akin to what we anticipate based on the allostatic load model[70].

It has been suggested that characteristics of modern society, such as the predominance of the Western diet and sedentary lifestyles, have contributed to positive energy balance and obesity[71, 75]. As described in section 1.3.2.1, this can initiate a number of biological pathways leading to adverse health outcomes. These stimuli can also stimulate the sympathoadrenal system. The HPA axis is a major neuroendocrine system that starts with the release of corticotropin-releasing hormone (CRH) from the hypothalamus, which then stimulates the release of adenocorticotropin from the anterior pituitary, and finally stimulates cortisol production from the adrenal cortex. Cortisol is transported through the circulation to promote a wide variety of biological responses, such as impaired glucose tolerance and hypertension in more chronic states of stress. At a more local level, the expression of local adipose tissue enzymes contributes to the metabolism of cortisol. The enzyme beta-hydroxysteroid dehydrogenase type 1 (11B-HSD1), which converts inactive cortisol to its active form, has been shown to associate with obesity in autocrine and paracrine activities on adipose and surrounding tissues[71, 76].

In conclusion, biological pathways associated with the development MetS, and ultimately chronic conditions, can arise from both proximal and distal influences that relate to a wide range of factors, as described in Figure 3.

1.3.3 Biomedical Factors

1.3.3.1 Genetics

Genetics is the study of genes, or portions of deoxyribonucleic acid (DNA) that code for known cellular processes. Heredity and variation in living organisms can be attributed to differences in genes and/or their expression. A genome-wide study by Love-Gregory et al. identified five genetic variants in the CD36 gene that were associated with an increased risk of metabolic syndrome. These genes have been shown to play an important role in fatty acid metabolism, which factors into the etiology of MetS [77]. There also appears to be an association between genetic markers of chronic conditions and MetS, as evidenced by polymorphisms in susceptibility genes for obesity and polycystic-ovarian syndrome (PCOS) (the FTO gene) and T2DM (the TCF7L2, WFS1, and IGF2BP2 genes) that have been shown to also predispose an individual to MetS [78, 79]. Genetic factors thus may also be associated with MetS status.

1.3.3.2. Age

Ageing is one of the main risk factors for disease.[80] Individuals accumulate the changes they've experienced through life as they age. This process is multidimensional, and captures not only physical changes through time, but also its social and psychological dimensions.

Older age is related to an increased odds of MetS. In an examination of MetS prevalence across age groups, Riedeger et al. found that rates jumped from 17.0% in Canadians aged 18-39 years to 39.7% in those aged 60-69 years.[37] Aging of adipocytes also contributes to the overflow hypothesis. The latter suggests that once the capacity of adipocytes has been exceeded, triglycerides accumulate in hepatocytes, skeletal muscles and visceral adipocytes. This then leads to a state of IR, which has been shown to associate with increased age[60, 81]. Complex hormonal changes associated with aging, such as decreases in growth hormone and testosterone, and the reduced responsiveness to leptin and thyroid hormone, further contribute to changes in body composition that promote IR[82-84].

1.3.3.3 Sex

Unique biological and physiological attributes differentiate the sexes. These include hormones that are specific to each sex, and which have been suggested to describe the variations in the prevalence of MetS by sex. For example, although reports suggest that the prevalence of MetS is not significantly different between the sexes[37, 85], some of its component factors are. For instance, one of the component risk markers for MetS, abdominal obesity, is well known to vary on the basis of sex. More specifically, women are known to have more subcutaneous fat and less visceral fat than men, but this changes after menopause[86-88].

In a study of men and women over 40 years of age, MetS was shown to be associated with all-cause, cardiovascular and non-cardiovascular mortality in women, but not in men. Furthermore, these associations were significant only among postmenopausal women (all-

cause mortality OR 1.87, 95% CI: 1.22-2.85 in women aged 65 and older vs. OR 1.48, 95% CI: 0.68-3.23 in women aged <65 years). Therefore, menopausal status is an effect modifier. This might be explained by biological changes specific to menopause, such as a propensity for central obesity and its associated occult T2DM [89]. As described in section 1.3.2.1, visceral fat induces sub-chronic inflammation, which then increases the risk for hyperinsulinemia and atherogenic dyslipidemia.

The contribution of sex hormones is not specific to women. In a study of men, higher levels of bioavailable testosterone were shown to be associated with lower odds of MetS and lower cardiovascular mortality among those with MetS (OR 0.80, CI: 0.76-0.84). Among those with MetS, cardiovascular death was more likely among those with low bioavailable testosterone vs. those with normal levels (Hazard ratio (HR) 1.90, CI: 1.12-3.22 vs. 0.82, 95%CI: 0.35-1.89 respectively). The influence of testosterone levels was not significantly associated with cardiovascular mortality in those without MetS. Decreased testosterone levels and MetS were similarly associated with all-cause and cancer mortality[90]. While the direction of causality linking MetS to testosterone is not clear, studies suggest that hyperinsulinemia and obesity may reduce testosterone production.[91] On the other hand, a reduction in androgens can contribute to IR, a major contributor to MetS.[92]

1.3.3.4 Ethnic Group

Ethnicity is a term used to socially identify categories of individuals who share common ancestral, social, and cultural experiences. This social identity can be a useful proxy for unique biologic features and genetic diversity as well, but should not limit consideration of

identity influences due to non-biologic factors.[93] Nonetheless, it is common for geneticists and researchers to use the term ethnicity to deconstruct the relationship between biologic identity and health.

In section 1.3.3.1, the associations of genetic factors with MetS were discussed. It is possible then that genetic variations between groups are partly responsible for the differences in MetS risk by ethnic groups. For instance, studies have demonstrated ethnic based differences in the rates of MetS. Compared to non-Hispanic white Americans, the odds of MetS in non-Hispanic Black and Hispanic Americans was 2.70 (CI: 1.96-3.73) and 4.18 (CI: 3.01-5.79) respectively[85]. However, since ethnicity is also associated with psychosocial and behavioural factors, the distinction is not always so clear-cut.

A common attribute confounding diagnosis with MetS is the discrepancies in the prevalence of individual risk markers by ethnicity. For example, using the NCEP definition, the prevalence of MetS is lower in Black men and this seems to be due to lower levels of triglycerides[94] and HDL[95] in this ethnic group despite their high levels of hypertension[95]. It is striking then to see the higher than expected rates of Coronary Artery Disease among Black men given their reported prevalence of MetS. The process underlying the etiology of MetS manifest differently by ethnic group[96-98], and the inclusion of ethnic-specific cutpoints in the Harmonized definition seeks to account for these patterns.

In their proposal for ethnicity-specific waist circumferences, the IDF demonstrated how the rates of MetS vary in different ethnic groups when consideration of ethnic background was not applied. They showed that, using the rNCEP definition, the rates of MetS in men was

19.5% in Australia, 10% in France and 10.6% in Mauritius. Citing clear differences in the relationship between adiposity, abdominal obesity and visceral fact accumulation, the IDF suggested ethnicity-specific waist circumferences as a better indicator of obesity related risk.[99] Taken altogether, these findings support ethnicity as a determinant of MetS status.

1.3.4 Psychosocial Factors

1.3.4.1 Socioeconomic Status (Income and Education)

An individual's combined economic and social status defines their socioeconomic status (SES)[100]. For this thesis, income and education will be used since they relate to an individual's access to resources and assets to support their success. Education, for example, is a social and knowledge resource. As such, it can serve as a "social" marker of an individual's status in the social hierarchy linked to ideas of rank and prestige. Income, in addition to signalling status, rank and prestige, is also proxy for material resources and represents the "economic" aspects of SES. These measures are certainly related, but not necessarily enough to be redundant[101]. Furthermore, SES has been linked to health. More specifically, the theory that social circumstances affect health outcomes has been described by the social causation hypothesis[102].

Education is an important marker of SES that generally chronologically precedes attributes such as income or job status. Its benefit as an SES marker includes the fact that it often is set prior to the development of major chronic conditions, allowing for simpler ascertainment of directionality, and does not require labour force involvement. However, the association of education with success can be moderated by a number of external factors such as access to

educational opportunities, sex, and country of residence[103, 104]. Meanwhile, income as a marker of SES is often subject to high nonresponse rates and doesn't always provide information about standard of living against community and demographic contexts. Associations between income and health are typically nonlinear, and tend to be steepest at the lower SES levels[105].

Studies into the association of SES with health have a long history[106]. Adler et al. demonstrate the putative protective benefit of higher education through its association with lower rates of chronic disease, cancer and arthritis.[107] In a prospective study of Canadians, McLeod et al. were able to demonstrate that household income, and not income inequality (the distribution of income with the population) was associated with health outcomes between 1994 and 1998 when adjusted for potential confounders. Orpana et al. demonstrated both cross sectional[108] and prospective[109] relationships of lower income with poor self-rated health. Across income adequacy groups, for instance, Orpana et al. report that exposure to stressors accounted for 16% to 26% of the relationship between income group and poor self-rated health among men and 6% and 15% among women[108]. Similarly, Ross et al. demonstrate that health-related quality of life is highest for the most affluent and the most educated individuals[110]. Therefore, not only do these SES factors influence the potential for an individual's success, but they have also been consistently related to health status.

In their assessment of SES and MetS, Kivimaki et al. demonstrated the increased odds of having 3 or more MetS risk factors in men (3.32, CI: 2.66-4.14) and women (2.39,CI: 2.03-2.82) in the lowest income tertile relative to the highest[111]. In a Canadian study, a lower prevalence of MetS was seen among individuals with lower income (21.3% in the lowest

income level, and 15.2% in the highest income level). The same study also demonstrated the decreased odds of MetS among post-secondary graduates compared to secondary school graduated (OR 0.45, CI: 0.25-0.81).[37] Thus, the relationship of SES with health is not isolated to chronic diseases only, but also to early disease risk states such as MetS. Both these gradients may be explained by the social causation hypothesis, which suggests that the social environment can negatively impact health through material, behavioural and psychosocial pathways.[112, 113] For instance, stressors arising from living circumstances determined by differential SES is a proposed psychosocial mechanism explaining the social gradient of health[114, 115].

1.3.4.2 Stress

Stress is widely considered a central problem in human life, whose precise definition is conceptualized differently based on the discipline[116]. In physiology, stress is the non-specific response humans have evolved to respond to any demand[74]. In psychology, Lazarus and Folkman define stress as a process that occurs when the demands of a situation outweigh the perceived ability to cope with it[117]. Stressors are agents that evoke a stress response, and may include negative events, physical strains or even emotional challenges. They can be characterized by their duration, acute or chronic, and their course, discreet or continuous[118]. However it arises, stress often prompts the body to respond acutely through the sympathetic-adrenal-medullary axis (SAM, through a fight or flight response) or the HPA-axis.

The acceptance of stress as a determinant of physical and mental health is a relatively recent phenomena. In their review of Navy medical records in 1967, Holmes and Rahe highlighted

the social nature of stress and its association to health outcomes. They proposed that major life events requiring extensive behavioural adjustments resulted in numerous changes over a short period of time, thus overtaxing an individual's ability to cope or adapt. This made these individuals more susceptible to infection, injury or disease. Furthermore, the accumulation of socially undesirable or negative life events were also shown to produce elevated levels of psychological distress [119]. Subsequent research by Brown and Harris[120], Marmot[121], and others continue to demonstrate an association between stressors (both acute and chronic) and negative health outcomes[122].

Studies have also associated MetS with stress. In the Whitehall II study, chronic work stress predicted higher odds of MetS after 14 years of follow-up (OR 2.25, CI: 1.31-3.85) [123]. Similarly, women who experienced life events as extremely stressful had an increased risk of developing MetS over 12 years [124]. Finally, in their population-based study, Pyykkonen et al. showed that life events perceived as stressful, most notably those related to economic status (finance and work), were related to MetS[125].

1.3.5. Behavioural Factors

1.3.5.1 Physical Activity and Sedentary Behaviour

The first law of thermodynamics states that the total energy of a system is constant; energy input is in equilibrium with energy output. This statement has been used to broadly represent the current understanding of obesity, where an imbalance towards energy input results in excess energy storage. Generally speaking, food consumption can be seen as one of several

factors impacting energy input while many factors influence energy output, such as physical activity and sedentary behaviour[126].

Physical activity is implicated in how we maintain the energy equilibrium, and its contribution to energy expenditure can vary depending on factors such as duration and intensity of the activity. Sedentary behaviour falls on the other end of the physical activity spectrum. It involves engaging in activities that are at the resting level of energy expenditure in a sitting or reclining position[127], such as reading, watching television, or using a computer[128]. Since sedentary behaviour is not defined in reference to physical activity, it is relevant to study it as an independent determinant of health. Furthermore, it is possible for individuals to be physically active, yet highly sedentary[129].

The benefits of physical activity appear to follow a dose-response effect. When examining the odds of MetS by levels of physical activity, Rennie et al. found that individuals who engaged in vigorous and moderate physical activity were less likely to have MetS (OR 0.52, CI: 0.40 – 0.67 for ≥12.5 hours/week of vigorous level activity relative to < 5 hours/week, and OR 0.78, CI: 0.63-0.96 for ≥24 hours/week of moderate activity relative to <24 hours/week) [130]. Furthermore, a study by Buscemi et al. found compared to individuals who did not engage in physical activity, the odds of MetS among those who engaged in light physical activity was 0.53, CI: 0.32-0.87 and among those who engaged in moderate or heavy exercise was 0.31, CI: 0.13-0.75[131]. Given that physical activity counterbalances to energy excess in regards to obesity, it is not surprising that physical activity associates with MetS as it does.

Canadians live in environments that are increasingly sedentary, with 68% of men's and 69% of women's waking hours spent engaging in sedentary activities[132]. The manner in which sedentary time is accumulated has also been demonstrated to be important. While total sedentary time is associated with obesity and MetS, breaks in sedentary time has been suggested to have beneficial associations[133]. A recent meta-analysis of MetS and sedentary behaviours found that higher time spent engaging in sedentary activities increased the odds of MetS by 73% (OR 1.73, CI: 1.55-1.94, p<0.0001)[134]. Using accelerometry data, a study by Healy et al. demonstrated that an increase in the percentage of time and duration of sedentary behaviours was associated with elevated metabolic risk, and more breaks in the sedentary activity reduced metabolic risk. For example, independent of total sedentary time, the latter was positively associated with lower waist circumference (standardized $\beta = -0.16$, 95% CI -0.31 to -0.02, $P = 0.027$), and triglyceride levels ($\beta = -0.18$, -0.34 to -0.02, $P = 0.029$)[133]. Given that we live in an environment that promotes low energy expenditure, this latter finding suggests that in addition to keeping energy intake low, breaks in sedentary activity such as by standing up or taking small walks can improve metabolic health[126, 133].

1.3.5.2 Alcohol

Alcohol consumption is a prevalent lifestyle habit, and is estimated to be the fifth leading risk factor for global disability adjusted-life expectancy for all ages and sexes. Drinking excessive amounts of alcohol regularly is known to have deleterious effects. In 2013, almost one in five Canadians over the age of 12 (17.4%) were considered to be heavy drinkers[135]. Globally, over 2.7 million deaths are attributed to alcohol use linked CVD, cancer, liver disease, injury and more[136, 137]. In addition to health effects of alcohol use, this habit also

negatively impacts psychosocial status of an individual. A recent study compared the relative harms of 20 drugs, including heroin, cocaine and alcohol, for harms to the user and others. Harms were defined to include crime, decline in social cohesion within community and family adversity. The study found that harms were the greatest for alcohol compared to all other drugs[138, 139].

The evidence associating alcohol and MetS in individual studies is conflicting. Associations between alcohol use and MetS have recently been described as protective[140, 141], detrimental[142] or J-shaped[136, 143] in nature. Complex mechanistic associations between alcohol use and each risk marker likely influence these discrepancies for MetS. Glucose metabolism, for example, exhibits similar conflicting associations. However, blood pressure, triglyceride levels and BMI levels worsen or follow a J-shaped pattern with alcohol use while cholesterol levels are protected by this habit[136].

In a meta-analysis of prospective studies assessing the link between alcohol use and MetS, Sun et al. reported that compared to non-drinkers, very-light alcohol drinkers (0.1 to 5 grams/day) had a decreased risk of MetS (pooled RR 0.86, CI: 0.75-0.99) while heavy drinking (>35 grams/day) was associated with an increased risk of MetS (pooled RR 1.84 CI: 1.34-2.52)[143]. Interestingly, this association differs when examining cross-sectional studies. More specifically, in a study by Frieberg et al., it was shown that alcohol consumption was inversely associated with MetS status, even at higher levels of alcohol[140].

1.3.5.3 Smoking

Smoking is prevalent in Canada, with 16.1% of Canadians aged 15 and over currently smoking. The rates of smoking are significantly higher among males than females (18.4% vs. 13.9% respectively)[144]. Smoking accounts for more than one in ten (12%) deaths worldwide among adults aged 30 and over. Within chronic conditions, tobacco use accounts or 10% of all deaths from CVD, 22% of all cancer deaths and 36% of all deaths associated with the respiratory system[145].

In their assessment of environmental tobacco smoke exposure and active smoking among adolescents, Weitzman et al. found that smoking was associated with an increased risk of MetS (OR 4.7, CI1.7-12.9 and OR 6.1, CI: 2.8-13.4 respectively)[146]. Among adults, current smokers had higher rates of MetS (OR 1.4, CI: 1.1-1.7), and the components of MetS were also associated with smoking status (waist circumference OR 1.9, CI:1.2-2.1, HDL-C OR 1.5, CI:1.3-1.8, and triglycerides OR 1.4, CI:1.2-1.7)[147]. These results were replicated by Slagter et al., except for the association of HDL-C with smoking [148].

1.3.5.4. Fruits and Vegetables

Fruits and vegetables are a good source of micronutrients, antioxidants, fibre, and anti-inflammatory agents[149] and diets high in fruits and vegetables are associated with better health[150-153]. Fibre intake, for instance, is inversely associated with systolic and diastolic blood pressure, waist circumference, and body weight[154]. Anti-inflammatory agents may reduce production of inflammatory cytokines[155], which have been suggested in the pathogenesis of obesity and metabolic syndrome[156]. Dietary factors such as fruit and

vegetable intake have been implicated as modifiable etiologic risk factors for chronic disease[149]. In a prospective analysis using the Nurses' health study, and inverse association between total fruit and vegetable and CVD was observed for each increment of five servings daily (RR 0.88, CI: 0.81-0.95)[151]. Similarly, in a meta-analysis examining the effectiveness of increased fruit and vegetable intake for the primary prevention of cardiovascular disease, favourable effects were observed with respect to systolic blood pressure, diastolic blood pressure and low-density lipoprotein levels[157]. As a result, many organizations have made dietary recommendations regarding fruit and vegetable intake, such as the "5-a-day" initiative, which reflects recommendations by the World Health Organization, the UK National Health Service, and Health Canada[158, 159].

Intake of fruit and vegetables has also been examined with respect to MetS. A meta-analysis of studies examining the association between fruit and vegetable consumption with MetS found that while there were no studies reporting changes in the prevalence of MetS on the basis of its intake, beneficial changes in diastolic blood pressure among those with MetS were observed (fixed-effect standardized mean difference -0.29, CI: -0.57 to -0.02). None of the other MetS risk markers were found to benefit from increased fruit and vegetable intake[160].

1.3.5.5 Milk

Milk is one of nature's most complex foods, providing all nutritional components necessary to support life and development[161]. In the western world, dairy accounts for more than half of the dietary intake of calcium[162], and is also an important source of protein, vitamin D,

potassium, phosphorous and magnesium. Because of the broad nutritional benefits of milk, this dietary behaviour has been widely studied in relation to many health outcomes.

In a meta-analysis of dairy consumption with cardiovascular disease, an inverse relationship was found for overall risk of CVD (RR 0.88, CI: 0.81-0.96) and of stroke (RR 0.87, CI: 0.77-0.99), but no significant association was found with coronary heart disease[163]. In a prospective analysis of MetS and diabetes in relation to milk consumption, an inverse relationship was found for MetS (OR for those who drink a pint or more of milk daily 0.38, CI: 0.18-0.78), but no association was found for diabetes[164]. Among US adults, a significant inverse relationship was found between MetS and one or more daily servings of yogurt (0.40, 95%I 0.18-0.89). Cheese consumption, however, was associated with a higher odds of MetS (OR 1.16, CI: 1.04-1.29), signalling the importance of examining different dairy products independently[165]. This might explain why in a meta-analysis of dairy consumption in relation to MetS, despite a suggestion of the potential benefit of dairy, the authors caution methodological limitations as a reason to not draw conclusions[166].

1.3.5.6 Sugar Sweetened Beverages

Fluid intake, especially from water, helps individuals stay healthy and hydrated[167]. Fluids can include a variety of beverages, such as milk, coffee, juice, and soda. Adults consumption of beverages drops with age; whereas Canadians aged 19 to 30 years old consumed 2610 grams of fluid for men and 2056 grams of fluid for women, these estimates became significantly lower at 1584 grams and 1532 grams respectively past the age of 71[168]. Beverages that are high in added sugar are of particular concern since they are major contributors to energy

intake. Patterns of beverage consumption in US children and adolescents suggest an increase in the consumption of sugar sweetened beverages (SSB), like sweetened fruit drinks and regular soft drinks, in parallel with a decrease in milk consumption[169]. This suggestion of a replacement of milk consumption by SSB is worrisome, particularly given that soft drinks and fruit drinks accounted for more than 40% of daily intakes of added sugars[170]. Certainly, consumption of soft drinks fall sharply with age from about 47% of men and 27% of women aged 19 to 30 years old to about 10% for both sexes past the age of 71[168], but the patterns of beverage frequency and type are noteworthy.

The negative health effects of these beverages associated with obesity, diabetes and heart disease have been well documented[171]. In a meta-analysis of the association of SSB consumption with MetS, Malik et al. describe a pooled relative risk of 1.20 (1.02-1.42). Based on follow-up studies, individuals who consumed one or more SSB per day were at an increased odds to develop MetS (OR 1.44, 1.20-1.74), including the various components of this condition: obesity (OR, 1.31; 1.02 - 1.68), elevated waist circumference (OR, 1.30; 1.09 - 1.56), impaired fasting glucose (OR, 1.25; 1.05 -1.48), high blood pressure (OR, 1.18; 0.96 - 1.44), hypertriglyceridemia (OR, 1.25; 1.04-1.51), and low high-density lipoprotein cholesterol (OR, 1.32; 1.06 - 1.64)[172].

1.4 Chronic Disease

1.4.1 Type 2 Diabetes

Diabetes is a chronic disease related to the body's ability to appropriately use insulin. Insulin is a hormone secreted by the pancreas that enables the body to absorb sugar from the blood

stream and use it as an energy source. Broadly speaking, diabetes occurs when an individual either does not produce insulin, as in the case of type 1 diabetes, or cannot sufficiently produce enough insulin or is unresponsive to insulin, as with T2DM. In all cases, diabetes represents an uncontrolled state of hyperglycemia wherein circulating levels of blood sugar are high. Over time, this state can damage blood vessels, nerves, and organs [173]. This thesis will focus on T2DM.

In 2008/09, 6.8% of Canadian adults were living with diabetes while approximately 20% of diabetes cases were undiagnosed based on data from the Canadian Health Measures Survey (CHMS). Between 1998/99 and 2008/09, the rates of diabetes increased almost 70% among Canadian adults. The greatest increase was among Canadians aged 35-44, where the rates doubled, as well as among younger age groups, where obesity played a significant contributing role. At every age group, individuals with diabetes experienced at least two times the mortality rate than those without. Diabetes notably impacts life expectancy and health related quality of life[173].

Diabetes and MetS share common risk factors. For example, obesity is a contributing factor to both conditions, as is elevated glucose levels. For the latter, the threshold for identifying MetS is lower than that for diabetes. Not surprisingly, the two conditions are related. In fact, MetS has been associated with a five-fold increase in T2DM[45]. In a systematic review of prospective studies looking at diabetes risk among individuals with MetS, the odds of diabetes was 2.99 (CI1.96-4.57) and the population attributable fraction for diabetes to MetS was approximately 30% using the NCEP definition for MetS [6].

1.4.2 Cardiovascular Disease

Cardiovascular diseases, which include heart disease, stroke and myocardial infarction, are major chronic diseases in Canada. In fact, heart disease and stroke represent the second and third leading cause of death at 19.7% and 5.5% respectively[3]. In 2007, 4.8% of Canadians reported being diagnosed with heart disease. Given the financial burden associated with CVD, and its indirect effects through factors such as short or long-term disability, CVD had the second highest cost among all diagnostic categories. That is, in 2000, the economic cost associated with CVD was estimated to be $22.2 billion. It is promising that the rates of CVD have been decreasing steadily since 1950, but they are still a leading cause of mortality in Canada[174].

The risk markers used to define MetS are also used to ascertain CVD risk, such as hypertension and impaired fasting glucose. In a recent meta-analysis of CVD, Motillo et al. found that MetS was associated with an increased risk of CVD (RR 2.35, CI: 2.02-2.73), CVD mortality (RR 2.40, CI: 1.87-3.08), stroke (RR 2.27, CI: 1.80-2.85), myocardial infarction (RR 1.99, CI: 1.61-2.46), and all-cause mortality (RR 1.58, CI: 1.39-1.78). Sensitivity analysis reinforced the validity of these estimates by showing that longer-follow up times provided similar risk estimates to studies with shorter follow up times. Their results also demonstrate the prognostic value of MetS for CVD even in the absence of diabetes[8]. This is noteworthy given the suggestion by some that the risk for CVD conferred by MetS is due to the fact that these patients have diabetes[27]. In his systematic review of prospective studies between 1998 and 2004, Ford reported that the population attributable fraction for CVD attributed to MetS was approximately 12%[6].

1.4.3 Additional chronic conditions

Because MetS comprises of risk factors that are associated with a number of physiological processes, it may also be expected that MetS has been associated with chronic conditions. While CVD and diabetes have been the two that have been the most widely studied and reported, there is growing interest in the association of MetS with other chronic conditions. As discussed previously, while there have been reports of the limited specificity of MetS, once might infer a broad sensitivity for chronic disease in general based on its wide associations. This may be attributed to common pathways, such as inflammation, atherogenesis, thrombosis, hypertension and dyslipidemia[25].

As discussed in section 1.1.1, the WHO included a marker of microalbuminuria in their definition for identifying MetS. This state describes when there is a moderate increase in the level of urine albumin, which can be attributed to an abnormally high permeability of the kidney for this protein. Microalbuminuria is thus an indicator of abnormal kidney function, and has been linked to endothelial dysfunction and MetS. Furthermore, it has been linked to CKD. In their review, Singh et al. discuss how renal dysfunction becomes apparent in MetS before the appearance of diabetes or hypertension[175]. Using national data from the US, Chen et al. reported the odds ratio (OR) of MetS for those with CKD as 2.60 (CI: 1.68-4.03) and microalbuminuria as 1.89 (CI: 1.34-2.67).

Cancer is the leading cause of mortality in Canada, accounting for 29.9% of all deaths in 2011. Emerging evidence has linked MetS to cancer. In their meta-analysis of this association, Esposito et al. found that the presence of MetS was associated with an increased relative risk of liver (1.43, CI: 1.23-1.65) and colorectal cancers (1.25, CI: 1.19-1.32) in men,

as well as colorectal cancer (1.34, CI: 1.09-1.64), endometrial (1.61, CI: 1.20-2.15) and breast postmenopausal (1.56, CI: 1.08-2.24) cancer in women.[5] MetS has also been associated with other chronic conditions, including rheumatic disease[176], and PCOS[178].

1.5 Public Health

Given its association with a number of chronic conditions, MetS is conceptually attractive as an encompassing multiple risk factor indicator that may provide benefits for early detection of multiple disease states. MetS became institutionalized in the medical vocabulary with its inclusion into the ninth revision of the International Classification of Diseases (ICD) in 2001 by the National Center for Health Statistics. Since then, uptake of this definition in clinical practice has been slow due to a range of factors including financial compensation and concerns over the practical utility of this diagnosis[179, 180]. For example, in the two years since the ICD code was created, hospital discharge records suggest a low use of the code in practice[179]. This underscores the discussion about which users such a diagnosis is most practical for.

In acute care settings, such as those captured by hospital discharge records, clinicians are most interested in managing the primary condition for admission. It is unlikely that a patient will be admitted for MetS and it is of limited practical value to capture its diagnosis. Therefore, it is not surprising that the use of the ICD code is low in such settings[180]. As a risk factor syndrome that is only meant to indicate increased relative risk and not absolute risk, MetS is likely better utilized by General Practitioners to identify patients at potential risk for future chronic disease[29]. In their assessment of health-centre records from Finland, Helminen

et al. also found that only half of those patients who qualified as having MetS were diagnosed with it (49.4% had the condition and 28.5% were diagnosed) and that the sensitivity and specificity of the code was limited (0.31 and 0.73 respectively). Furthermore, less than 10% of patients were aware that they were considered to have MetS[181].

In spite of its slow adoption in clinical practice, there are still supporters of its use since it provides a way to identify people at high risk without the need for advanced technology. Moreover, treatment of patients at this stage often involves less invasive preventive measures to avoid long-term burden of disease, such as lifestyle modification or sometimes pharmacotherapy[29]. Aside from its slow and wavering adoption in clinical practice, MetS has had steady and growing interest from public health organizations that survey and monitor its prevalence so as to gauge potential future chronic disease. For instance, while there were only 7655 PubMed citings for MetS in the 50 years leading up until Jan 1, 2000, there have since been 47,892 citings until August 4, 2015[182]. In this respect, while its practical use in clinical settings is still being determined, MetS' didactic use in academic and broader public health settings is well established.

1.6 The Current Thesis

1.6.1 Goal, Objectives, and Hypotheses

The overarching goal of the current thesis is to contribute to the understanding of MetS as an indicator through which material, psychosocial and behavioural factors link to chronic diseases. This will be achieved through the following objectives:

Article 1:

1) To describe the prevalence of MetS using current definitions (NCEP, IDF, Harmonized);
2) To demonstrate the association between MetS and diagnosed chronic conditions (hypertension, diabetes, CKD, and dyslipidemia) in Canada; and
3) To establish the association of MetS with current, though undiagnosed conditions (hypertension, diabetes, CKD, and dyslipidemia), and predicted chronic disease in Canada.

Article 2:

4) To demonstrate that lower socioeconomic status, as measured by household income and individual educational attainment, is associated with greater likelihood of MetS; and
5) To examine whether psychosocial (stress, work stress, sense of community, mood disorders, perceived quality of life, and life satisfaction) and behavioural factors (alcohol use, smoking, sleep, physical activity, and consumption patterns of milk, sugar sweetened beverages, and fruits and vegetables) mediate this association.

Article 3:

6) To examine whether physical activity guideline adherence (150 minutes of moderate-to-vigorous physical activity (MVPA) per week) and non-movement behaviours (NMBs, including sleep time, screen time, measured sedentary time) are independently associated with MetS; and

7) To examine whether MVPA guideline adherence moderates the association of NMBs with MetS; and
8) To examine the combined effects of physical activity guideline adherence and NMBs on the risk of MetS.

It is hypothesized that:

H1) MetS is prevalent in Canada, and its prevalence varies depending on the definition used.

H2) MetS is associated with chronic conditions (hypertension, diabetes, CKD, and dyslipidemia) in Canada.

H3) MetS is associated with undiagnosed conditions (hypertension, diabetes, CKD, and dyslipidemia) and future risk of chronic disease (diabetes and CVD) in Canada.

H4) Lower socioeconomic condition is associated with increased odds of MetS.

H5) Psychosocial and behavioural factors mediate the association of SES with MetS.

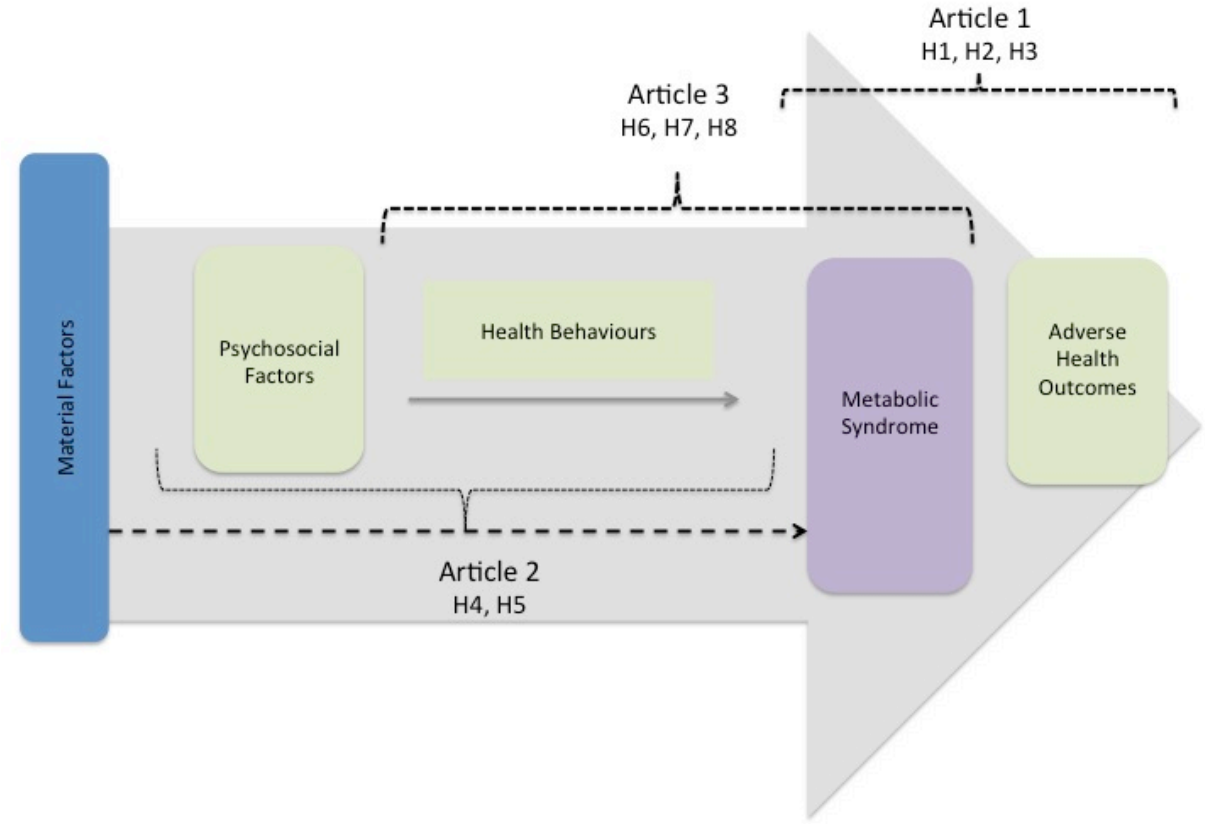
H6) Physical activity guideline adherence reduces the associations of NMBs with MetS.

H7) Physical activity guideline adherence will moderate associations of NMBs with MetS.

H8) The association of different combinations of physical activity guideline adherence and NMBs with the risk of MetS will vary.

These hypotheses are presented in the explanatory model (Figure 5), which is meant to provide a representation of the relationships to be tested in the current thesis, but not be exhaustive of all the factors involved

Figure 5. Hypothesized explanatory model of associations and pathways to be tested in the present thesis.



1.6.2 Outline of the thesis

This current thesis is organized as a collection of manuscripts that guide the reader through an examination of the three above-mentioned articles (in Chapters 2, 3 and 4 respectively). Chapter 5 will be a general discussion of the findings from the collection of manuscripts.

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CHAPTER 2

Metabolic Syndrome and Chronic Disease

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Abstract

Introduction: Metabolic syndrome (MetS) is a risk condition that appears to promote the development of chronic disease. We examined the burden of MetS in Canada through its current and projected association with chronic disease.

Methods**:** The Canadian Health Measures Survey 2007–2009 was used to identify the prevalence of MetS in Canadian adults and to examine associations between sociodemographic factors and chronic diseases. We estimate the projected risk for diabetes and fatal cardiovascular events using the Diabetes Population Risk Tool (DPoRT) and Framingham algorithms.

Results**:** After adjusting for age, 14.9% of Canadian adults were identified as having MetS. Rates were similar in both sexes, but higher in those who are non-Caucasian or overweight or obese ($p < .001$). The importance of MetS for public health was demonstrated by its significant association with chronic disease relative to the general population, particularly for diagnosed (11.2% vs. 3.4%) and undiagnosed (6.0% vs. 1.1%) diabetes. The ten-year incidence estimate for diabetes and mean percent risk of a fatal CVD event were higher in those with MetS compared to those without (24.8% vs. 8.8% for diabetes, and 4.1% vs. 0.8% for CVD).

Conclusion**:** MetS is prevalent in Canadian adults, and a high proportion of individuals with MetS have diagnosed or undiagnosed chronic conditions. Projection estimates for the incidence of chronic disease associated with MetS demonstrate higher rates in individuals with this condition. Thus, MetS may be a relevant risk factor in the development of chronic disease.

KEY WORDS: Metabolic syndrome, chronic disease risk, Framingham risk tool, Diabetes Population Risk Tool

Introduction

The vast majority of patients in the Canadian healthcare system are living with one or more chronic diseases.[1] Cardiovascular disease, chronic obstructive pulmonary disease, cancer and diabetes are the most common causes of hospitalization and premature death in Canada, accounting for almost three-quarters of all deaths.[2] Together, these chronic diseases account for 80% of primary care visits and more than two-thirds of medical costs.[1, 3] Knowing more about the risk factors and indicators for chronic disease may, therefore, help public health efforts aimed at addressing this growing concern.

Metabolic syndrome (MetS) is a condition that describes the clustering of risk markers that increase an individual's likelihood of developing chronic disease.[4] A number of leading chronic conditions have been shown to be associated with MetS. These include cardiovascular disease (CVD)[5], type 2 diabetes,[6] cancers,[7] and chronic kidney disease (CKD)[8].

The growing prevalence of obesity and sedentary lifestyles contributes to the prevalence of MetS.[9-11] While the pathogenesis of MetS may be attributed to obesity and metabolic susceptibility[12], a variety of socioeconomic factors have also been shown to influence the prevalence of MetS. For example, Canadian adults with a postgraduate degree had half the odds of acquiring MetS compared with those who have completed high school (OR = 0.45, 95% confidence interval (CI): 0.25–0.81).[13] Likewise, ethnicity also affects observed prevalence rates (OR = 0.54, CI: 0.4–0.73 in non-Hispanic Blacks relative to non-Hispanic Whites).[14] Considering differences based on ethnicity has resulted in a variety of official MetS definitions being sanctioned by international health authorities.[4, 15, 16] MetS has also

been described as a progressive disorder; the several components of MetS tend to worsen over time and collectively contribute to an increased risk for chronic disease.[17]

Hivert et al.[18] demonstrated the utility of MetS as a relevant public health tool. Using electronic health records to identify and track patients with MetS for future development of CVD and diabetes, they showed that patients with MetS had a higher incidence of these chronic conditions and incurred higher healthcare costs than did those patients without MetS.[18] This signifies an important role for MetS as a chronic disease indicator that could benefit individual health as well as healthcare costs and resources.[18] The limited availability of prevalence estimates derived from Canadian data to date has meant that international estimates are often used instead. It is therefore important to develop Canadian findings on MetS and its association with chronic conditions.

In this study, our aim was to (1) estimate the prevalence of MetS in the Canadian adult population; (2) examine the relationship between MetS, risk factors and chronic disease; and (3) characterize the future risk of chronic diseases associated with MetS through measures of undiagnosed disease, as well as through 10-year projections for diabetes and CVD using established prediction tools.

Methods

Data source

We used data from the 2007–2009 Canadian Health Measures Survey (CHMS).[19] This cross-sectional survey, conducted by Statistics Canada, recruited a representative sample of 5600

Canadians aged 6 to 79 years, which covers about 96.3% of the Canadian population. The survey used a mobile examination clinic to measure, for example, participants' blood pressure (BP) and serum factors. Information about current health status, socioeconomic variables, etc., was gathered through a general household interview.[19] Statistics Canada provides weights for each participant that capture the number of people represented by that participant in the population, and account for non-response and the demographic distribution of the population. Additional information on sampling and estimations is described elsewhere.[20, 21]

Study population

Some of the CHMS study participants (n = 2634) were asked to fast before the tests at the mobile examination clinic, and we used data from this subsample in this study. The response rate for this subsample was 85.2%, which when combined with the overall response rate for the CHMS, makes the overall fasting subsample response rate 46.3%.[19, 20, 22] Pregnant women (n = 8) and individuals aged under 20 years (n = 933) were excluded from the analysis, leaving a study population of 1693 participants. For analyses using this subsample, Statistics Canada provided separate weights, based on the 2006 Census, for fasting participants, to ensure that analyses in this restricted subpopulation would remain representative of the entire Canadian population. These weighting factors account for non-response and for the demographic distribution of the country.

To test for potential selection bias as a result of various exclusion criteria, we performed a sensitivity analysis to compare the baseline demographic status of our study population with national-level estimates. Comparing our study population with recent Canadian estimates, we

found that our study population (Table 1) showed similar estimates for age,[23] education,[24] gender,[25] ethnicity[26] and income,[27] indicating that our study population is representative of the general Canadian population.

Key definitions

Metabolic syndrome. We used the revised National Cholesterol Education Program (rNCEP) Adult Treatment Panel III definition for MetS, which uses revised waist circumference criteria.[4] We also examined prevalence rates of MetS using the International Diabetes Federation (IDF) and Harmonized definitions. [15, 16]

Undiagnosed and diagnosed chronic conditions. In the absence of any longitudinal data to determine whether individuals with MetS may develop chronic diseases with time, we determined whether participants may have had an undiagnosed condition. This is treated as a proxy measure for future chronic disease risk. Individuals were deemed to have a particular condition undiagnosed if they said that they did not have the condition but had measurable physical attributes of the condition.

Diagnosed hypertension was based on a positive response to the question "Do you have high blood pressure?" or from self-reported use of specific medications (list available from the authors on request). Average systolic BP and diastolic BP were derived from an average of six blood pressure measurements.[22, 28, 29] We determined that individuals had undiagnosed hypertension if they reported no diagnosed hypertension but had BP readings above 140/90 mmHg (for either reading).

Diagnosed diabetes (type 2) was based on a positive responses to the questions, "Do you have diabetes?" and "Were you diagnosed with non-insulin dependent diabetes (type 2)?" or from self-reported use of specific medications (list available from the authors on request).[22] As with BP, we determined that individuals had undiagnosed diabetes if they gave a negative response to questions about having physician-diagnosed diabetes but their fasting plasma glucose levels measured at 7.0 mmol/L or more. Individuals with type 1 diabetes were not included in the analysis.

Diagnosed CKD was based on a positive response to the question "Do you suffer from kidney dysfunction or disease?"[22] Undiagnosed CKD was based on a negative response to this question plus either a low measured glomerular filtration rate (≤ 60 mL/min using the Modification of Diet and Renal Disease Study equation[30]) or a high measured microalbumin to creatinine ratio (> 2.65 mg/mmol).

Diagnosed dyslipidemia was based on a positive response to the question "Have you ever been told by a health professional that your blood cholesterol was high?"[22] Undiagnosed dyslipidemia was based on a negative response to this question plus the participant either meeting both the total cholesterol to HDL-C ratio (≥ 5.5 in men, ≥ 4.5 in women) and LDL-C criteria (≥ 3.5 mmol/L) or using appropriate medications (list available from the authors on request).

Descriptive variables: Analyses are described by sex, age (at clinic visit), education, ethnicity (self-reported cultural or racial group) and total household income. Lifestyle factors

include measured body mass index (BMI) and self-reported leisure time physical activity and smoking status.[19]

Analysis

We undertook multivariate analyses using statistical software SAS Enterprise Guide 4.1 (Cary, NC, US).[31] National estimates were calculated with the CHMS weights for the subsample of the population who had fasted and were age adjusted using Canadian Census data. We calculated variance estimates using Statistics Canada Bootvar software (Statistics Canada, Ottawa, ON) and followed their reporting guidelines. Horvitz-Thompson estimation was used to analyze statistical significance following a *t* distribution with 11 degrees of freedom.

We examined prevalence estimates using the frequency procedure on SAS Enterprise Guide 4.1, and adjusted for these as described for individual reported estimates in the Results section. OR estimates were calculated from logistic regression models and adjusted for age and sex, where mentioned. Ten-year cumulative incidence projections for type 2 diabetes were estimated using the Diabetes Population Risk Tool (DPoRT).[32] Originally developed using the 1996 National Population Health Survey, this prediction tool uses commonly collected survey data, such as self-reported estimates for health behaviours and sociodemographic factors, to predict the risk of developing incident physician-diagnosed diabetes. Sex-specific Weibull survival models were used to create DPoRT for individuals without diabetes mellitus, who are not pregnant, and who are aged over 20 years. Predictive variables used in the model include age, sex, self-reported ethnicity, BMI, immigrant status

(for women), education, smoking status and history of hypertension and heart disease, all of which were available for our analysis.[32]

We used the lipid-based Framingham 10-year risk calculator to estimate the risk of a fatal general CVD event, defined as either coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease or heart failure. This risk prediction tool was originally created using data from the Framingham Heart Study and Framingham Offspring Study. Sex-specific Cox proportional hazards regressions were used to relate various risk factors to the incidence of fatal general CVD events. Mathematical CVD risk functions derived from this were then used in the development of the Framingham Risk Tool. Results are presented as high risk (≥ 20%) or intermediate and high risk (≥ 10%). The population subset for CVD projections was restricted to individuals aged 30 to 74 years who have no previous history of a CVD event.[33]

Ethics approval

Approval to conduct our study was obtained from the Ottawa Hospital Research Ethics Board (Protocol # 20120767-01H) prior to commencement.

Results

The majority of the survey participants were Caucasian, physically inactive and former or current smokers. Most had at least some post-secondary education and an annual household income of more than $50 000. The mean age of the study population was 45 years, and the population was equally represented by each sex (Table 1).

Table 1. Characteristics of the study population

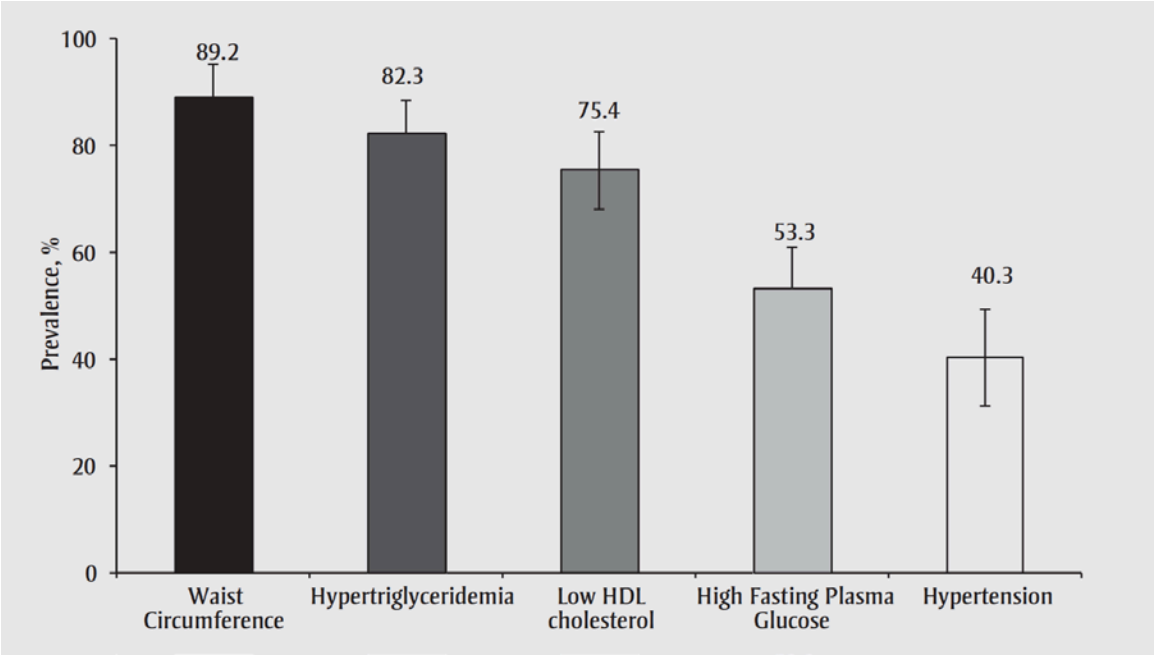
Characteristics	N	%	95% CI
Sex			
Women	886	50.4	49.8–50.9
Men	807	49.6	49.1–50.2
Age, years			
20–39	536	37.8	37.1–38.4
40–59	603	41.3	40.8–41.8
60–80	554	20.9	20.6–21.2
Mean age (SE), years		45.3 (0.2)	
Cultural / ethnic background			
Caucasian	1441	84.3	74.2–94.4
Non-Caucasian	205	15.7[E]	5.6–25.8
Total household income, $			
≤ 29 999	290	14.6	11.6–17.7
30 000–49 999	324	18.4	16.3–20.5
50 000–79 999	400	26.4	22.5–30.3
≥ 80 000	583	40.6	33.6–42.9
Highest level of education			
Less than secondary	206	11.4	7.6–15.2
Secondary graduate	289	18.8	13.1–24.5
Some post-secondary / post-secondary graduate	1178	69.8	61.5–78.2
Smoking status			
Never smoked	810	45.7	41.8–49.5
Former smoker	553	31.2	27.9–34.5
Current smoker – daily or occasional	325	23.1	20.6–25.6
Leisure time physical activity			
Active / moderately active	800	44.3	37.2–51.5
Inactive	893	55.7	48.5–62.8
BMI, kg/m^2			
< 25	676	43.5	37.8–49.2
25–29	638	37.8	33.8–41.8
≥ 30	351	18.7	15.6–21.2

Abbreviations: BMI, body mass index; CI, confidence interval; SE, standard error.
[E] Interpret with caution (coefficient of variation: 16.6%–33.3%).
Missing data (not applicable, not stated, don't know) not included in calculation of proportions.

Participants were deemed to have MetS when they met three or more rNCEP MetS criteria, resulting in a crude prevalence of 15.5% and an age-adjusted prevalence of 14.9%. In the overall population, 34.9% had no MetS risk markers, whereas 29.5% had one and 20.2% had two. The most prevalent MetS risk markers among those identified as having MetS were

waist circumference (89.2%), hypertriglyceridemia (82.3%), low HDL-C(75.4%), high fasting plasma glucose (53.3%) and high systolic or diastolic BP (40.3%) (Figure 1).

Figure 1. Prevalence of different metabolic syndrome risk markers in individuals with metbolic syndrome



Abbreviations: HDL, high density lipoprotein; LDL-C, low density lipoprotein.

The rNCEP estimates were compared to prevalence estimates based on the IDF and Harmonized definitions, both of which resulted in significantly larger prevalence estimates (crude prevalence: IDF = 23.1%, Harmonized = 19.6%; age-adjusted prevalence estimates: IDF = 22.3%, Harmonized = 19.1%) (Table 2).

Table 2. Metabolic syndrome prevalence and odds ratios according to population characteristics

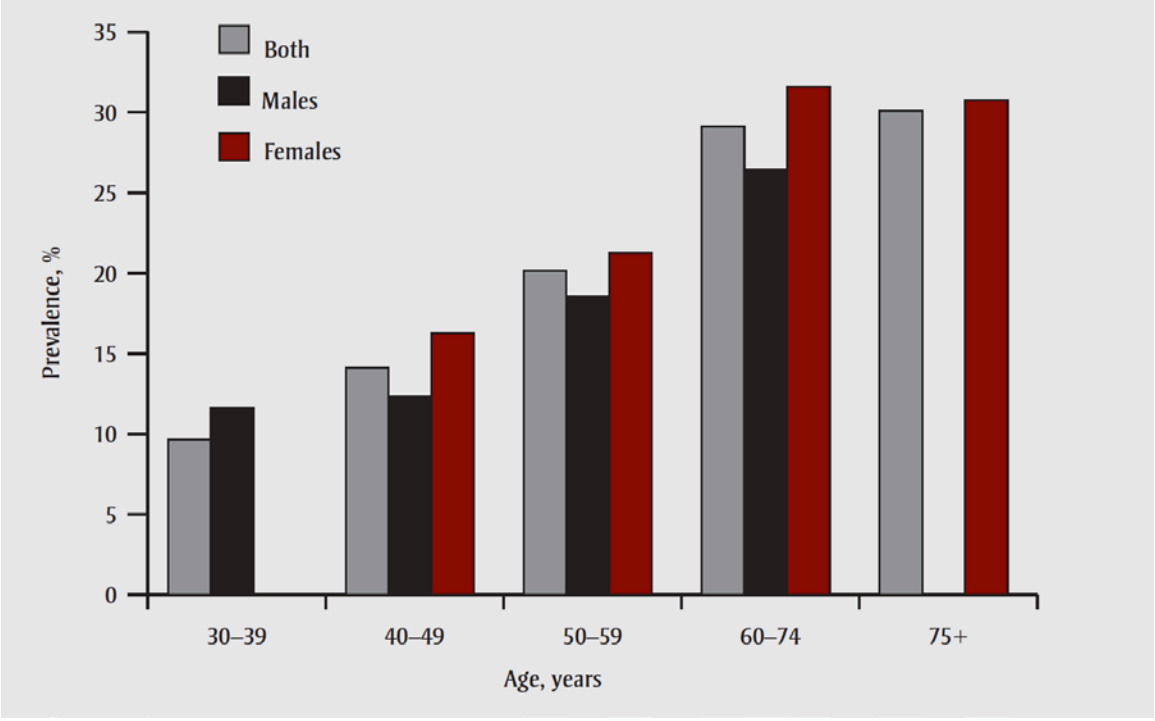
Definitions		Prevalence %	Prevalence 95% CI	*p* value	Odds Ratios OR	Odds Ratios 95% CI
rNCEP ATP III						
	Crude	15.5	12.0–19.0	—		
	Adjusted	14.9	13.3–16.6			
IDF						
	Crude	23.1	20.4–25.8	< .001		
	Adjusted	22.3	20.4–24.3			
Harmonized						
	Crude	19.6	15.9–23.2	< .001		
	Adjusted	19.1	17.3–20.9			
Characteristics						
Overall population						
Sex [a,b]						
	Men (ref)	14.5	10.4–18.6	—	1	—
	Women	16.5	12.6–20.3	.25	1.12	0.87–1.42
Ethnicity [a,b,c]						
	Caucasian (ref)	15.5	12.1–18.8	—	1	—
	Non-Caucasian	16.6[E]	5.4–27.7	< .001	2.66	1.29–5.45
Men						
Age [b]						
	20–39 (ref)	8.0[E]	4.4–11.5	—	1	—
	40–59	14.5[E]	6.7–22.4	.05	1.48	0.67–3.26
	60–80	26.9	21.3–32.5	.012	3.33	2.07–5.34
Smoking status [a,b]						
	Current	6.6[E]	2.0–11.1	.01	0.65	0.23–1.86
	Former	24.1	15.5–32.7	.12	1.54	0.66–3.61
	Never (ref)	11.4[E]	5.6–17.3	—	1	—
LTPA [a,b]						
	Active	12.0	8.5–15.6	—	1	—
	Inactive	16.9[E]	10.0–23.9	.001	1.39	0.69–2.78
BMI, kg/m^2 [a]						
	< 25 (ref)	—[F]		—	1	—
	25–29	15.8	10.4–21.2	< .001	—[F]	—
	≥ 30	38.6	25.5–51.8	< .001	—[F]	—
Women						
Age [b]						
	20–39 (ref)	—[F]		—	1	—
	40–59	18.7[E]	11.7–25.7	.003	3.67	1.20–11.17
	60–80	31.5	24.3–38.6	< .001	7.43	2.62–21.05
Smoking status [a,b]						
	Current	21.1	13.6–28.5	.71	3.15	1.63–6.07
	Former	21.3[E]	10.8–31.8	.38	2.06	0.93–4.59
	Never (ref)	11.0	8.7–13.3	—	1	—
LTPA [a,b]						
	Active (ref)	10.5[E]	6.6–14.5	—	1	—
	Inactive	20.2	15.4–25.0	< .001	1.76	1.13–2.73
BMI, kg/m^2 [a]						
	< 25 (ref)	—[F]		—	1	—

	25–29	22.9	16.1–30.0	< .001	—[F]	—
	≥ 30	43.2	34.2–52.2	< .001	—[F]	—

[a] Odds ratio adjusted for age.
[b] Odds ratio adjusted for BMI.
[c] Odds ratio adjusted for sex.
[E] Interpret with caution (coefficient of variation: 16.6%–33.3%).
[F] Cannot be reported (coefficient of variation: > 33.3%).

The prevalence of MetS varied by age group, but the difference by sex for each age group was not statistically significant (Figure 2). Variation occurred according to smoking status as well, although these patterns varied by sex (Table 2). On the other hand, ethnic background significantly influenced prevalence rates, with people of non-Caucasian origin having a higher prevalence than those of Caucasian origin. For both sexes, a high BMI and being physically inactive were significantly associated with a higher prevalence of MetS.

Figure 2. Prevalence of metabolic syndrome by gender and by age group



Note: At all reported age groups, except for ages 60–74 years, estimates should be interpreted with caution (coefficient of variation: 16.6%–33.3%). Estimates that could not be reported (coefficient of variation: > 33.3%) were not included in the figure.

The odds of MetS varied according to participant characteristics, and was significantly associated with being non-Caucasian and older (Table 2). Other characteristics were also significant, although this varied based on sex. For example, the odds of MetS was significantly associated with being a current smoker in women but not in men.

We examined the prevalence of chronic conditions across three population groups: the overall population, individuals with obesity (BMI $\geq$ 30 kg/m^2) and individuals with MetS. Undiagnosed disease was more prevalent in those with MetS compared with those with obesity or the overall study population for all conditions examined, and was most prominent for dyslipidemia (28.3% vs. 18.5% and 10.0%, respectively) (Table 3). Note that the rate of undiagnosed diabetes was more than five times higher in those with MetS than in the overall population (6.0% vs. 1.1%, p = .009, interpret with caution).

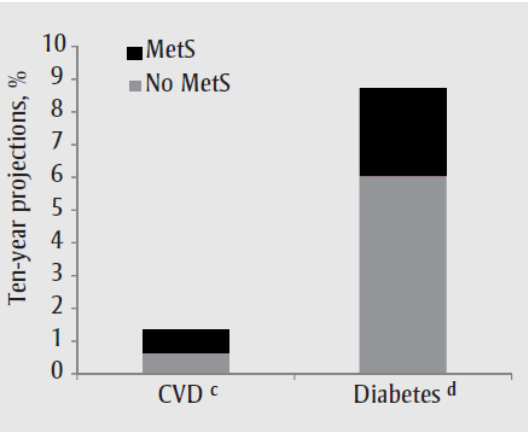
Table 3. Prevalence of diagnosed and undiagnosed chronic conditions in the overall population and in individuals with obesity and with metabolic syndrome

	Overall		Obesity			Metabolic Syndrome			
	%	95% CI	%	95% CI	*p* value[a]	%	95% CI	*p* value[a]	*p* value[b]
Hypertension									
Diagnosed	17.2	14.2–20.1	33.6	25.2–41.9	.001	36.1	29.0–43.1	< .001	.61
Undiagnosed	0.7[c]	0.2–1.1	—[F]	—	—	—[F]	—	—	—
Diabetes									
Diagnosed	3.4	2.4–4.5	8.0	5.2–10.8	.003	11.2[c]	6.7–15.6	.003	.07
Undiagnosed	1.1[c]	0.6–1.7	4.4[c]	1.5–7.2	.02	6.0[c]	2.2–9.8	.009	.27
Chronic Kidney Disease									
Diagnosed	1.9	1.4–2.4	—[F]	—	—	4.0[c]	1.2–6.8	.13	—
Undiagnosed	10.0	8.1–11.9	15.2[c]	9.0–21.5	.11	22.2	14.9–29.5	.002	.10
Dyslipidemia									
Diagnosed	29.4	26.5–32.3	37.0	31.3–42.6	.02	50.8	46.6–55.1	< .001	< .001
Undiagnosed	10.0	6.9–13.1	18.5	12.3–24.7	.006	28.3	22.5–34.1	< .001	.006

[a] These *p* values represents the significance of the difference between population subgroups and the overall population.
[b] This *p* value represents the significance of the difference between population subgroups.
[c] Interpret with caution (coefficient of variation: 16.6%–33.3%).
[F] Cannot be reported (coefficient of variation: > 33·3%).

We estimated the future burden of type 2 diabetes and CVD that can be attributed to MetS using existing algorithms. The mean 10-year predicted risk of diabetes in individuals with MetS, as opposed to those without, is 24.8% (95% CI: 18.9–30.7) versus 8.8% (95% CI: 7.4–10.3). The proportion of Canadian adults anticipated to develop diabetes between 2007 and 2017 is thus approximately 11.2% (Figure 3). Similarly, the mean predicted risks for fatal CVD are 4.1% (95% CI: 2.3–6.0; interpret with caution) vs. 0.8% (95% CI: 0.6–1.0). The risk of CVD can be further analyzed as being high, that is, a 20% or higher risk of a CVD event in 10 years, or as intermediate to high, a 10% to 20% CVD risk in 10 years,. The proportion of Canadian adults with MetS with a high risk of a CVD event is 6.81% (95% CI: 3.2–10.4, $p = .004$ relative to those without MetS; interpret with caution). Furthermore, the proportion of Canadian adults at intermediate to high risk of a CVD event is 8.9% (95% CI: 4.3–13.6; interpret with caution) in those with MetS, compared with 2.0% (95% CI: 1.3–2.7, $p = .008$) in those without MetS.

Figure 3. Ten-year projections for the cumulative incidence of diabetes[a] and mean percent risk of a fatal CVD[b] event in individuals with or without metabolic syndrome [c]



[a] Estimated using the Diabetes Population Risk Tool (DPoRT).[32]
[b] Calculated using the lipid-based Framingham 10-year risk calculator.[33] The population subset for CVD projections was restricted to adults aged 30–74 years who have no previous history of a CVD event.
[c] Projections: With MetS = 4.1% (95% CI: 2.3–6.0), $p < .01$; without MetS = 0.8% (95% CI: 0.6–1.0), $p < .01$.
[d] Projections: With MetS = 24.8% (95% CI: 18.9–30.7), $p < .01$; without MetS = 8.8% (95% CI: 7.4–10.3), $p < .01$
Note: Given the identified population prevalence of MetS among Canadian adults (85.1% without MetS, 14.9% with MetS), this suggests a projected 10 year risk of a fatal CVD event as 1.29%, and a projected 10 year cumulative incidence of diabetes as 11.2%.

Discussion

Prevalence of metabolic syndrome

Comparing prevalence for MetS using the same rNCEP definition, the age-adjusted rate in Canada is less than half that reported in the United States (14.9% vs. 34.4%), [14] but similar to previously published findings for the Canadian population.[34] Using newly suggested IDF definitions, which take into account variations in waist circumference for different ethnic groups, or the Harmonized definition, the age-adjusted prevalence of MetS in Canada is higher than with the rNCEP (22.3% and 19.1%, respectively), showing that the choice of definition for MetS does appear to matter.

We chose to use the rNCEP definition for MetS in our study to facilitate comparisons with previously published epidemiological data.[14] The rNCEP definition was reasonably accurate in representing the ethnic composition of our study population (84% Caucasian; Table 1). While sample size limitations did not allow us to explore variations in MetS prevalence based on self-reported ethnic origin, when this information was used to apply the IDF definition of MetS, it appears as though more people are being included as having MetS.[15]

Risk factors and metabolic syndrome

Our findings indicate that the prevalence of MetS in Canada is associated with age, ethnicity, BMI and leisure time physical activity. Older age was significantly associated with MetS, but the patterns of prevalence varied by age and sex. Prevalence was higher in men than in women in the 30- to 39-year age group. Thereafter, the prevalence of MetS increases steadily in women, exceeding the prevalence of MetS in men, from age 40 through 60 to 74 years, after which time it levels off. In men, the steady increase in prevalence seems to occur after the age of 40. Tjepkema[35] suggested that this transition reflects the marked increase in rates of obesity in men after age 45 years. In the same study, Tjepkema[35] also showed that obesity rates increase steadily in women until age 65 years. The changes in prevalence that we observed align with reported increased rates of MetS in peri- and post-menopausal women.[36]

The odds of MetS were significantly higher in non-Caucasian individuals, and we found greater risk of MetS in non-Caucasian Canadians than was found in Mexican American and in non-Hispanic white individuals in the United States.[14] In addition to Hispanic and African Canadians, we included Filipino, Chinese, South Asian, Arab and other populations in our

study. It is possible that the inclusion of these additional groups may account for the difference in the odds of MetS by ethnicity between the two studies. Previous findings using the rNCEP definition also showed higher prevalence rates in some of the ethnic groups included in our study relative to our overall population. [37, 38]

Our results indicate that being physically active lowers the odds of MetS compared with being inactive, although this lower risk is only statistically significant in women. Our analysis clearly shows that rates of overweight and obesity are high in adults, with a prevalence of almost 57%. This is of concern given the close association of obesity with MetS, as well as with pre-diabetes.[39]

MetS is commonly associated with pre-diabetes, wherein individuals have elevated plasma glucose levels as well as systemic inflammation. It is also associated with characteristics such as prothrombotic state and dyslipidemia, which may account for its link to cardiovascular risk.[40] The increased risk of type 2 diabetes and of a fatal CVD event in individuals with MetS is thus not surprising, given the research demonstrating these associations.[5, 41] The proportion of individuals identified as being at risk of developing diabetes in the next 10 years, relative to those without MetS, indicates the role of MetS as a potential chronic disease indicator. These findings are corroborated by a 2010 study that estimated risk of diabetes for Canadians at 8.9%;[42] the use of self-reported information in that study rather than measured values may explain the differences between their and our results. When considering the projections for CVD, which estimate the risk of a fatal event, the concern is clear.

We need to be aware of a possible overlap in definitions for chronic disease risk factors and for MetS. In the case of dyslipidemia, this overlap may contribute to the high rates of abnormal lipid levels in those with MetS. The risk marker of low HDL-C was prevalent in 75% of the population with MetS, but it is worth noting that the definition of dyslipidemia was based on a high total cholesterol to HDL-C ratio combined with elevated LDL-C levels. Similarly, MetS is defined based on waist circumference, not BMI, which makes both populations distinct but potentially related.

Public health impact of metabolic syndrome

Independent of race/ethnicity, age, sex and health status, evidence shows an increased risk of developing certain chronic diseases with each additional MetS risk marker.[41] Reaven[43] suggests that even though an individual may not meet the number of risk markers (3 or more) necessary to be diagnosed with MetS, they may still be at risk of future disease and should therefore not be overlooked. We found that 50% the study population had one or two MetS risk markers, by no means a small proportion.

We compared MetS with a well-studied chronic disease risk factor, obesity. Our findings demonstrated a higher prevalence of chronic disease in individuals with MetS compared with those with obesity (shown in Table 3), although the differences were not statistically significant. A previous study has described MetS as more predictive of future disease than obesity alone.[44] The greater association between chronic disease and MetS in our study may, therefore, further signify a public health utility for MetS as a key indicator of disease risk.

Limitations

Working with the CHMS data, sample size proved to be a limiting factor in providing reportable estimates for key covariates, such as for sociodemographic characteristics, and limited the scope of the study to a national viewpoint, since it is not built to produce regional estimates. Further, the use of self-reported information for activities such as smoking or leisure time physical activity may have proven to be a limitation. Due to the lack of pertinent variables to measure undiagnosed diabetes, our definition is limited in scope and interpretations should be made with caution. To limit the effects of confounders, BMI, age and sex were all controlled for in multivariate analyses.

Conclusion

MetS represents a condition that is strongly associated with factors such as obesity, ethnicity and leisure time physical activity. Our study demonstrates the differential pattern by which MetS affects specific subpopulations and indicates an association between MetS and major chronic conditions.[45] Since Canadians with MetS have significantly higher rates of undiagnosed chronic diseases than the overall population and higher predicted rates of future chronic disease, it may be of value for clinicians to include MetS, in addition to obesity, as an indicator for chronic disease and useful for public health policy-makers to consider MetS when directing preventive population health efforts.

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CHAPTER 3

The Social Gradient of Chronic Disease Risk: Examining factors contributing to Metabolic Syndrome

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Current Status: Under Review with the Public Library of Science

Abstract

Introduction: Metabolic syndrome (MetS) is a risk condition associated with higher odds of leading chronic conditions such as diabetes and cardiovascular diseases. Risk factors for MetS include those within the material, behavioural and psychosocial paradigm. Indeed, a social gradient of MetS has been previously described linking lower income and educational status with higher odds of MetS. This paper seeks to explore whether behavioural and psychosocial factors mediate this social gradient.

Methods: The Canadian Health Measures Survey was analysed to examine mediation pathways that may underlie the relationship between socioeconomic status (SES) and MetS in Canadian adults ages 18 and over. The association of (i) SES with MetS, (ii) SES with behavioural and psychosocial risk factors, and (iii) behavioural and psychosocial risk factors with MetS were examined to identify possible mediators of the social gradient of MetS. Logistic regression, multinomial regression, and standardized logit coefficients were used to identify possible mediators and calculate percent reductions in MetS associated with them.

Results: A social gradient in metabolic syndrome exists in the Canadian adult population. Psychosocial risk factors were not identified as mediators of this gradient. However, the behavioural risk factors of alcohol use, smoking, physical inactivity, and screen time were found to be partial mediators of this pathway. Relative to the highest socioeconomic level, these mediators account for 17% and 44% of the social gradient of the second lowest and lowest income adequacy levels, and to 22% and 10% of the second lowest and lowest education levels.

Discussion: Disparities in metabolic syndrome exist in Canadian adults according to income adequacy and education status. These disparities appear to be accounted for, in part, by patterns in alcohol use, smoking behaviours and measures of physical inactivity.

KEY WORDS: Metabolic syndrome, social gradient, income adequacy, lifestyle risk factors, psychosocial risk factors

Introduction

Studies of the links between socioeconomic status (SES) and health have a long history. Since the industrial revolution, scientists have noted how gradients in social class and standards of living adversely impact health [1, 2]. With their landmark study, Marmot et al. revealed such an association with cardiovascular health[3], and subsequent studies have linked this gradient to chronic conditions, such as diabetes[4] and coronary heart disease[5], as well as to risk behaviours and states, like tobacco use[6], alcohol use[7] and obesity[8, 9].

The phenomenon of the social gradient in health is often examined using hierarchies of SES as measured by educational attainment and income[10, 11]. Both these indicators are associated with better access to material resources, through income, and social resources consistent with Bourdieux's theory of social capital[12 13]. Material risk factors impact health through direct effects on absolute living standards, but also through indirect effects by way of the unequal circumstances giving rise to relative disadvantage [13, 14]. As suggested by the social causation hypothesis, a social environment of financial and economic uncertainty negatively affects health[15]. Accordingly, lower income has been associated with pathways to chronic disease and shorter life expectancy[10, 16-18]. In a study of diabetes mortality, a twofold higher risk was associated with having less than a high-school education (Relative hazard (RH) 2.05, 1.78-2.35) and having a family income below the poverty line (RH 2.41, 2.05-2.84)[19]. SES also impacts drivers of health inequality through behavioural[6] and psychosocial mechanisms[20]. For instance, in an analysis of Canadians aged 15 to 85, current-smoking rates were lower, and quitting rates higher, in parallel with increasing education levels[6].

The potential impact of modifiable health determinants, such as those under the behavioural paradigm, has led to them being explored as avenues for chronic disease prevention [21, 22]. Unlike socio-demographic risk factors, which are impossible or more difficult to modify, factors such as tobacco use[23], physical activity [24], and healthy diets have gained momentum as pathways to reduce health disparities[21, 25]. Beyond these lifestyle factors, psychosocial constructs, including thoughts, feelings and experiences are being increasingly recognized as important determinants of health[26]. For example, the ability to adapt and cope with adverse life events has been linked to better health outcomes[27, 28]. In a meta-analysis of 10 prospective studies, Russ et al. demonstrated a dose-response association between subclinical distress, a psychosocial concept, and increased risk of mortality[29].

Metabolic syndrome (MetS) is a risk condition associated with chronic disease. It describes the co-expression of three or more (of five) risk markers, such as elevated glucose levels and triglycerides. While each risk marker may be independently associated with chronic disease, they are collectively thought to confer a greater risk based on the number and patterning of risk markers[30-32]. MetS has been associated with health status and mortality, such as with hypertension[33], diabetes[33, 34], cardiovascular disease(CVD) [31, 34] and all-cause mortality[34]. For instance, a population attributable fraction of 6-7% for all-cause mortality, 12-17% for CVD, and 30-52% for diabetes has been linked to MetS. As such, MetS has also been proposed as an indicator of chronic disease risk in primary care guidelines [35]. In addition to its association with chronic disease, MetS has also been shown to associate with factors from each of the paradigms of heath determinants discussed above. Material factors, such as education[33, 36, 37] and income[36], behavioural factors, such as physical activity[38, 39], or inactivity[40, 41] and diet [39],

and psychosocial factors, such as chronic work stress[42] and stressful life events[43], have all been linked to MetS.

This paper seeks to examine whether the social gradient of MetS[33, 44] is mediated by behavioural and psychosocial factors.

Methods

Data source

The Canadian Health Measures Survey (CHMS) is a nationally representative population survey aimed at collecting information related to the health of Canadians. This survey, which covers the population living in the 10 provinces aged 6 to 79 years, uses a complex sampling design and is cross-sectional in nature. Data were collected from respondents living near sixteen collection sites in Nova Scotia, New Brunswick, Quebec, Ontario, Alberta and British Columbia. Residents of Indian Reserves or Crown lands, institutions and certain remote regions, and full-time members of the Canadian Forces were excluded.

Data collection involved a combination of general household interview and, for physical measures, a visit to a mobile examination clinic (MEC). The former enabled collection of self-reported information regarding current health status, socioeconomic status, nutrition, smoking habits, alcohol use, medical history, current health status, sexual behaviour, lifestyle and physical activity. The latter permitted collection of physical, blood, urine, indoor air, and tap water measures. Physical measures included anthropometric data regarding measured height and weight, waist circumference, accelerometer-based physical activity, and blood

pressure. Blood measures included fasting plasma glucose levels, lipid profiles, and vitamin D status.

Study population

Data from the household, laboratory, and fasted subsamples were used in this analysis, and the response rates for each were 89.2%, 83.4%, and 87.6% respectively. We pooled the previously mentioned subsamples, and restricted to individuals who participated in the fasted subsample (represents 45% of total population) in Cycles 1 (2007-2009) and 2 (2009-2011) of the CHMS. This was done to increase total sample size and therefore statistical power. The overall combined response rate for the fasted subsample used in the analysis was 47.2%.[45] From the combined fasted subsample (n=5427), pregnant women (n = 17) and individuals aged less than 18 years (n = 1693) were excluded from the analysis.

Key definitions

Metabolic syndrome. The harmonized definition of MetS[46] was used to identify individuals with this condition on the basis of anthropometric measures, self-reported physician diagnosed risk conditions, or medication use related to the condition, and laboratory measures. More specifically, (1) ethnicity and gender specific waist circumference cut points, (2) elevated triglycerides, (3) reduced high-density lipoprotein cholesterol (HDL), (4) elevated blood pressure, and (5) elevated fasting plasma glucose were collectively used based on Harmonized definition specifications to identify MetS status. As per this definition, when an individual was identified to have 3 or more of the 5 risk markers for MetS, they were considered to have MetS.

Socioeconomic Status. SES was determined based on an individual's household income adequacy and education level. Since household income alone is not sufficient to understand an individual's standard of living because it does not capture how many people are sharing it, we chose to use a measure of income adequacy.[47] This measure was derived by Statistics Canada based on self-reported total household income and number of individuals living within the household into a four category variable, which we then recoded into a three category measure for our analyses (lowest and lower middle income grouping, upper middle income grouping, and highest income grouping). Education level was based on self-reported information, and was coded as less than secondary education, secondary school graduate, and some post-graduate education or more.

Behavioural Risk Factors.

Physical activity, screen time and sleep.

Self-reported measures were used to report on lifestyle factors, including those in the movement continuum of sleep, screen time and physical activity [48]. Physical inactivity was coded using responses to leisure-time physical activity participation over the last 3 months. Frequency and intensity of physical activity participation were used to derive energy expenditure values that were then coded by Statistics Canada into three levels of physical activity: active, moderately active, and inactive. We used this variable as a dichotomous measure, where active was categorized as a combination of the active and moderately active responses. Hours of sleep was based on self-reported hours of sleep over a 24-hour period, excluding time spent resting. In the absence of specific guidelines for screen time in adults, which we use as a proxy for sedentary behaviour, we chose to apply youth guidelines to our population, [49] which recommend less than 2 hours per day of sedentary behaviours based on

questions about the typical number of hours per week that a respondent was in front of a computer, television, video game, or watching DVDs or videos over the last 3 months to code for a binary variable of daily sedentary behaviour hours.

Alcohol and smoking.

Alcohol consumption was coded to align with definitions used internationally. This involved coding for the weekly number of grams of alcohol consumed number of drinks and conversion for a standard drink (1 drink = 14g alcohol) [50, 51] so as to identify sex-specific categories of alcohol consumption: abstainer, average, hazardous, and harmful categories. Smoking patterns were coded using self-reported type of smoker and number of cigarettes per day among those who smoke. Non-smokers and former smokers were identified based on self-report, and current smokers were categorized as light, moderate and heavy smokers based on their daily number of cigarettes[52].

Dietary Behaviours.

Dietary variables examined include milk, sugar-sweetened beverage (SSB) and fruit and vegetable consumption. Milk consumption was measured according to daily intake of milk, not including those non-dairy forms such as rice milk, soy milk or other. A binary variable was created to compare one or more serving per day with less than one serving per day. SSB was coded as a dichotomous variable of more than one serving per day, vs. less than or equal to one serving, based on daily intake of sports drinks, soft drinks and fruit drinks (such as fruit punch, Sunny Delight or Kool-Aid). Finally, fruit and vegetable intake was calculated based of 5 or more serving per day of fruit and vegetables intake, not including potato or potato products (french/home fries/hash brown potatoes).

Psychosocial Risk Factors. Self-perceived stress was captured using an individual self-report question "Thinking about the amount of stress in your life, would you say that most days are…", which were then recoded into three categories (not at all or not very stressful, a bit stressful, or quite a bit or extremely stressful). Work stress was also collected based on self-report and recoded in a similar manner into three categories. Self-reported job status was captured based on an individual question. Individuals who reported being unemployed were coded as not having work stress, and logistic models assessing work stress were adjusted for employment status. Self-reported sense of belonging to community was recoded into a dichotomous variable of very strong and somewhat strong vs. somewhat weak and very weak sense of belonging. Self-reported diagnosed mood disorder, which captures whether an individual has a disorder such as depression, bipolar disorder, mania, or dysthymia, was included. Finally, self-perceived quality of life was assessed through a single question recoded to 3 categories: excellent and very good, good, or fair and poor, and life satisfaction was similarly assessed, with responses recoded to 3 categories: very satisfied or satisfied, neither satisfied or dissatisfied, or somewhat or very dissatisfied.

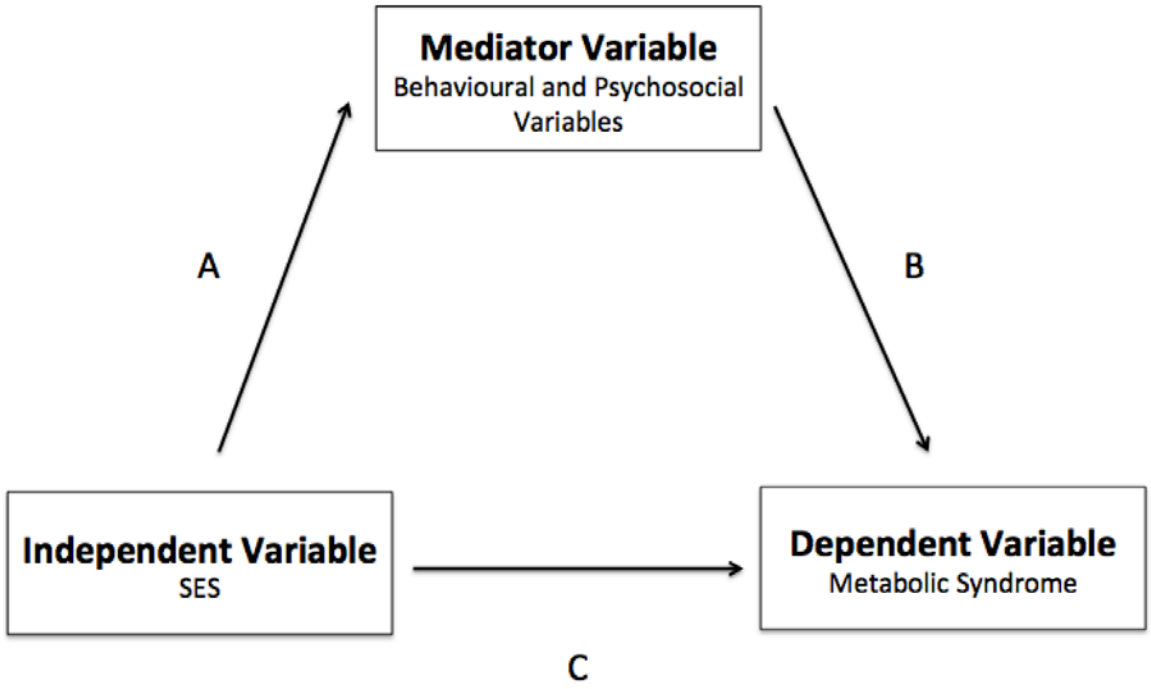
Analysis

Univariate and multivariate analyses were conducted using SAS Enterprise Guide 6.1 (Cary, NC, US). The CHMS uses two sampling frames for sample selection: an area frame of geographic units for selecting collection sites, and an area frame of dwellings within each site. Sampling weights were calculated using the selection weights for collection sites multiplied by the selection weights for households, and adjusted for non-response. Estimates were calculated using sample weights for the merged fasted subsample, and appropriate degrees of freedom were applied[45, 53, 54]. We examined prevalence of socioeconomic,

behavioural and psychosocial risk factors and MetS using the survey frequency procedure on SAS, and calculated appropriate variance using the balanced repeated replication method. This method uses bootstrap weights to estimate sampling variability from complex stratified sampling.

Logistic regression and multinomial regression were used to calculate crude and age- and sex- adjusted odds ratios. In order to identify possible mediators and associated percent reductions, mediation analysis[55] and standardized logit-coefficients were used. According to accepted methodologies widely used in several disciplines, "a variable functions as a mediator when it meets the following conditions: (a) variations in levels of the independent variable significantly account for variations in the presumed mediator (Figure 1, path A) (b) variations in the mediator significantly account for variations in the dependent variable (Figure 1, Path B), and (c) when Paths A and B are controlled, a previously significant relation between the independent and dependent variables (Figure 1, path C) is no longer significant…(or is reduced)….If the residual Path C is not zero, this indicates the operation of multiple mediating factors."[55] Mediators were tested separately for their association with SES (Figure 1, Path A), and independent effects were examined for their association with MetS (Figure 1, Path B). Since it is not appropriate to directly compare logit-coefficients from models with different variable standard deviations, we standardized these estimates for initial and final models using a method described by Menard [56]. Based on comparisons between standardized logit-coefficients from initial and final models, a reduction in odds demonstrates a potential mediating effect by the suggested mediators[55].

Figure 1. Mediation model



Ethics approval

Approval was obtained from the University of Ottawa Research Ethics Board (File # H10-14-23).

Results

Of the 3731 Canadian adults ages 18 to 79 included in our analysis, 20.3 %(17.3-23.2) met the criteria for MetS. The average number of MetS components among the overall population, those without MetS, and those with MetS were 1.4(1.2-1.5), 0.8(0.7-0.9) and 3.5(3.4-3.5) respectively. Canadian adults with lower income adequacy and education, who were inactive and watched more screen time, and who experienced mood disorders and a lower sense of community-belonging were more likely to experience MetS. Greater hours of sleep, lower alcohol consumption, heavy smoking, lower perceived quality of life, lower life

satisfaction, and lower levels of both work stress and general stress were also associated with this condition (Table 1). MetS showed a graded association with SES (prevalence of 25.6%(20.0-31.2), 21.5%(17.9-25.0) and 17.3%(13.1-21.6) as income level increases, and 33.6%(25.5-41.6), 24.6%(19.2-29.9) and 16.4%(13.5-19.3) as education level increases) (Figure 2). Furthermore, among those with MetS, the average number of MetS components was observed to be higher, but not significantly so, among those in lower SES categories (for each increasing level of income, the average number of MetS components was 3.6 (3.5-3.8), 3.4 (3.3-3.6), and 3.5 (3.4-3.6), and for each increasing education level it was 3.7(3.5-3.8), 3.5(3.3-3.6), and 3.5 (3.4-3.6)).

Table 1. Population characteristics in the overall population, and the population without and with metabolic syndrome.

		All		No MetS		MetS	
		N	%	N	%	N	%
Male		1756	49.6 (49.3-49.9)	1321	49.1(47.6-50.7)	435	51.5(45.5-57.4)
Age (± s.e)		3717	44.8±0.2	2869	42.3±0.2	848	54.6±0.9
Income Adequacy							
	Lowest	805	19.8 (16.9-22.8)	575	18.5(15.3-21.8)	230	25.0(19.5-30.6)
	Middle	1203	31.4(27.9-34.8)	900	30.9(27.3-34.6)	303	33.3(27.9-38.7)
	Highest	1709	48.8(44.8-52.7)	1394	50.6(46.0-55.1)	315	41.7(34.8-48.6)
Education							
	< Secondary	493	13.5(11.4-15.5)	322	11.2(8.8-13.5)	171	22.6(17.0-28.1)
	Secondary Graduate	591	16.3(13.4-19.2)	437	15.4(12.5-18.3)	154	20.0(15.3-24.7)
	>Some Post-Secondary	2599	70.2(66.4-74.0)	2090	73.4(69.4-77.5)	509	57.4(51.1-63.7)
Alcohol Use							
	Abstainer	580	16.8(14.0-19.7)	403	15.2(11.7-18.7)	177	23.2(17.8-28.6)
	Responsible	2803	75.5(72.7-78.3)	2193	76.6(73.2-80.0)	610	71.2(65.8-76.7)
	Hazardous	169	4.8(3.4-6.1)	139	5.1(3.5-6.7)	30	3.5(2.0-5.0)[E]
	Harmful	90	2.9(1.8-4.0)[E]	70	3.1(1.9-4.3)[E]	20	2.1(0.7-3.5)[E]
Smoking							
	Never	1860	50.1(46.8-53.5)	1511	52.3(48.5-56.1)	349	41.4(35.3-47.6)
	Former	1126	28.2(25.7-30.6)	770	25.3(22.4-28.2)	356	39.4(34.8-44.1)
	Light	464	13.4(11.2-15.6)	387	14.2(12.0-16.4)	77	10.2(6.4-14.1)[E]
	Moderate	149	4.6(3.4-5.8)	122	4.9(3.4-6.4)	27	3.3(1.5-5.1)[E]
	Heavy	107	3.7(2.5-4.9)	75	3.2(1.9-4.6)[E]	32	5.6(3.2-7.9)[E]
Sleep							
	< 6.5 h	888	24.7(22.1-27.3)	671	24.8(21.9-27.6)	217	24.3(20.8-27.8)
	6.5 - 8.5 h	2469	65.5(62.9-68.1)	1941	66.5(63.6-69.4)	528	61.4(56.6-66.1)
	> 8/5h	360	9.9(8.1-11.7)	257	8.7(6.7-10.8)	103	14.3(10.2-18.4)

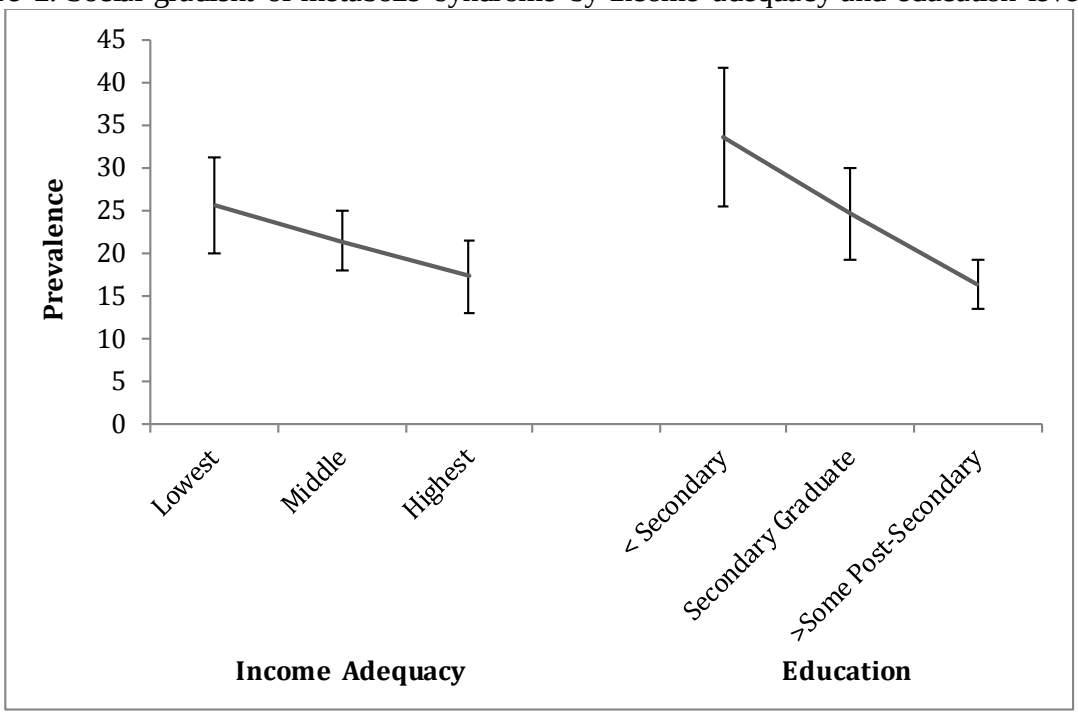
		All		No MetS		MetS	
		N	%	N	%	N	%
Inactive		1934	53.8(50.2-57.3)	1421	52.2(48.1-56.3)	513	60.1(54.6-65.6)
Excessive Screen time		1360	39.2(35.5-42.9)	996	37.1(32.6-41.6)	364	47.4(40.9-53.9)
Milk (≥1/day)		1857	51.0(48.5-53.5)	1446	51.4(48.0-54.7)	411	49.6(43.8-55.5)
Sugar Sweetened Beverages (>1/day)		419	13.2(11.2-15.2)	340	13.4(11.2-15.5)	79	12.3(7.8-16.9)[E]
Fruits and Vegetables (≥5/day)		642	17.0(14.7-19.2)	509	16.8(14.3-19.2)	133	17.8(11.9-23.8)
Stress		715	20.5(18.4-22.7)	548	21.0(18.4-23.7)	167	18.6(13.8-23.4)
Work Stress		750	22.8(20.5-25.1)	604	23.2(20.3-26.0)	146	21.3(15.5-27.1)
Limited sense of community		2475	62.1(58.6-65.5)	1886	61.2(57.3-65.2)	589	65.3(59.3-71.4)
Mood Disorder		379	9.7(8.2-11.2)	268	8.8(7.1-10.5)	111	13.0(9.3-16.7)
Perceived Quality of Life							
	Low	199	5.9(4.7-7.1)	131	5.6(3.9-7.2)	68	7.4(4.9-9.9)
	Moderate	969	27.1(24.6-29.6)	735	26.6(23.7-29.4)	234	29.3(23.6-35.1)
	High	2534	67.0(64.3-69.6)	1994	67.9(65.0-70.7)	540	63.2(57.0-69.5)
Life Satisfaction							
	Low	144	4.2(3.1-5.3)	95	3.9(2.3-5.5)[E]	49	5.5(3.4-7.6)[E]
	Moderate	234	7.0(5.2-8.9)	182	7.2(5.3-9.1)		[F]
	High	3321	88.7(86.7-90.8)	2581	88.9(86.8-91.1)	740	88.0(83.1-92.9)

Legend

[E] Interpret with caution (16.6<=Coefficient of Variation <33.3)

[F] Not suitable for release (Coefficient of Variation >=33.3)

Figure 2. Social gradient of metabolic syndrome by income adequacy and education levels.



A number of significant associations between SES (income and education) and potential mediators were observed (Table 2a-e). As compared to higher income and education groups, middle and lower income and education groups were significantly less likely to be in higher drinking categories than be abstainers and significantly more likely to in higher smoking categories than those who never smoked. Across these same SES levels, the movement continuum variables of sleep in excess of 8.5 hours and physical inactivity were significantly more prevalent. The only dietary variable to factor significantly was consumption of SSBs, which was significantly more prevalent across lower income and education levels. Compared to the highest levels of education attainment, a low perceived quality of life was the only significant psychosocial variable. However, across lower levels of income, mood disorder, lower life satisfaction, and lower life satisfaction were all significant.

Table 2: Odds of reported Behavioural (a,b,c) and Psychosocial (d, e) risk factors by income and education levels

(a) Lifestyle Habits: Alcohol use and smoking behaviours

		Alcohol Use				Smoking				
		1	responsible	hazardous	harmful	1	former	light	moderate	heavy
Income Adequacy	Lowest	1	0.4(0.3-0.6)	0.3(0.1-0.8)	0.1(0.1-0.3)	1	0.8(0.5-1.3)	1.8(1.3-2.5)	3.9(1.58-9.35)	2.6(1.3-5.1)
	Moderate	1	0.6(0.4-0.7)	0.5(0.2-1.1)	0.2(0.1-0.7)	1	0.7(0.5-0.9)	0.9(0.6-1.3)	2.2(1.0-4.6)	2.9(1.4-6.0)
	Highest	1	1	1	1	1	1	1	1	1
Education Level	< Secondary	1	0.5(0.3-0.7)	0.6(0.2-1.5)	0.2(0.0-1.1)	1	0.9(0.6-1.4)	2.4(1.3-4.2)	2.7(1.2-5.9)	4.5(1.9-10.9)
	Secondary Graduate	1	0.7(0.4-1.0)	1.0(0.5-2.4)	0.2(0.1-0.6)	1	1.3(0.9-1.8)	1.3(0.9-1.9)	2.7(1.2-5.8)	1.6(0.7-3.9)
	>Some Post-Secondary	1	1	1	1	1	1	1	1	1

Category 1 for alcohol use refers to abstainers and for smoking refers to individuals who never smoked.

(b) Non-movement behaviours: Sleep, physical inactivity and screen time

		Sleep			Inactive	Excessive screen time
		< 6.5 h	6.5 - 8.5 h	> 8/5h		
Income Adequacy	Lowest	1.3(1.0-1.8)	1	2.4(1.3-4.6)	1.4(1.0-1.9)	1.5(1.1-1.9)
	Moderate	1.2(0.8-1.6)	1	1.3(0.8-2.2)	1.3(1.0-1.7)	1.1(0.8-1.6)
	Highest	1	1	1	1	1
Education Level	< Secondary	1.7(1.2-2.2)	1	2.8(1.7-4.6)	1.8(1.3-2.4)	1.4(0.9-2.1)
	Secondary Graduate	1.3(0.9-1.8)	1	1.3(0.7-2.3)	1.2(0.9-1.6)	1.0(0.7-1.4)
	>Some Post-Secondary	1	1	1	1	1

(c) Dietary behaviours: Consumption of milk, sugar sweetened beverages, and fruits and vegetables

		Milk (≥1/day)	Sugar Sweetened Beverages (>1/day)	Fruits and Vegetables (≥5/day)
Income Adequacy	Lowest	0.8 (0.6-1.2)	1.6 (1.0-2.8)	0.6 (0.4-0.9)
	Moderate	1.1 (0.8-1.5)	1.6 (1.0-2.7)	0.7 (0.5-1.0)
	Highest	1	1	1
Education Level	< Secondary	0.7 (0.5-1.0)	2.9 (1.7-4.9)	0.7 (0.4-1.3)
	Secondary Graduate	1.0(0.8-1.4)	1.3 (0.9-1.8)	0.5 (0.4-0.8)
	>Some Post-Secondary	1	1	1

(d) Mental Health: Stress, work stress and mood disorder

		Stress	Work Stress	Mood Disorder
Income Adequacy	Lowest	1.5(0.8-2.5)	0.5(0.3-0.8)	2.3(1.2-4.2)
	Moderate	0.8(0.6-1.0)	0.5(0.4-0.6)	1.1(0.8-1.5)
	Highest	1	1	1
Education Level	< Secondary	1.0(0.6-1.7)	0.6(0.4-1.1)	0.9(0.6-1.2)
	Secondary Graduate	0.8(0.6-1.1)	1.0(0.8-1.4)	1.0(0.6-1.6)
	>Some Post-Secondary	1	1	1

(e) Well-being: Sense of community, life satisfaction and perceived quality of life

		Limited sense of community	Perceived Quality of Life			Life Satisfaction		
			Low	Moderate	High	Low	Moderate	High
Income Adequacy	Lowest	1.1(0.8-1.5)	10.3(4.8-22.2)	2.6(1.9-3.8)	1	8.4(3.7-19.1)	3.1(1.4-6.9)	1
	Moderate	1.2(0.9-1.5)	4.3(2.1-8.6)	1.8(1.3-2.5)	1	4.3(2.5-7.3)	1.6(0.9-3.1)	1
	Highest	1	1	1	1	1	1	1
Education Level	< Secondary	1.1(0.8-1.7)	2.8(1.5-5.4)	2.0(1.3-3.0)	1	1.1(0.6-2.2)	1.3(0.8-2.2)	1
	Secondary Graduate	1.1(0.8-1.5)	2.2(1.1-4.4)	2.2(1.6-3.0)	1	2.6(1.3-5.5)	1.4(0.8-2.7)	1
	>Some Post-Secondary	1	1	1	1	1	1	1

Models adjusted for age and sex
E: Interpret with caution (16.6<=Coefficient of Variation <33.3)
F: Not suitable for release (Coefficient of Variation >=33.3)

Examining the associations of these same behavioural and psychosocial factors with MetS, the odds ratios for MetS were significantly lower among hazardous alcohol drinkers relative to those who abstain (OR 0.4, 0.2-1.0), former smokers relative to never smokers (OR 1.5, 1.1-2.0), those who were physically inactive as compared to active (OR 1.2, 1.0-1.6), and those who accumulated greater than two hours per day of screen time relative to those who accumulated less (OR 1.6, 1.1-2.4) (Table 3, Model 3). It is noteworthy that the odds ratios observed when examining behavioural factors and psychosocial factors separately changed when they were all included in the model to examine independent associations. While they still remained significant, the magnitude of the associations of hazardous alcohol consumption and physical inactivity decreased. Further, the significant association of harmful alcohol consumption became an insignificant association. Similar changes occurred with psychosocial factors, but none became significant. Taking the results of these two models (Tables 2 and 3) together suggested that alcohol use, smoking, physical inactivity and screen time should be included in the final meditational model (Table 4).

Table 3. Odds ratio for metabolic syndrome according to behavioural and psychosocial risk factors

Risk Factor		Model 1 – Behavioural Factors	Model 2 – Psychosocial Factors	Model 3 – Both
		OR	OR	OR
Alcohol Use				
	Abstainer	1	1	1
	Responsible	0.6 (0.4-1.1)		0.6 (0.4-1.2)
	Hazardous	0.5 (0.2-0.9)		0.4 (0.2-0.9)
	Harmful	0.1 (0.2-0.9)		0.4 (0.2-1.0)
Smoking				
	Never	1	1	1
	Former	1.5 (1.1-2.0)		1.5 (1.1-2.0)
	Light	1.0 (0.6-1.6)		1.0 (0.6-1.7)
	Moderate	0.7 (0.3-1.6)		0.7 (0.3-1.6)
	Heavy	1.8 (0.9-3.7)		1.8 (0.9-3.7)
Sleep				
	< 6.5 h	1.0 (0.8-1.3)		1.0 (0.7-1.3)
	6.5 - 8.5 h	1	1	1
	> 8/5h	1.4 (0.9-2.4)		1.4 (0.8-2.6)
Inactive		1.3 (1.0-1.7)		1.2 (1.0-1.6)
Excess screen time		1.6 (1.1-2.3)		1.6 (1.1-2.4)
Milk (≥1/day)		1.0 (0.7-1.4)		1.0 (0.7-1.4)
Sugar Sweetened Beverages (>1/day)		1.3 (0.8-2.1)		1.3 (0.7-2.2)
Fruits and Vegetables (≥5/day)		1.1 (0.6-1.9)		1.1 (0.6-1.9)
Stress			0.8 (0.5-1.3)	0.8 (0.5-1.4)
Work Stress			1.5 (0.9-2.6)	1.6 (0.9-2.8)
Limited sense of community			1.1 (0.8-1.5)	1.2 (0.8-1.6)
Mood Disorder			1.3 (0.9-1.9)	1.2 (0.8-1.8)
Perceived Quality of Life				
	Low		1	1
	Moderate		0.9 (0.4-1.8)	0.8 (0.3-2.0)
	High		0.8 (0.4-1.6)	0.8 (0.3-2.0)
Life Satisfaction				
	Low		1	1
	Moderate		0.7 (0.2-2.5)	0.7 (0.2-3.1)
	High		0.8 (0.4-1.8)	0.8 (0.3-1.8)

Models adjusted for age and sex

Table 4. Identifying mediators for final mediation model

Mediators	Significant associations in Path A	Significant associations in Path B	Include in Final Model
Alcohol Use	X	X	X
Smoking	X	X	X
Sleep	X		
Physical Inactivity	X	X	X
Screen time	X	X	X
Milk			
SSB	X		
FV	X		
Stress			
Work Stress	X		
Limited sense of community			
Mood Disorder	X		
Perceived Quality of Life	X		
Life Satisfaction	X		

Paths A and B refer to pathways identified in the Mediation Model (Figure 1)

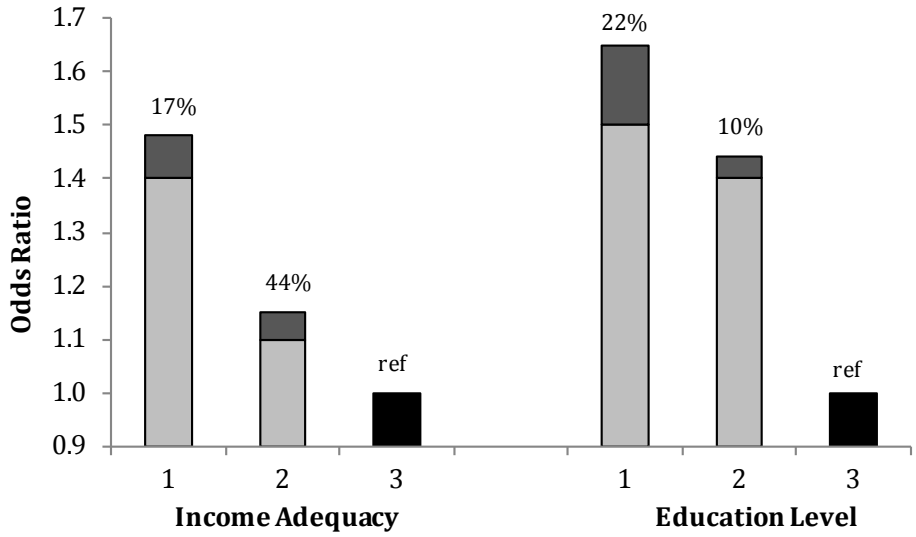
Our initial model assessing the association of SES with MetS, and adjusted by sex and age, was compared to our final model with identified mediating variables (alcohol use, smoking, inactivity and screen time). After calculating standardized regression coefficients for the respective SES levels, percent reductions after accounting for behavioural variables (those identified for inclusion in the model) were calculated. Across SES categories, these behavioural risk factors accounted for a 17.0% and 43.7% reduction in the association between the two lowest income levels and MetS, and a 22.2% and 9.8% reduction in the association between the lowest education levels and MetS (Table 5, Figure 3). Analyzed individually, alcohol consumption explained a 20.6% and 36.4% reduction across income levels, and a 10.6% and 9.6% reduction across education levels, and movement continuum variables accounted for 7.5% and 14.8% reductions across income levels and a 12.1%

reduction and 0.5% increase across education levels. It is noteworthy that smoking exhibited a suppressor effect across income categories, resulting in a 13.6% and 3.8% increase in standardized coefficients across income levels, compared to a 1.7% and 0.1% reduction across education levels.

Table 5. Odds ratio for metabolic syndrome according to social position and percentage change due to mediating factors

	Initial Model		**Final Model**		**Percent Difference**
	OR	**b***	**OR**	**b***	
Income					
Lowest	1.43 (0.91-2.26)	0.0489	1.35(0.84-2.18)	0.0406	-17.0
Middle	1.10(0.80-1.50)	0.0151	1.05(0.77-1.45)	0.0085	-43.7
Highest	1	-	1	-	
Education					
< Secondary	1.62(1.04-2.51)	0.0550	1.47(0.94-2.32)	0.0428	-22.2
Secondary Graduate	1.45(1.04-2.02)	0.0516	1.41(1.01-1.96)	0.0465	-9.8
>Some Post-Secondary	1	-	1	-	

Figure 3. Percent reductions in the odds of metabolic syndrome accounted for by identified mediators.



Percent reductions are identified by the listed estimates which describe differences in standardized logit-coefficients. Identified mediators are alcohol use, smoking, physical inactivity and screen time. (Income adequacy 1: lowest, 2: middle, 3: highest; Education level 1: < secondary education, 2: secondary graduate, 3: > some post-secondary).

Discussion

This study examines the extent to which socioeconomic gradients in MetS may be explained by behavioural and psychosocial factors. MetS was prevalent in our population, at roughly one in five. This estimate is in keeping with previous Canadian reports using the Harmonized definition for MetS[33, 57], and higher than 14.9% prevalence reported using the NCEP definition[33, 58]. The discrepancy in these estimates may be due to the fact that the Harmonized definition recognizes that the risk associated with specific waist circumferences varies by population group, making it more sensitive to risk variation that may occur due to sex or ethnicity[46]. The co-expression of MetS risk markers was also interesting. Comparing

the mean number of risk markers in those with and without MetS, our results suggest that once one risk marker is present, the others tend to accompany it. The observation that individuals with MetS in the lower SES categories had a higher average number of MetS components was also interesting, although not significant. The numbering and patterning of these combinations may be important. There are age and sex differences in the way that MetS combinations relate to mortality risk, and this risk is not necessarily related to the number of MetS risk markers one may exhibit[32, 59-62].

Our findings confirm the inverse social gradient of MetS in our population, which aligns with previous studies [36, 37], but which was only significant by education level based on logistic regression analyses controlled for age and sex. Those with less than post-secondary education, or a secondary graduate degree were significantly more likely to have MetS than those with some post-secondary education or more. While not statistically significant, a similar stepwise gradient was observed for income levels as well. Based on a review of the literature, no study was identified to have examined the mediating role of psychosocial and behavioural risk factors in the social gradient of MetS in Canada as we do here. In our study, only mediators captured within the behavioural paradigm (alcohol use, smoking, screen time, and physical inactivity) were identified as significant for inclusion in the final mediation model. Heavy smoking has been previously described as related to MetS, and we found a close to significant association, although our estimate may have been affected by power due to sample size limitations [63-65]. Our finding of elevated MetS risk among former smokers has been described previously by Calo et al., who also reported elevated levels of triglycerides, blood pressure, and fasting glucose among this smoking group compared to never and

current smokers[66]. Although income and education were inversely associated with MetS (negative direct effect), inclusion of current smoking behaviours increased the magnitude of this association, thereby suggesting a suppression (or negative mediation) effect due to smoking[67]. The previous association of smoking as a mediator between SES and CVD risk (as measured through waist circumference) can serve as a replication study affirming the mediating, and not confounding, effect of smoking[68].

The remaining mediators exhibited a positive mediation effect. Alcohol use did not follow the J-shaped association with MetS as described previously based on a meta-analysis of prospective studies[69], but did mimic the association shown from other cross-sectional analyses[70]. Higher levels of alcohol use were associated with a lower risk of MetS, although the association was attenuated and no longer significant in the harmful consumption category when the models included psychosocial variables. Examining the movement continuum variables identified, our findings aligned with previous studies suggesting that both physical inactivity[38] and higher levels of accumulated screen time[71] were associated with MetS. The description of a mediating effect of alcohol consumption and physical activity with all-cause mortality and cardiovascular disease in a prospective study supports the distinction of our identified mediators as being mediators and not simply confounders[68].

Pathways for psychosocial factors as mediators of the SES – health gradient have been described and have called attention to the need for further research[10]. Although psychosocial factors such as chronic stress[72], work stress[42], job control[73], life satisfaction[74], and social isolation[75] have previously been shown to associate with MetS, they were not significant in

this study. This could be attributed to the inclusion of weak measures of psychosocial variables, and that the use of individual questions as opposed to validated scales resulted in reduced sensitivity to psychosocial states. Response biases could also influence the results, and objective measures of psychosocial concepts, where possible for concepts such as social networks, could strengthen this work. Conceptually, however, it is worth continuing to investigate how the psychosocial paradigm associates with behavioural risk factors and ill health given the strong and significant relationships observed in other studies[10, 76].

Behavioural and lifestyle risk factors represent specific actions taken at the individual level. Ajzen's theory of planned behaviour suggests that volitional behaviours, such as our movement continuum variables, are actions that may be influenced by perceived behavioural control[77]. Perceived behavioural control represents an individual's perceived ability to perform a given activity and ties into theories of self-efficacy[78]. So, we might infer that psychosocial factors influence behaviours more directly, and health indirectly through behaviours. While this hypothesis is one that should be explored further, there is some evidence for this suggestion. In a study by Giles-Corti et al., adults living in low SES neighbourhoods were less likely to use nearby recreational facilities compared to those living in high SES areas, but not for a lack of available facilities. Instead, this difference was attributable to perceived access and neighbourhood environment acting as a barrier. [79]. The positive association between life satisfaction[80] and health risk perceptions[81, 82] with health behaviours like not smoking, engaging in physical activity and eating a healthy diet further lend evidence to the suggestion that psychosocial variables affect behavioural actions. Finally, in a mediation analysis looking at the association of SES with CVD risk,

psychosocial variables were identified as significant mediators, but ones that follow a pathway towards risk. More specifically, income was observed to affect psychosocial stress and psychosocial distress, both of which were analysed to create a relational pathway placing them before behavioural risk and subsequent CVD risk[83].

Examining the association of mediators with the social gradient of MetS, movement continuum variables (sedentary behaviours as measured through screen time, and physical activity), smoking patterns and alcohol consumption were identified as significant predictors of MetS. Our indicators of socioeconomic status included income and education, and our final mediation model showed noticeable reductions in the odds of MetS on the basis of these mediators. For income, it is interesting that the mediators contributed to a greater attenuation in the middle-income adequacy group than the lowest. For education, reductions were less notable, but the MetS gradient steeper. The smaller reductions in the SES gradient may be explained by the reduced salience of education as an indicator of SES as time since graduation increases, especially given the mean age of our study population was 45 years old. A previous study by Prescott et al. conducted a similar analysis, and found that psychosocial and behaviour risk factors did not mediate the pathway of the social gradient of MetS, as measured by education level[84]. Similarly, our findings report a smaller association of education level with mediators of the social gradient of MetS relative to income adequacy. We did observe more pronounced mediation effects using measures of income rather than education. Although this difference may be due to the fact that the majority of our study population had some post-secondary education or more, the observed stronger association of income rather than education with CVD risk may in fact be a real effect, and has been

described elsewhere as well[83]. Regardless of the SES indicator considered, partial mediation of between 10% and 44% across all SES categories are noteworthy, particularly since they involve mediators that are modifiable risk factors. As preventive medicine gains importance as a way to tackle rising rates of chronic disease in Canada, it has become increasingly relevant to identify modifiable risk factors that both reduce inequities in health and chronic disease overall.

Strengths and Limitations

Much of the literature on MetS uses the NCEP definition. It is possible that our use of the Harmonized definition attenuated significant associations of MetS with behavioural and psychosocial factors by way of pathways linked to the parameters modified within this newer definition. Furthermore, our study combined two cycles of the cross-sectional CHMS survey and made use of self-reported data. It is possible that risk factors, behaviours, and observed associations changed over the four-year time frame and were affected by respondent bias[8]. Small sample size and measurement issues, such as differences and lack of precision for psychosocial variables, may have further limited the ability to identify significant associations. This lack of significant findings in this study, however, should not be interpreted as an absence of a relationship given that associations have been observed in other studies. Further research is needed before concluding that psychosocial factors do not play into the social gradient of MetS. As discussed previously, it is possible that behavioural factors mediate the relationship of psychosocial factors with MetS, so further analyses into complex pathways would be beneficial.

Cross-sectional studies constrain causal inference and allow for the possibility that an individual's health status may have influenced their behaviours (health selection), instead of the reciprocal. However, our final mediation model identified mediators previously described as avenues to manage MetS[86], which suggests that our findings align with current evidence and practice and do not reflect health selection processes. Replication studies further provide the ability to distinguish between mediation and confounding, and can help reject the possibility of type I error from mediation analyses[67]. Therefore, prior cross-sectional[83] and prospective[68] studies affirming the mediators identified in our study lend support to the mediation effects identified in this analysis.

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CHAPTER 4

Physical Activity and Non-Movement Behaviours: Their independent and combined associations with Metabolic Syndrome

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Abstract

Introduction: Metabolic syndrome (MetS) is a prevalent risk condition associated with a higher risk of chronic conditions, including diabetes and cardiovascular diseases. Non-movement behaviours (NMB), including sleep, screen time and sedentary activity, as well as physical activity have been associated with MetS. In light of the increasing prevalence of NMBs, and the moderate rates of physical activity guideline adherence in Canada, this analysis examines the independent and combined associations of NMB and physical activity with MetS.

Methods: Data on Canadians 18 years and older from the Canadian Health Measures Survey (n = 2901) were used to examine the moderating effect of moderate-to-vigorous physical activity (MVPA) guideline adherence (150 minutes or more of MVPA/week, based on accelerometer) on the association of NMBs (sleep based on self-report, screen time based on self-report, and sedentary time based on accelerometer) with MetS. Logistic regression analyses were conducted and sampling weights were applied to represent the Canadian adult population.

Results: A graded association between PA and MetS was observed, with those achieving less MVPA than guidelines having a higher odds of MetS (OR 2.9, 95 % CI: 1.9–4.5 for < 75 mins/week of MVPA, and OR 1.8, 95 % CI: 1.2–2.8 for 75–150 mins/week, as compared to those accumulating 150 mins/week or more). When examining the moderating effect of PA on the association between NMBs and MetS, we found that (1) for participants who met guidelines, no level of any NMB was significantly associated with MetS and (2) for those who did not achieve guidelines, there was an increased odds of MetS based on excess NMB time(OR 3.2, 95 % CI: 1.5–6.8 for 1.4–2.1 h/day and OR 4.4, 95 % CI: 2.5–7.9 for ≥2.1

h/day of screen time and 75–150 mins/week of MVPA, OR 1.7, 95 % CI: 1.1–2.5 for ≥8 h/day of sleep time and <75 mins/week of MVPA, and OR 2.2, 95 % CI: 1.3–3.8 for 9.2–10.3 h/day of sedentary time and <75 mins/week of MVPA).

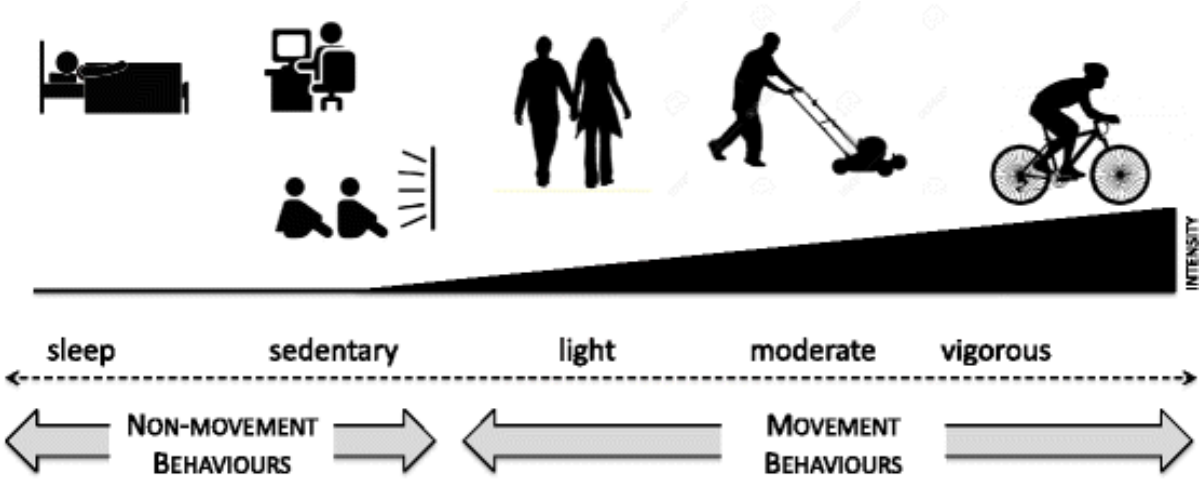
Conclusion: Adhering to physical activity guidelines may mitigate the associations of NMBs with MetS. Given that associations between NMBs and MetS were not significant among Canadians meeting PA guidelines, these findings suggest the beneficial role of physical activity to prevent chronic disease risk.

KEY WORDS: metabolic syndrome, sedentary behaviours, non-movement behaviours, physical activity guideline adherence, chronic disease risk

Introduction

In the past 50 years, data have demonstrated a change in the way we engage in physical activity. This includes movement behaviours, such as walking, but also non-movement behaviours (NMB) like sleep and sedentary behaviours (Figure 1). In 1970, 20% of adults were in jobs involving light physical activity, and 30% in ones requiring more intense energy expenditure. By 2000, this balance changed, and 40% were in the former category, while only 20% were in the latter. Similarly, screen behaviours have increased reflecting the jump in households with a computer and internet between 1989 to 2009 from 15% to 69%[1, 2]. Today, approximately 29.2% of Canadian adults watch 15 hours or more of television per week and 14.8% engage in 11 hours or more of computer use[3]. Taking the various forms of sedentary behaviours together, the majority of Canadian adults' waking hours (~68% of their day) are sedentary, with men spending 9.6 hours, and women 9.8 hours, in such activity[4]. As adults spend increased amounts of time in environments built for comfort, such as through using cars for transport or engaging in screen-based behaviours, a shift in daily patterns of physical activity has emerged.

Figure 1. Range of physical activity and non-movement behaviours over a 24-hour day



Morris' 1953 study of the association of cardiovascular disease (CVD) with occupation-based physical activity patterns among London Transport and Post Office employees set the stage for subsequent epidemiological studies regarding physical activity and health [5]. In the 60 years since then, inquiry into the particulars of physical activity have led to an appreciation of it as a continuum[6], with types of physical activity identified on the basis of their intensity as measured in metabolic equivalents (METs), which is a ratio of energy expended during an activity relative to at rest[7], or on accelerometer based counts per minute (cpm)[4]. Accordingly, moderate (3-5.9 METs, 1535-3961 cpm) to vigorous (≥6 METs, ≥3962 cpm) levels of physical activity[4, 8] (MVPA) are most recommended based on their inverse associations with obesity and chronic disease risk[9-11]. While an appreciation for physical activity as a continuum has long been acknowledged, MVPA has been the focus of most research, with only a recent renewed interest in the rest of the spectrum. For example, in a meta- analysis of all-cause mortality cross domains of physical activity, Samitz et al. reported a 0.86 (0.80–0.92) risk ratio for all-cause mortality in individuals with 150 minutes per week of MVPA compared to those with the lowest level of MVPA[12]. Similar reports of

dose-response associations with CVD, stroke, hypertension, colon cancer, breast cancer and all-cause mortality[13] have led to current physical guidelines for adults, which suggest accumulating at least 150 minutes of MVPA per week in bouts of 10 minutes or more[7, 14].

For the average Canadian, MVPA accounts for less than 5% of the 24-hour day. The rest of the day is comprised of other forms of physical activity and NMBs along the movement continuum (Figure 1) [6]. These include light physical activity (1.6-2.9 METs, 100-1534cpm), which includes standing and walking slowly, sedentary behaviours (1-1.5 METs in a sitting or reclining posture, < 100cpm), and sleep (0.9 METs) [4, 6, 8, 15, 16]. While sedentary behaviours may be identified on the basis of energy expenditure, they can also be identified based on the type of activity. In contemporary society, this can include sitting-related activities, such as transport, television viewing, and seated work-related activities. Prospective studies have demonstrated the association of premature mortality with sitting time[17, 18], television and screen based activities[19-21], and other sedentary behaviours[22].

Sleep also has associations with chronic disease. In a meta-analysis of prospective sleep studies, Cappuccio et al. describe how short sleep duration (≤5-6 hours/night) was associated with greater odds of coronary heart disease (CHD, RR 1.48, 1.22-1.80) and stroke (RR 1.15, 1.00-1.31), while long sleep duration (≥8-9 hours/night) was associated with odds of CHD (RR 1.38, 1.15-1.66), stroke (RR 1.65, 1.45-1.87) and total CVD (RR 1.41, 1.19-1.68)[23]. Sleep describes an NMB that has reciprocal interactions with exercise[24] and, unlike sedentary behaviour, also has an important role in physiologic function. These two non-movement behaviours (NMB) are distinct from light physical activity, which is highly negatively

correlated with sedentary time, thereby suggesting a public health benefit of replacing sedentary time with light physical activity[25].

Metabolic Syndrome (MetS) has been suggested as an early indicator of chronic disease risk [26]. This condition describes the co-existence of several cardiometabolic risk factors, which collectively contribute to an increased risk of CVD[27], diabetes[28, 29] and various cancers[30]. Physical activity levels have been associated with a higher risk of MetS overall, but also with its component risk markers. For instance, for each hour of daily sitting, there is a 1.03 and 0.37 percent increase in triglyceride and waist circumference measures respectively [31].The odds of MetS were 2.07 (1.49-2.88) and 1.48 (0.95-2.31) greater, in women and men respectively, for watching ≥14 hours/week of screen time as compared with those who watched ≤ 7 hours[20]. In a longitudinal analysis of sleep behaviours, Chaput et al. reported that short sleep duration (≤ 6 hours) was associated with MetS (RR 1.74, 1.05-2.72), but not long sleep duration (≥ 9 hours)[32]. Examining the independent associations of sleep time, screen time and sedentary behaviours with MetS, Saleh et al. described a significant association for the highest level of the latter two behaviours[33]. When examining movement behaviours on the other end of the continuum, the inverse is noticed. More specifically, adults engaging in vigorous activity hours had half the odds (OR 0.52, 0.40-0.67) of having MetS than among those who engaged in none. Moderate activity was similarly beneficial (OR 0.78, 0.63-0.96 among those with ≥ 24 hours of moderate METs/week, relative to <24 hours)[34]. Even light physical activity was observed to associate with beneficial MetS outcomes (OR 0.44, 0.24-0.81 in the highest and OR 0.51, 0.29-0.89 in the middle tertile of

light physical activity relative to the lowest)[35]. It is not surprising then that moderate and vigorous physical activity are suggested as behaviours to manage MetS [36].

In light of the increasing prevalence of NMBs, and their suggested risk for future chronic disease, this analysis examined the independent associations of NMB with MetS, and the joint associations of NMB with MVPA guideline adherence.

Methods

Data source

The Canadian Health Measures Survey (CHMS) is a nationally representative population survey aimed at collecting information related to the health of Canadians[37]. This survey, which covers the population living in the 10 provinces aged 6 to 79 years, uses a complex sampling design and is cross-sectional in nature. For each survey cycle, data was collected from respondents living near sixteen collection sites in Nova Scotia, New Brunswick, Quebec, Ontario, Alberta and British Columbia. Residents of Indian Reserves or Crown lands, institutions and certain remote regions, and full-time members of the Canadian Forces were excluded.

Data collection involved a combination of general household interview and, for physical measures, a visit to a mobile examination clinic (MEC). The former enabled collection of self-reported information regarding current health status, socioeconomic status, nutrition, smoking habits, alcohol use, medical history, current health status, sexual behaviour, sleep hours and physical activity. The latter permitted collection of physical, blood, urine, indoor

air, and tap water measures. Physical measures included anthropometric data regarding measured height and weight, waist circumference, accelerometer-based physical activity, and blood pressure. Blood measures included fasting plasma glucose levels, lipid profiles, and vitamin D status.

Following their visit to a MEC, ambulatory respondents were asked to wear an Actical accelerometer (Phillips – Respironics, Oregon, USA) over their right hip on an elasticized belt during their waking hours for 7 days. At the first occurrence of midnight after the MEC visit, the accelerometers were initiated to monitor counts of physical activity[38]. The accelerometer measured and recorded time-stamped acceleration in all directions, which allows for calculation of the intensity, duration and frequency of movement[39]. The digitized values are summed over a user-specified interval or epoch of 1 minute, resulting in a measure of cpm. Accelerometer based physical activity data were then cleaned to ensure individuals had 10 hours of data per day, and at least 4 days of valid collection days. The monitors were returned to Statistics Canada, the data were downloaded and the monitor was checked to determine if it was still within the manufacturer's calibration specifications[4, 38].

Study population

Data from the household, laboratory, fasted, and activity monitor subsamples were used in this analysis, and the response rates for each were 89.2%, 83.4%, 87.6%, and 79.4% respectively. We pooled the previously mentioned subsamples, and restricted to individuals who participated in both the fasted (represents 45% of total population) and activity monitor subsample in Cycles 1 (2007-2009) and 2 (2009-2011) of the CHMS. This was done to

increase total sample size and therefore statistical power. The combined response rate for the full sample with the fasted subsample used in the analysis was 47.2% (N=5427), and with the activity monitor subsample was 42.1% (N=9339). Individuals who participated in both these subsamples were retained (N=4273)[40]. Pregnant women (N=10) and individuals under the age of 18 (N=1362) were excluded, leading to the study population used for this analysis (N=2901).

Key definitions

*Metabolic syndrome***.** The harmonized definition of MetS[41] was used to identify individuals with this condition on the basis of anthropometric measures, self-reported physician diagnosed risk conditions, or medication use related to the condition, and laboratory measures. More specifically, (1) ethnicity and gender specific waist circumference cut points, (2) elevated triglycerides, (3) reduced high-density lipoprotein cholesterol (HDL), (4) elevated blood pressure, and (5) elevated fasting plasma glucose were collectively used based on Harmonized definition specifications to identify MetS status. As per this definition, when an individual was identified to have 3 or more of the 5 risk markers, they were considered to have MetS.

Physical Activity Measures. Accelerometer based information allowed for the determination of daily minutes of moderate and vigorous physical activity per day. MVPA guideline adherence was determined using the activity monitor based measure of daily minutes of moderate and vigorous physical activity and the current Canadian guidelines for adults. Full guideline adherence (≥150 minutes of MVPA per week) and a threshold at half guideline

adherence (75 minutes of MVPA per week) were used to create three levels of MVPA for analyses (less than ½ the guidelines as low MVPA, between ½ the guideline and guideline adherence as moderate MVPA, and more than or equal to guideline adherence as high MVPA)[14]. Sedentary behaviour was also captured based on activity monitor based cpm, and tertiles were accordingly created (<9.2 hours/day, 9.2-10.3 hours/day, ≥10.3 hours/day). Sleep behaviours were identified based on self-reported hours of sleep over a 24-hour day, excluding time spent resting, and tertiles were calculated as <7hours/day, 7-8 hours/day, and ≥8 hours/day. Screen time was measured using responses to questions measuring the typical number of hours per week that a respondent was in front of a computer, television, video game, or watching DVDs or videos over the last 3 months, which was then recoded to determine daily hours in these screen-based activities. From this, tertiles were identified as <1.4 hours, 1.4-2.1 hours and ≥2.1 hours/day.

Combined variables were coded that took into account the tertiles of each NMB with levels of MVPA. In the case of sleep, for example, this led to a 9-category variable for sleep-MVPA (low sleep-low MVPA, low sleep-medium MVPA, low sleep-high MVPA, medium sleep-low MVPA, medium sleep-medium MVPA, medium sleep-high MVPA, high sleep-low MVPA, high sleep-medium MVPA, high sleep-high MVPA). Similar variables were created for screen time and sedentary behaviour.

Sociodemographic risk factors. Age, sex, and ethnicity (Caucasian vs. non-Caucasian) were used to identify individual demographic characteristics based on self-reported estimates. Sample size limitations did not permit more granularity on the basis of ethnic background.

Income adequacy was derived by Statistics Canada based on self-reported total household income and number of individuals living within the household into a four category variable, which we then recoded into a three category measure for our analyses (lowest and lower middle income grouping, upper middle income grouping, and highest income grouping). Education level was based on self-reported highest attainment, and was coded as less than secondary education, secondary school graduate, and some post-graduate education or more.

Behavioural risk factors. Alcohol consumption was coded to align with definitions used internationally. This involved coding for the weekly number of grams of alcohol consumed based on self-reported number of drinks and conversion for a standard drink (1 drink = 14g alcohol) [42, 43] so as to identify sex-specific categories of alcohol consumption: abstainer, average, hazardous, and harmful categories. Smoking patterns were coded using self-reported type of smoker and number of cigarettes per day among those who smoke. Non-smokers and former smokers were identified based on self-report, and current smokers were categorized as light, moderate and heavy smokers based on their daily number of cigarettes[44]. Time spent reading was included based on a self-reported measure, and daily minutes of light physical activity was included in analyses based on activity monitor based estimates.

Analysis

Physical activity measures of interest were the NMBs of screen time, sedentary behaviour and sleep, as well as MVPA. Statistical analyses were conducted using SAS Enterprise Guide 6.1 (Cary, NC, US). All analyses were weighted to account for unequal probabilities of selection and variance was calculated using the balanced repeated replicate weight

approach. Tertiles for NMBs were created based on the 33rd and 66th percentile as determined using univariate analysis. Patterns along the various physical activity measures were described using mean estimates and mean differences were determined using t-tests for independent samples. All other analyses were controlled for by identified confounders, determined based on a p-value <0.1 for any of the four physical activity measures of interest. This led to the adjustment by age, alcohol consumption, education level, and light physical activity. Models were also adjusted by sex, even though it was not significantly related to any of the four physical activity measures of interest. Other measures considered but not retained due to non-significance included income level, time spent reading, and smoking behaviours.

The independent association of the four physical activity measures of interest with MetS were calculated using logistic regression analyses . Effect modification, or moderation, was examined for the three NMBs by stratifying logistic regression results by the 3 levels of MVPA [45, 46]. Combined associations were examined using the combined variables for each NMB with MVPA levels using logistic regression analyses with the referent category being the level with the least expected risk of MetS. Analyses using the survey suite of procedures were adjusted for variance using the balanced repeated replication method. This method uses bootstrap weights to estimate sampling variability from complex stratified sampling.

Ethics approval

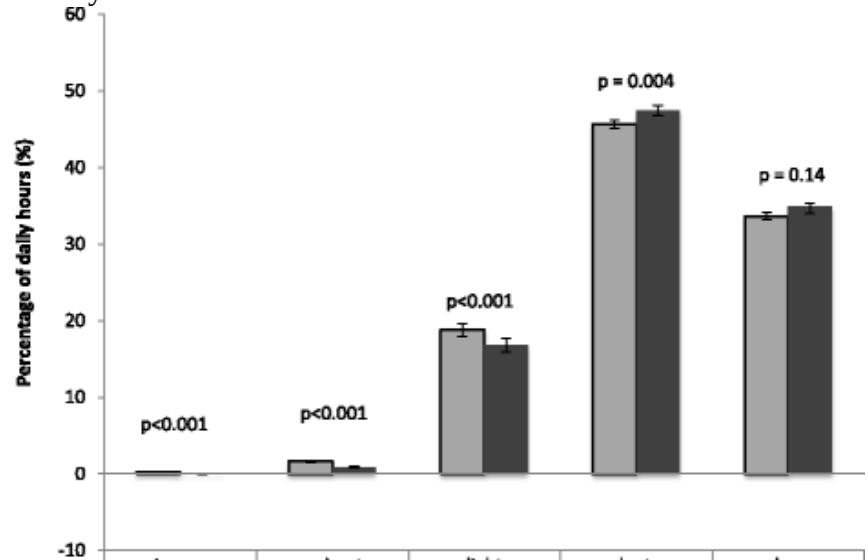
Approval was obtained from the University of Ottawa Research Ethics Board (File # H10-14-23).

Results

When combining accelerometer and self-reported information to describe behaviours over the course of an average day, behaviours for 21 h of the day were captured, with waking hours accounting for 66 % of the day, and sleep for the remaining 34 %. On average, 46 % of Canadian adults' hours were spent in sedentary time, and vigorous (0.2 %), moderate (1.5 %) and light (18.4 %) physical activity accounted for the remaining hours. Not including the 3 h that are unaccounted for based on data collection, Canadians spent 0.04 h/day in vigorous, 0.3 h/day in moderate, 3.9 h/day in light physical activity, and 9.7 h/day in sedentary time, as well as 7.2 h/day asleep.

MetS was prevalent in the Canadian adult population (19.0 %, 95 % CI: 15.7–22.4 %), and physical activity patterns varied by MetS status. Since the total hours of the day accounted for by MVPA and NMBs varied based on MetS status (21.23 hours for those without MetS and 20.97 hours for those with), results are discussed using percentage of total reported hours accounted for by the respective behaviours (Fig. 2). Comparing activity patterns between those with and without MetS, MetS was associated with significantly higher proportion of hours of sedentary time ($p = 0.004$), and significantly lower levels of vigorous ($p < 0.001$), moderate ($p < 0.001$) and light physical activity ($p < 0.001$). NMBs appear to be more prevalent among those with MetS, although sleep was not significantly different between those with and without MetS (sleep: $p = 0.14$).

Figure 2. Percentage of hours spent in various forms of physical activity among those with or without metabolic syndrome.



	vigorous	moderate	light	sedentary	sleep
No MetS	0.3	1.7	18.8	45.6	33.7
MetS	0.1	0.8	16.8	47.4	34.9

A similar pattern emerged when comparing hours between both groups. Individuals without MetS spent 0.06 (0.04-0.07) hours in vigorous, 0.4 (0.3-0.4) hours in moderate, 4.0(3.8-4.2) hours in light physical activity, and 9.7(9.6-9.8) hours in sedentary behaviour, as well as 7.2(7.0-7.3) hours asleep, while individuals with MetS spent 0.01(0.00-0.02) hours in vigorous, 0.2 (0.2-0.2) hours in moderate, 3.5(3.3-3.7) hours in light physical activity, 9.9 (9.8-10.1) hours in sedentary behaviour, as well as 7.3 (7.1-7.5) hours asleep.

Examining the independent relationships of physical activity behaviours with the odds of MetS, elevated odds was observed for those not achieving weekly MVPA guidelines (OR 2.9, 95 % CI: 1.9–4.5 for low MVPA, and OR 1.8, 95 % CI: 1.2–2.8 for moderate MVPA, as compared to those achieving MVPA guidelines). Similarly, excess screen time (≥2.1 h/ day, OR 1.8, 95 % CI: 1.2–2.8) was significantly associated with increased odds, as was excess

sleep time (≥8 h/ day, OR 1.4, 95 % CI: 1.0–2.1) and moderate sedentary time (9.2–10.3 h/ day, OR 1.5, 95 % CI: 1.2–2.1) (Table 1).

Table 1. Independent relationships of MVPA and NMB on the risk of metabolic syndrome

		N	Odds ratio
MVPA minutes	<75 mins/wk	1061	2.9 (1.9-4.5)
	75–150 mins/wk	707	1.8 (1.2–2.8)
	≥150 mins/wk	1133	ref
Screen Time	<1.4 h/d	1211	ref
	1.4–2.1 h/d	706	1.4 (0.9–2.1)
	≥2.1 h/d	982	1.8 (1.2–2.8)
Sleep Time	<7 h/d	957	1.2 (0.8–1.7)
	7–8 h/d	958	ref
	≥8 h/d	986	1.4 (1.0–2.1)
Sedentary Behaviour Time	<9.2 h/d	815	ref
	9.2–10.3 h/d	996	1.5 (1.2–2.1)
	≥10.3 h/d	1089	1.0 (0.7–1.4)

Models adjusted for age, sex, alcohol consumption, education level, income adequacy, and smoking behaviours. The respective remaining behaviours were included in the models so as to test independent relationships. (h/d = hours/day, mins/wk = minutes/week)

To examine whether the relationship between NMB and odds of MetS vary by adherence to MVPA guidelines, stratified analysis was employed and the remaining NMBs were kept in the model to test the independent effects. Indeed, the differential patterns of association for all NMBs across MVPA guideline strata suggest effect modification by the latter. Referent categories were created within each MVPA strata on the basis of the lowest risk category of NMB. Among individuals engaged in moderate MVPA, 1.4 to 2.1 and ≥ 2.1 h/day of screen time was significantly associated with an increased odds of MetS (OR 3.2, 95 % CI: 1.5–6.8 and 4.4, 95 % CI: 2.5–7.9 respectively). Similarly, among those engaged in low MVPA, there was a 1.7, 95 % CI: 1.1–2.5 increased odds of MetS for those who slept ≥8 h/day, and a 2.2, 95 % CI: 1.3–3.8 increased odds among those who engaged in 9.2–10.3 h of sedentary activity per day. There was no significant association of NMBs with MetS among those

individuals who adhered to physical activity guidelines and accumulated 150 min of MVPA/week (Table 2).

Table 2. Effect modification of the risk of metabolic syndrome associated with NMBs by MVPA guideline adherence

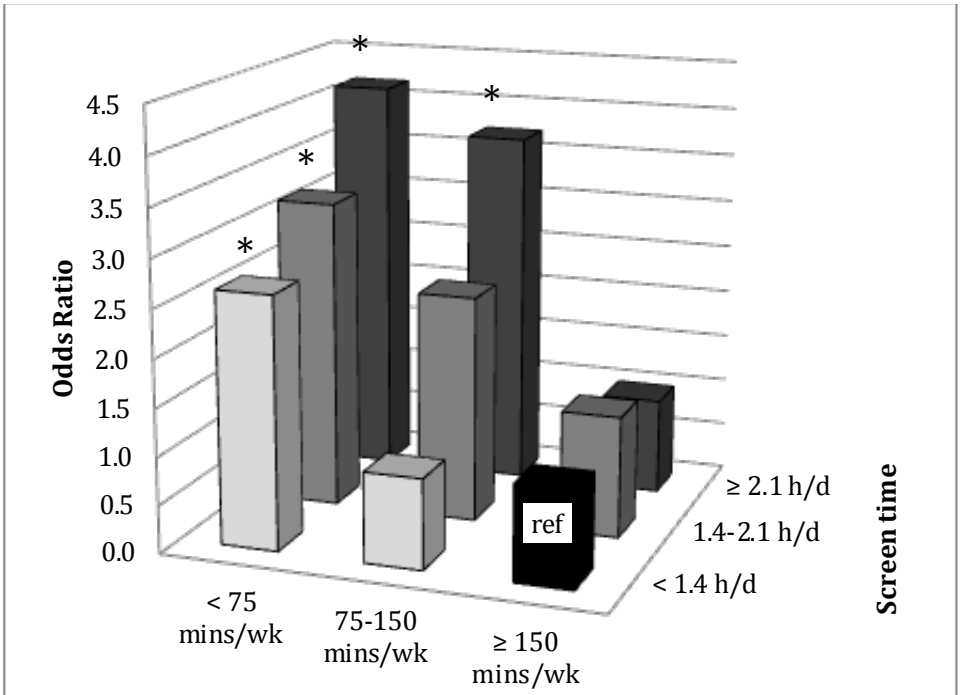
		Moderate to Vigorous Physical Activity					
		< 75 mins/wk		75-150 mins/wk		≥ 150 mins/wk	
		N	OR	N	OR	N	OR
Screen Time	<1.4 h/d	383	ref	298	ref	530	ref
	1.4-2.1 h/d	256	1.3 (0.7-2.1)	179	3.2 (1.5-6.8)	271	1.0 (0.3-2.9)
	≥ 2.1 h/d	421	1.7 (0.9-3.3)	230	4.4 (2.5-7.9)	331	1.3 (0.6-2.6)
Sleep Time	<7 h/d	315	1.2 (0.7-2.1)	202	1.1 (0.7-2.0)	298	1.3 (0.6-2.6)
	7-8 h/d	333	ref	247	ref	416	ref
	≥ 8 h/d	413	1.7 (1.1-2.5)	257	1.1 (0.5-2.4)	419	1.2 (0.5-2.8)
Sedentary Behaviour Time	<9.2 h/d	234	ref	215	ref	508	ref
	9.2-10.3 h/d	375	2.2 (1.3-3.8)	242	1.6 (0.9-3.0)	341	0.7 (0.3-1.6)
	≥ 10.3 h/d	452	1.6 (0.8-2.9)	250	0.5 (0.2-1.1)	284	1.0 (0.5-1.9)

Models adjusted for age, sex, alcohol consumption, education level, income adequacy, and smoking behaviours. The respective remaining behaviours were included in the models so as to test independent relationships. (h/d = hours/day, mins/wk = minutes/week)

To examine the joint association of NMB and MVPA behaviours, logistic regression analysis was conducted using variables reflecting all combinations of NMB and MVPA categories, as described in methods.. The referent category was the one with lowest expected risk. For all NMBs, when MVPA guidelines were achieved, there were no increased odds of MetS regardless of level of the NMB (Figure 3).

In the case of screen time, the referent category were those individuals who engaged in high MVPA and who accumulated <1.4 h of screen time per day. Relative to this group, all levels of screen behaviours for individuals who participated in low MVPA were associated with an increased odds of MetS (OR 2.6, 95 % CI: 1.4–4.8 for <1.4 h/day, OR 3.2, 95 % CI: 2.0–5.3 for 1.4–2.1 h/day, and OR 4.2, 95 % CI: 2.2–8.0 for ≥ 2.1 h/day). Among those who participated moderate MVPA, an increasing stepwise gradient was observed with increasing screen time (OR 0.9, 95 % CI: 0.5–1.8 for <1.4 h/day, OR 2.4, 95 % CI: 0.9–6.0 for 1.4–2.1 h/day, and OR 3.7, 95 % CI: 2.2–6.4 for ≥2.1 h/day). Finally, among those who adhered to MVPA guidelines, there were no significant associations of MetS with screen time (1.3, 95 % CI: 0.7–2.4 for 1.4–2.1 h/day, and 1.0, 95 % CI: 0.4–2.7 for ≥2.1 h/day) (Fig. 3a).

Figure 3a. Combined association of screen time and MVPA guideline adherence on MetS risk.



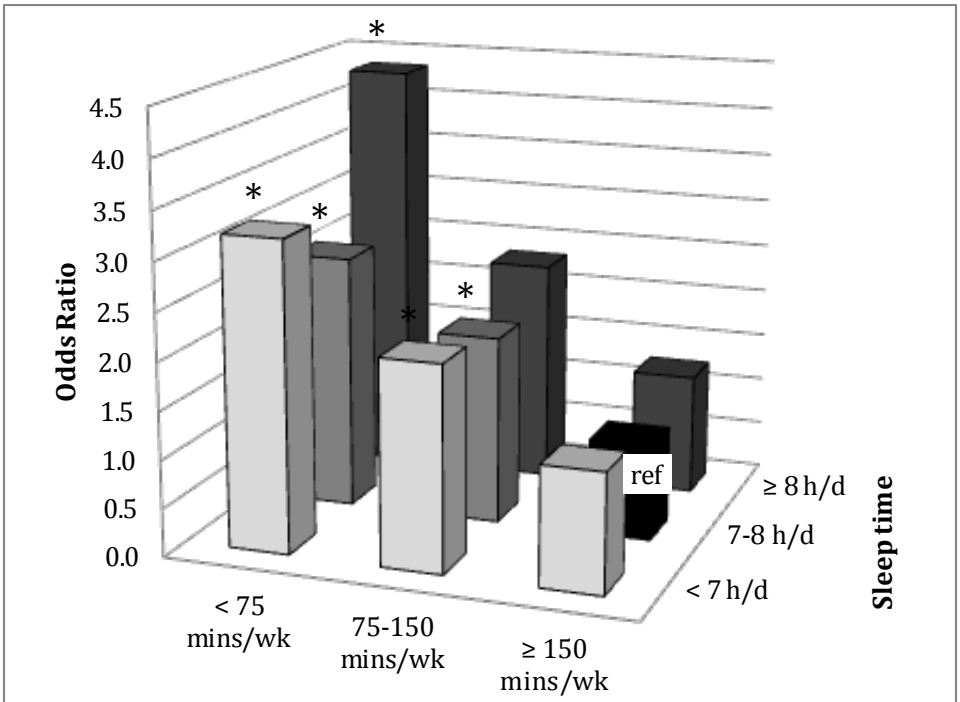
	< 75 mins/wk	75-150 mins/wk	≥ 150 mins/wk
< 1.4 h/d	2.6	0.9	1.0
1.4-2.1 h/d	3.2	2.4	1.3
≥ 2.1 h/d	4.2	3.7	1.0

Note: Models adjusted for age, sex, alcohol consumption, education level, income adequacy, smoking behaviours, sleep time, and sedentary time (h/d = hours/day, mins/wk = minutes/week, * = $p<0.05$).

Sleep behaviour exhibited a U-shaped risk association with MetS, with the 7–8 h/day of sleep and MVPA guideline adherence used as the reference category. Similar to screen behaviours, all levels of sleep hours were associated with increased odds of MetS for individuals who achieved low MVPA (OR 3.2, 95 % CI: 1.6–6.5 for <7 h/day, OR 2.6, 95 % CI: 1.4–4.9 for 7–8 h/day, and OR 4.3, 95 % CI: 2.1–9.1 for ≥ 8 h/day). Among those who achieved moderate MVPA, associations were only significant for those with moderate or low sleep time (OR 2.1, 95 % CI: 1.1–4.1 for <7 h/day, OR 2.0, 95 % CI: 1.0–3.8 for 7–8 h/day,

and OR 2.3, 95 % CI: 0.9–6.2 for ≥ 8 h/day). There were no significant associations of MetS with sleep time among those who adhered to MVPA guidelines, (1.2, 95 % CI: 0.6–2.4 for <7 h/day, and 1.3, 95 % CI: 0.6–2.6 for ≥ 8 h/day) (Fig. 3b).

Figure 3b. Combined association of sleep time and MVPA guideline adherence on MetS risk.



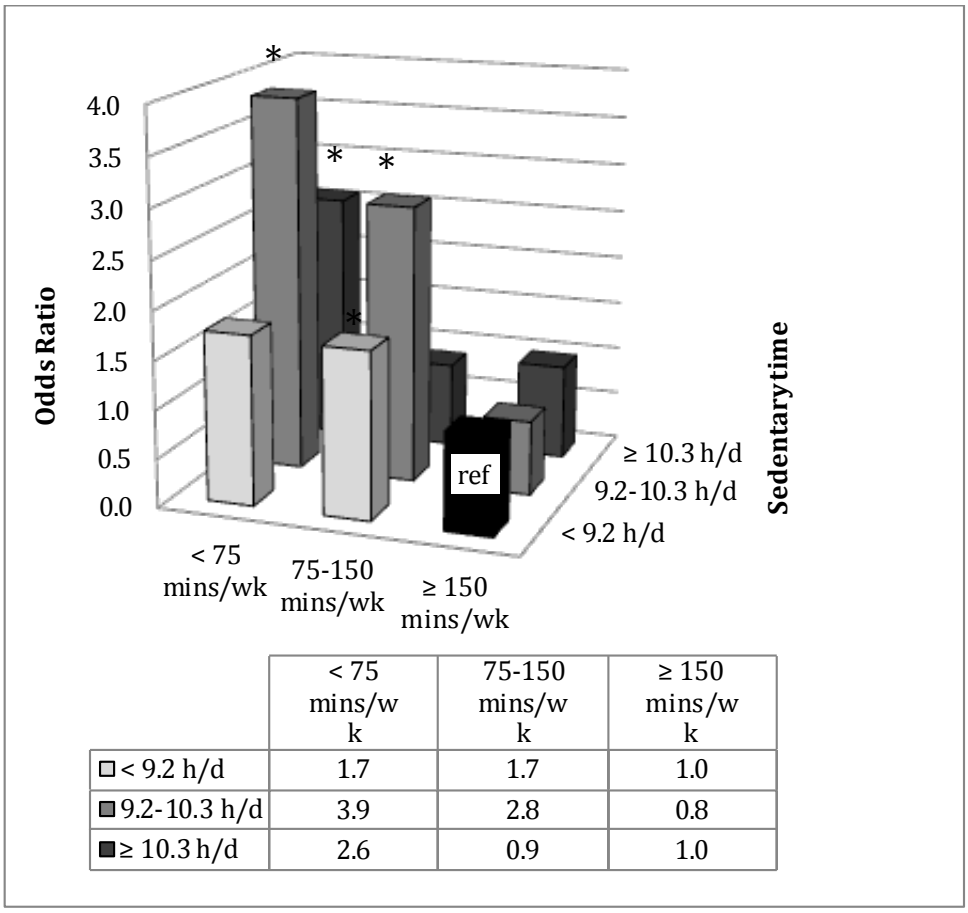
	< 75 mins/wk	75-150 mins/wk	≥ 150 mins/wk
< 7 h/d	3.2	2.1	1.2
7-8 h/d	2.6	2.0	1.0
≥ 8 h/d	4.3	2.3	1.3

Note: Models adjusted for age, sex, alcohol consumption, education level, income adequacy, smoking behaviours, screen time, and sedentary time (h/d = hours/day, mins/wk = minutes/week, * = p<0.05).

Finally, when examining sedentary time, there appears to be an inverse U-shaped curve, with individuals engaged in 9.2–10.3 h/day of sedentary time at most risk of MetS compared to the referent category of <9.2 h/day of sedentary time and MVPA guideline adherence. Among those who achieved low MVPA, sedentary time in excess of 9.2 h each day were

associated with MetS odds (OR 1.7, 95 % CI: 0.9–3.4 for <9.2 h/day, OR 3.9, 95 % CI: 2.1–7.1 for 9.2–10.3 h/day, and OR 2.6, 95 % CI: 1.5–4.6 for ≥ 10.3 h/day). Achieving moderate MVPA was only associated with increased odds of MetS for those in the moderate category of sedentary time (OR 1.7, 95 % CI: 1.0–3.0 for <9.2 h/day, OR 2.8, 95 % CI: 1.5–5.4 for 9.2–10.3 h/day, and OR 0.9, 95 % CI: 0.4–1.7 for ≥ 10.3 h/day). For those who did achieve MVPA guidelines, the associations of sedentary time with MetS were not significant (0.8, 95 % CI: 0.4–1.6 for 9.2–10.3 h/day and 1.0, 95 % CI: 0.6–1.7 for ≥ 10.3 h/day) (Fig. 3c).

Figure 3c. Combined association of sedentary time and MVPA guideline adherence on MetS risk.



	< 75 mins/wk	75-150 mins/wk	≥ 150 mins/wk
< 9.2 h/d	1.7	1.7	1.0
9.2-10.3 h/d	3.9	2.8	0.8
≥ 10.3 h/d	2.6	0.9	1.0

Note: Models adjusted for age, sex, alcohol consumption, education level, income adequacy, smoking behaviours, screen time, and sleep time (h/d = hours/day, mins/wk = minutes/week, * = p<0.05).

Discussion

This article explores the associations of MVPA and NMBs and MetS. The findings suggest that adhering to MVPA guidelines may mitigate MetS risk. MetS was prevalent among the study population, with almost one in five meeting criteria. This finding parallels other Canadian studies using the Harmonized definition for MetS[47, 48], but is higher than the 14.9% prevalence reported using the NCEP definition[47, 49], likely due to the fact that the former uses sex- and ethnicity- specific cut-offs.

Canadian adults spend approximately two-thirds of their day awake, and of these hours, a majority of time is spent in sedentary behaviour. Although roughly 9.7 hours per day or 66% of waking hours in sedentary behaviour reflects previous Canadian reports[4], it is noteworthy that such behaviour comprises a greater proportion of waking hours than those reported for Australia (57%) [25] or the U.S. (56.8%[50] to 58%[1]). This is concerning given the suggestion that time spent in sedentary behaviours displaces time spent in lower intensity movement behaviours, such as light physical activity, and can result in an overall reduction on physical activity levels[51]. Not surprisingly, individuals with MetS were more likely to engage in sedentary behaviours than those without MetS, and the reciprocal was true for active behaviours. In an examination of physical activity patterns with a clustered metabolic risk score, Healy et. al also described a similar differential pattern of physical activity based on MetS status(β-estimate and 95% CI: sedentary behaviour 0.23,0.08 to 0.38, light physical activity -0.20, -0.35 to -0.04, MVPA -0.17, -0.34 to -0.01)[25].

Given that movement and NMB do indeed associate with MetS, the independent and combined associations of these activity levels were of interest. Independent of sleep and sedentary behaviour, this study found that MVPA and screen time are associated with an increased odds of MetS. Similar to this study, Clarke et al. found that weekly volume of MVPA was strongly associated with MetS. Their findings, like ours, suggest the benefits of adhering to weekly MVPA guidelines. While our suggestion is based on testing independent associations of weekly MVPA, their study also examined the daily patterning of MVPA and did not find an association of this with MetS [52]. Similarly, the independent association of MVPA with MetS has been described elsewhere[53]. With regard to screen time, its association with MetS independent of physical activity has also been described previously for adolescents[54] and adults[53].

It is noteworthy that sedentary behaviour was not a significant predictor of MetS, given previous cross-sectional[25] and prospective[55] reports suggesting it would. It is possible that the non-significance observed in this study may be due to the absence of considering the ways in which this time was accumulated. That is to say, it may be that not total sedentary time, but rather bouts and length of bouts of sedentary behaviour are what is important for preventing MetS. In their assessment of this phenomenon, Healy et al. reported that the majority of sedentary activity breaks fell under light physical activity behaviours, and that independent of total sedentary time, the intensity and frequency of these breaks were negatively associated with MetS[56]. Furthermore, objective measures of sedentary behaviour fail to differentiate 'bad' forms of sedentariness with 'good' forms, such as reading. This points to the benefit of considering both objective and self-report measures of sedentary behaviour.

The independent association of sleep is also worth considering. Sleep levels identified in this analysis reflected recommended sleep durations, but unlike previous reports, showed a non-significant U-shaped pattern [57]. This distinction is likely due to the fact that we considered independent associations, which suggests that previous reported associations of sleep with MetS are possibly impacted by other physical activity patterns[58].

Given reports that sedentary behaviours appear to be increasing among adults[59], we sought to explore whether MVPA behaviour moderates the association of NMBs with MetS. Through stratified analysis examining the associations of MVPA levels on their association, significant associations were observed for NMBs at levels below MVPA guideline achievement. Most noteworthy is how, for any level of NMB, if adherence to physical activity guidelines was achieved, then no association of NMB with MetS was observed. The differential patterns, whether significant or not, do suggest a moderating role of guideline adherence. However, given that the independent associations of NMBs on MetS were non-significant in some instances, it is not surprising that the moderating associations by MVPA on these behaviours were not significant either.

While the stratified analysis enabled within strata comparisons, combined analyses permitted comparisons between combined levels of NMB-MVPA with categories associated with the least MetS odds. Patterns observed within strata in Table 2 persisted in Figure 3. However, Figure 3 permitted across strata comparisons, which appear to be more informative. Indeed, among participants adhering to MVPA guidelines, no elevated odds for MetS for any NMB was observed. While sedentary behaviours also showed significant associations, the unexpected inverse U-shaped pattern suggests that more study is required to better

understand this pattern of results. As mentioned previously, the lack of consideration made for breaks in sedentary behaviour may obscure true representation of sedentary time. Nevertheless, in a prospective analysis of the combined association of MVPA and leisure-time sitting, which represents a sedentary behaviour, Bell et al. reported 5- and 10- years estimates of incident MetS that mimic the inverse U-shape we report here. They suggest this U-shape may be attributed to misclassification error due to changing behaviour patterns over time [60]. In contrast, a similar prospective analysis reported a linear trend for risk of MetS with sedentary behaviour[55]. Therefore, further examination into the associations of sedentary behaviour, MVPA and MetS may be warranted.

Continuing the examination of combined associations, screen time and sleep time yielded some significant associations. Examining their joint associations in relation to obesity, Dunton et al. described the interaction associations between MVPA and TV or movie time[61]. For both screen time and sleep time, achieving less than half the guideline per week was associated with an increased risk. These results give credence to the importance of achieving MVPA guidelines, regardless of NMB behaviours, much as was observed in the present analysis. Furthermore, while achieving MVPA guidelines seems to eclipse the associations of NMBs with MetS, it is important to note that at lower levels of MVPA, NMBs have a strong association with MetS. Therefore, even in the absence of MVPA, NMBs continue to be important to MetS.

Based on a review of the literature, no previous study was identified to have examined the utility of MVPA guideline adherence independent of NMB, and its combined utility across different NMB behaviours. Indeed, physical activity has been supported for the primary and

secondary prevention of a number of chronic conditions[62-65], including MetS[36]. As with a previous study examining the combined associations of sedentary behaviour with MVPA in children[66], this study highlights the potential importance of MVPA guideline adherence independent of NMB behaviours in adults.

Limitations

This study used pooled cycles of the cross-sectional CHMS survey and it is possible that patterns of physical activity and non-movement behaviours changed over the four-year time frame. The cross-sectional nature of the study also restricted exploration of temporality of events, it is possible that MetS preceded the adoption of NMB behaviours or the decrease in MVPA participation. Furthermore, much of the literature on MetS uses the NCEP definition for MetS, while our study used the Harmonised definition. Differences in these definitions on the basis of ethnic and sex-specific cut-offs may account for differences between studies.

The combination of measured and self-report information might account for the missing 3 hours from the full 21-hour day used in this analysis. This is possibly due to reporting bias for self-reported sleep data. However, it is possible that accelerometer data may provide for some error. The accelerometer used in this study was meant to be worn during waking hours, and valid data were identified based on having at least 4 days of valid days, i.e. days with a minimum of 10 hours of wear time. This guideline is widely used, but was originally not developed using empirical evidence[39]. Failing to wear the accelerometer during the full waking period may have thus affected results. This is important since accelerometers worn for too few hours may lead to underestimation of time spent in different intensities of physical activity. In an semi-simulated analysis of the adequacy of wear times for different

physical activity intensities, wear times below 14 hours, it was shown that wear times at 10h/day resulted in 30% less recorded time spent in inactivity relative to the reference period of 14 h/day [39]. Accelerometer data capture for sedentary and light physical activity are also affected by the epoch duration of data capture, which might misclassify record of physical activity in either category as a result, resulting in very different interpretations. This too may have affected sedentary estimates in this study[38, 67]. Similarly, the inability to access information regarding sedentary breaks may have limited the accurate representation of sedentary risk for MetS[56, 68]. Future studies should look further into optimizing data collection for sedentary behaviours, including information regarding bouts of sedentary behaviour and addressing possible misclassification concerns.

Conclusions

Adhering to physical activity guidelines may mitigate the associations of NMBs with MetS. Given that associations between NMBs and MetS were not significant among Canadians meeting PA guidelines, these findings suggest the beneficial role of physical activity to prevent chronic disease risk.

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CHAPTER 5: Discussion

5.1 Summary of key findings

The goal of the current thesis was to contribute to the understanding of MetS as an indicator through which material, psychosocial and behavioural factors associate with chronic disease. The thesis explored the associations of MetS with upstream risk and protective factors, through their mediating role in the social gradient of MetS and associated risk based on differential patterns of health behaviours, and with downstream health outcomes, through the association of MetS with current and predicted chronic disease.

This thesis analyzed data from the 2007-2009 (cycle 1)[1] and 2009-2011 (cycle 2)[2] Canadian Health Measures Survey (CHMS) to address the following hypotheses. First, that MetS is not uniformly distributed across the Canadian population, and is associated with current and predicted risk of chronic disease. Second, that social gradients in MetS by income and education are mediated by psychosocial and behavioural risk factors. Finally, that patterns of physical activity and NMBs are differentially associated with MetS risk. The three articles included in the thesis address the three hypotheses above accordingly.

The first article, "Metabolic Syndrome an Chronic Disease", provided an updated estimate of MetS prevalence in Canada using cycle 1 of the CHMS according to three leading definitions; the NCEP, Harmonized and IDF definition of MetS. The observed prevalence was between one in six to one in five of the Canadian adults population, consistent with reports by Riediger et al[3]. Due to the cross-sectional nature of this data source, associations with downstream chronic disease were examined in two ways. First, associations with

current chronic conditions were identified through regression analyses with current and undiagnosed chronic conditions. The latter was used a proxy for future chronic disease, owing to the fact that a respondent would have identified themselves as not having a physician diagnosed condition, but their laboratory measures suggested the presence of condition of interest. This revealed a higher prevalence of diagnosed and undiagnosed hypertension, diabetes, chronic kidney disease and dyslipidemia among individuals with MetS than the overall population or among those who are considered to be obese, which is consistent with expected findings. This supports the utility of MetS as a chronic disease risk indicator which associates with several chronic conditions and which may precede diagnosis with chronic disease (as demonstrated by the association with undiagnosed disease). Next, to supplement this analysis with a validated approach to examining future chronic disease risk, we utilized the lipid-based Framingham 10-year risk calculator[4] and the DPoRT[5] algorithm to identify future risk of CVD and diabetes respectively among those with and without MetS. Given the literature associating MetS with risk of these conditions[6-8], this analysis allowed the identification of projected risk among Canadian adults on the basis of MetS status. Both these methods further reinforced our hypothesis that MetS is associated with risk of future chronic disease, and lend support to our hypothesis that MetS serves as an indicator of chronic disease risk.

Finally, to build our understanding of the distribution of MetS in Canada in paper 1, we included descriptive analyses. This facilitated the transition to papers 2 and 3, which discuss MetS as it relates to upstream risk factors. As anticipated, descriptive analyses revealed an age gradient of MetS, but also some notable associations with behavioural risk factors. Smoking and leisure-time physical inactivity, for instance, were significantly associated with

MetS among women. Although only behavioural risk factors were examined for their association with MetS, this provided initial suggestions that population patterns of MetS in Canadian adults may be worth exploring.

The second article, "The Social Gradient of Chronic Disease Risk: Examining factors contributing to Metabolic Syndrome", further delves into the association of upstream risk factors with MetS. Given the abundance of research suggesting social gradients in health[9-11], this paper first provides evidence of such a gradient for MetS across education and income. Subsequently, we conducted a mediation analysis[12] to examine the role behavioural and psychosocial risk factors may have in this social gradient. Through this analysis, alcohol use, smoking behaviours, leisure-time physical inactivity and screen time were identified as potential mediators of the social gradient of MetS. This suggests that actions on these modifiable risk factors may change, and hopefully reduce, the associations of SES with MetS.

The third paper, "Physical Activity and Non-Movement Behaviours: Their independent and combined associations with Metabolic Syndrome", set out to explore the associations of physical activity in more depth than in the previous two papers. Instead of isolating analyses to self-reported physical activity behaviours, this article also utilized accelerometer data to independently examine different levels of physical activity as they relate to MetS. This analysis explored the moderating effect of MVPA guideline adherence on various NMBs, namely self-reported screen time behaviours, self-reported sleep time, and measured sedentary behaviours. Our findings reiterate the utility of achieving recommended MVPA guidelines, as suggested by the lack of association of NMBs with MetS when guidelines

were adhered to. Different patterns of association emerged when exploring moderating effects, as well as combined effects.

5.2 Strengths

When this thesis began in 2010, there was a gap in reporting on MetS based on national measured data in Canada since the Canadian Heart Health Survey (CHHS) in 1989[13]. Based on a review of the literature, much of the research on MetS in the 20 years since the CHHS were based on provincial or hospital subsamples, or extrapolations using non-Canadian resources. Then, at that point in time, the recent release of the CHMS consequently opened doors to reviving research on this topic due to the availability of objectively measured national level data regarding MetS risk markers.

Given the importance of Canadian data to inform our understanding of patterns of health and risk and protective factors, the collection of papers included in this thesis lends value to our understanding of MetS in Canada. Based on a review of the literature, this thesis includes papers that contribute new and relevant information on MetS in Canada.. The first article is the first to use DPoRT and FRS algorithms to associate MetS (vs. no MetS) with future disease risk among Canadians. The second paper is a first for its examination of the mediating role of behavioural and psychosocial risk factors in the social gradient of MetS in Canada. Finally, the third paper is a first in its examination of independent and combined effects of MVPA and NMBs on the association with MetS. All the studies in this thesis are also benefitted by having a solid conceptual underpinning that is well supported in the literature and that aligns with the biologic plausibility of associations discussed.

This thesis made use of the CHMS, which enabled findings to be generalized to the majority of the Canadian population (approximately 96% of Canadians)[14]. Using cycles 1 and 2 of the CHMS permitted objective measures for all risk markers needed to identify MetS, and also provided the added benefit of being the first Canadian survey to objectively measure physical activity among Canadian adults through the use of accelerometers. This allowed for objective and comprehensive collection of physical activity profiles allowing for discernment of different levels of intensity of physical activity and inactivity. The use of measured data provides rigor to the analyses in this thesis. Other measures, however, were collected using self-reported data, which can impact the accuracy of reporting. Using data from the Canadian Community Health Survey, for instance, it was shown that participants tended to under report their weight when interviewed by phone than when interviewed in person[15]. While measures of BMI were obtained objectively in this thesis, other measures may have been subject to similar measurement error.

5.3 Limitations

Despite being a nationally representative survey with a large sample size, the complex nature of this survey serves as one limitation of this thesis. The small number of degrees of freedom, as determined based on the limited number of primary sampling units (15 collection sites), may have impacted the variability of estimates and their statistical power[16]. The cross-sectional nature of the dataset limited us to examining association, and did not allow an examination of temporal sequencing of cause and effect. This also restricted our ability to comment on directionality of observed associations. However, using evidence from

other studies, some suggestions of what the directionality might be were ascertained. For example, it is reasonable that material, psychosocial and behavioural risk factors precede MetS, and that MetS precedes chronic conditions[6, 7, 17].

Furthermore, this dataset was limiting in the sample size available for more detailed analyses. To start, all analyses were limited to adults 18+. Further, measures of fasting glucose were needed to identify MetS, thereby limiting the study sample to less than half of the original sample since not all respondents were asked to fast[18]. Finally, for the third paper, we only included individuals with valid accelerometer and fasting data. This restricted analyses to a smaller sample population, which disallowed the candidate from examining sex-specific associations or more detailed analyses. Self-reported variables also provided some limitations in that validated tools were not always employed to accurately capture psychosocial variables, and that bias may have affected reporting for self-reported behavioural factors[15].

While these factors limited our study sample, they were also what enabled us the wealth and variety of variables used in this thesis, including both the upstream and downstream factors associated with MetS. Such a varied, accurate, and nationally representative resource is not available elsewhere for the Canadian population, either as a cross-sectional, longitudinal or administrative data source. The latter resource, administrative data, would particularly be a limited data source given the low adoption rates of the MetS diagnosis code in clinical settings[19]. However, as Reynolds points out, it will take further research to build evidence as to the utility of MetS to support confidence with the adoption of MetS as a diagnostic category[20].

5.4 Future Directions

Studies into the factors contributing to chronic disease risk are important towards efforts to control their rising rates here in Canada. The studies included in this thesis supported proposed pathways associated with chronic disease risk, but were unable to explore concepts of causality. As a result, it would be prudent of future studies to explore suggested pathways through studies using longitudinal data and larger sample sizes. In addition to future studies that address study design limitations noted here, replication studies that reaffirm our findings would also be worthwhile for showing the generalizability of the present findings.

The scientific community has already embraced the idea of simple screening tools to identify chronic disease risk. MetS is one such risk tool that an individual is considered to have when they meet the diagnostic criteria, rendering it an absolute state that an individual has or does not. While this perspective of the co-expression of risk markers enables easy identification of MetS, there has been interest in examining MetS as an ordinal[21] and even continuous[22] measure, as well as for its individual components[23]. These latter approaches are informative in studies examining the nature of associations, and are as such exploratory. However, the approach of considering MetS as an absolute state is most appropriate in the public health setting since it offers a way to label a risk state applicable to a wider range of chronic diseases. Risk tools that identify risk in the population, and possibly prevent the development of chronic disease, have been developed using Canadian resources. For example, the DPoRT[5] and CANHEART[24] risk tool were each Canadian risk indices developed and validated to identify diabetes and CVD risk respectively using routinely captured data from

national surveys. Both use upstream socio-demographic and anthropometric variables to give an estimate of risk, but are specific to the condition they were built to examine. There is also the Framigham[4] risk tool, which uses clinical measures to assess CVD risk and which is thus less accessible to the general population. The development of these various tools reiterate the desire by the health community identify disease risk so as to possibly mitigate their development. The three prior examples were developed for specific conditions, and may thus be limiting in this respect. With regards to measures needed to estimate risk, the DPoRT and CANHEART tools have the advantage of using routinely collected national estimates so as to keep track of disease risk at the population level, while the FRS tool has the advantage of using clinical data that enables individual level assessment of risk in clinical settings. In this spectrum of screening tools, MetS is situated somewhere in between. It uses a combination of anthropometric and clinical estimates, and also has been shown to associate with several chronic conditions[7, 8, 17]. Unlike the other three tools, it uses a yes/no approach to identifying risk, as opposed to providing a percentage estimate of absolute risk. Studies assessing the utility of MetS do exist, and they compare MetS with FRS for their value as comparable risk tools[25], which they are often not. For instance, the utility of MetS and importance of age-based considerations was highlighted in a comparison of these two risk tools in an assessment of coronary artery disease (CAD) among Asians, a population who develop CAD at a younger age and also have a higher prevalence of MetS. Risk estimates were compared with angiographic CAD, and highlighted the utility of MetS at being more sensitive to risk. Among those younger than 45 years, no one was identified as having high risk based on FRS despite having angiographic CAD. MetS aligned better with observed angiographic CAD.[26] Future studies to address the utility of MetS as a screening tool, and to compare it with other available tools so as to better explain how or where to use it, are warranted.

The health community also has a great interest in upstream approaches to target chronic diseases. In Canada, the recent Canadian Cardiovascular Harmonized National Guidelines Endeavour (C-CHANGE)[27] initiative recognizes the substantial responsibility and load put on first-line of care primary care physicians to manage risk factors associated with CVD risk. Many of their recommendations involve tracking risk factors that are component risk markers of MetS, and their recommendations include behavioural approaches also used to intervene with MetS[27]. Their suggestions, which reflect harmonized recommendations from collaborations with non-governmental organizations in the fields of tobacco, cardiovascular disease, exercise physiology, and obesity, suggest that whether overt or inadvertent, efforts by the health community to identify and address MetS like states are already taking place[27].

5.5. Conclusion

This thesis builds support for viewing MetS through a health promotion and chronic disease prevention lens, which aligns better with the original intention of Reaven when he first discussed MetS as a conceptually attractive construct[28]. Reaven conceptualized MetS as a framework to discuss a substantial number of apparently unrelated biological events to use as a pragmatic approach to obtain better health outcomes[29]. Exploring MetS in this perspective, we demonstrate associations with modifiable risk factors already targeted by chronic disease prevention efforts. For instance, dietary and lifestyle modification have already been recommended[27, 30, 31] for many of the same conditions that MetS has been associated with.

The finding that modifiable risk factors can prevent, or slow the progression of, chronic diseases such as CVD, diabetes, and some cancers has been important since it suggests that these diseases are not inevitable consequences of modern society[32]. Similarly, the findings in this thesis are suggestive that lifestyle modifications may be associated with lower odds of MetS, an early risk state associated with these chronic conditions. Consequently, an interesting take away from this thesis is that whatever the risk tool or guideline, healthy behaviours may be a powerful route to mitigate chronic disease risk.

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APPENDICES

Appendix A: Ethics and Approvals

This appendix includes

(1) Ethics approval from the Ottawa Hospital Research Ethics Board

(2) Ethics approval from the University of Ottawa Ethics Board

(3) Data Centre access approval from the Social Sciences and Humanities Research Council

(1)

UNIVERSITY OF OTTAWA HEART INSTITUTE
INSTITUT DE CARDIOLOGIE DE L'UNIVERSITÉ D'OTTAWA

THE OTTAWA HOSPITAL
L'HÔPITAL D'OTTAWA

uOttawa

Ottawa Hospital Research Ethics Boards / Conseils d'éthique en recherches

725 Parkdale Avenue, Box 411, Ottawa, Ontario K1Y 4E9 613-798-5555 ext. 14902 Fax: 613-761-4311
http://www.ohri.ca/ohreb

November 8, 2012

Dr. Deepa Rao

Dear Dr. Rao:

Re: Protocol # 20120767-01H **Metabolic Syndrome and Public Health in Canada**

Protocol approval valid until - November 7, 2013

I am pleased to inform you that this protocol underwent delegated review by the Ottawa Hospital Research Ethics Board (OHREB) and is approved. No changes, amendments or addenda may be made to the protocol without the OHREB's review and approval.

Approval includes the following:
- Electronic OHREB Application
- Thesis Proposal, 2012
- Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1, April 2011

If the study is to continue beyond the expiry date noted above, a Renewal Form should be submitted to the OHREB approximately six weeks prior to the current expiry date. If the study has been completed by this date, a Termination Report should be submitted.

The Ottawa Hospital Research Ethics Board is constituted in accordance with, and operates in compliance with the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; Health Canada Good Clinical Practice: Consolidated Guideline; Part C Division 5 of the Food and Drug Regulations of Health Canada; and the provisions of the Ontario Health Information Protection Act 2004 and its applicable Regulations.

Raphael Saginur, M.D.
Chairman
Ottawa Hospital Research Ethics Board

RS/ll

(2)

File Number: H10-14-23 Date (mm/dd/yyyy): 11/11/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

Ethics Approval Notice

Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

First Name	Last Name	Affiliation	Role
Daniel	Krewski	Health Sciences / Others	Supervisor
Heather	Orpana	Social Sciences / Psychology	Co-Supervisor
Deepa	Rao	Health Sciences / Others	Student Researcher

File Number: H10-14-23

Type of Project: PhD Thesis – Secondary Use of Data

Title: Taking Control of Chronic Disease: The Role for Metabolic Syndrome in Public Health

Approval Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
11/11/2014	11/10/2015	

(Ia: Approval, Ib: Approval for initial stage only)

Special Conditions / Comments:
N/A

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www.recherche.uottawa.ca/deontologie/ www.research.uottawa.ca/ethics/

File Number: H10-14-23 Date (mm/dd/yyyy): 11/11/2014

Université d'Ottawa University of Ottawa
Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

This is to confirm that the University of Ottawa Research Ethics Board identified above, which operates in accordance with the Tri-Council Policy Statement (2010) and other applicable laws and regulations in Ontario, has examined and approved the ethics application for the above named research project. Ethics approval is valid for the period indicated above and subject to the conditions listed in the section entitled 'Special Conditions / Comments".

During the course of the project, the protocol may not be modified without prior written approval from the REB except when necessary to remove participants from immediate endangerment or when the modification(s) pertain to only administrative or logistical components of the project (e.g., change of telephone number). Investigators must also promptly alert the REB of any changes which increase the risk to participant(s), any changes which considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project and safety of the participant(s). Modifications to the project, including consent and recruitment documentation, should be submitted to the Ethics Office for approval using the "Modification to research project" form available at: http://www.research.uottawa.ca/ethics/forms.html.

Please submit an annual report to the Ethics Office four weeks before the above-referenced expiry date to request a renewal of this ethics approval. To close the file, a final report must be submitted. These documents can be found at: http://www.research.uottawa.ca/ethics/forms.html.

If you have any questions, please do not hesitate to contact the Ethics Office at extension 5387 or by e-mail at: ethics@uOttawa.ca.

Signature:

Germain Zongo
Protocol Officer for Ethics in Research
For Daniel Lagarec, Chair of the Health Sciences and Sciences REB

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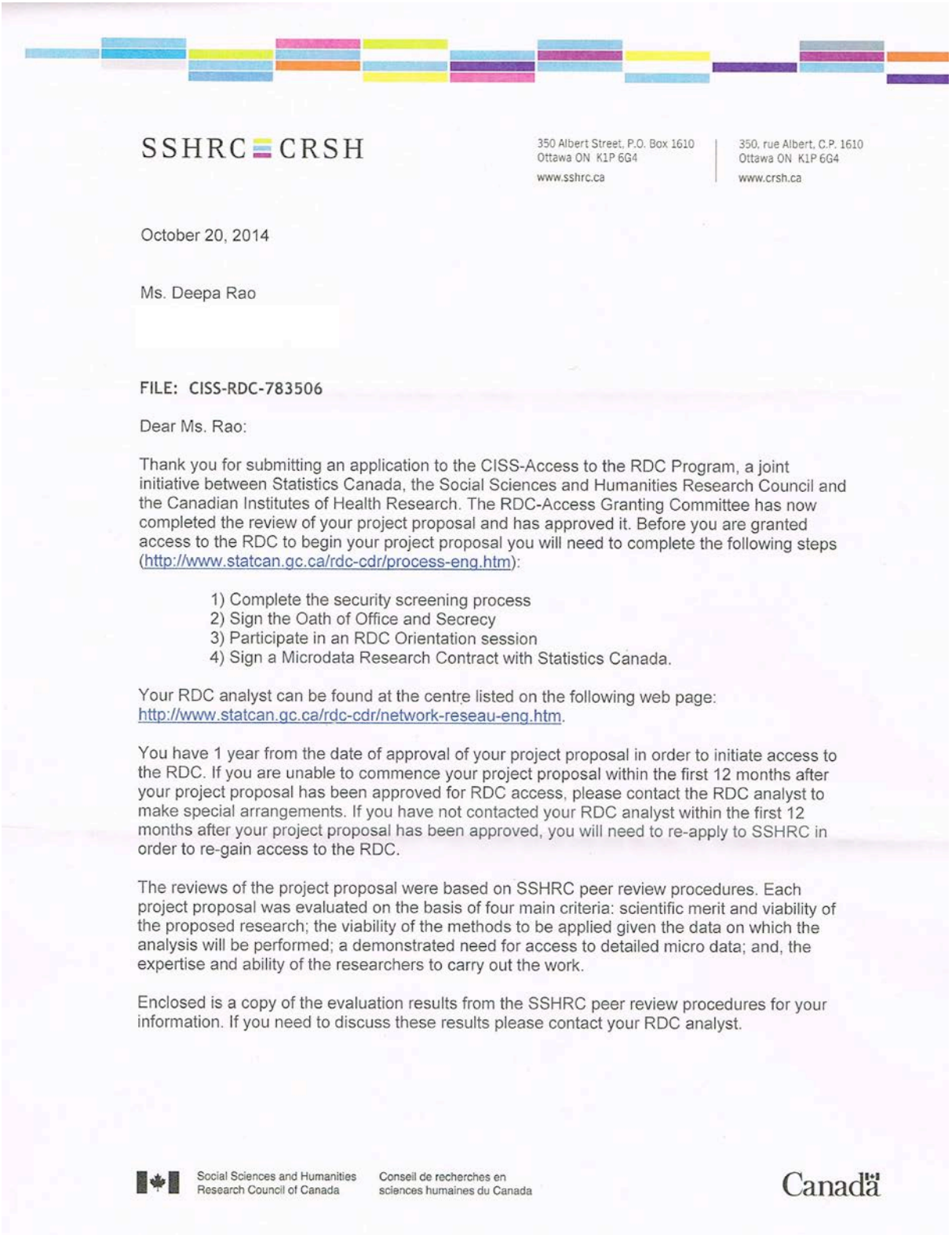
(3)



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October 20, 2014

Ms. Deepa Rao

FILE: CISS-RDC-783506

Dear Ms. Rao:

Thank you for submitting an application to the CISS-Access to the RDC Program, a joint initiative between Statistics Canada, the Social Sciences and Humanities Research Council and the Canadian Institutes of Health Research. The RDC-Access Granting Committee has now completed the review of your project proposal and has approved it. Before you are granted access to the RDC to begin your project proposal you will need to complete the following steps (http://www.statcan.gc.ca/rdc-cdr/process-eng.htm):

1) Complete the security screening process
2) Sign the Oath of Office and Secrecy
3) Participate in an RDC Orientation session
4) Sign a Microdata Research Contract with Statistics Canada.

Your RDC analyst can be found at the centre listed on the following web page: http://www.statcan.gc.ca/rdc-cdr/network-reseau-eng.htm.

You have 1 year from the date of approval of your project proposal in order to initiate access to the RDC. If you are unable to commence your project proposal within the first 12 months after your project proposal has been approved for RDC access, please contact the RDC analyst to make special arrangements. If you have not contacted your RDC analyst within the first 12 months after your project proposal has been approved, you will need to re-apply to SSHRC in order to re-gain access to the RDC.

The reviews of the project proposal were based on SSHRC peer review procedures. Each project proposal was evaluated on the basis of four main criteria: scientific merit and viability of the proposed research; the viability of the methods to be applied given the data on which the analysis will be performed; a demonstrated need for access to detailed micro data; and, the expertise and ability of the researchers to carry out the work.

Enclosed is a copy of the evaluation results from the SSHRC peer review procedures for your information. If you need to discuss these results please contact your RDC analyst.

Social Sciences and Humanities Research Council of Canada | Conseil de recherches en sciences humaines du Canada | Canada

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Should you have further questions, please feel free to contact the officer responsible for the administration of the CISS-Access to the RDC Program, Mika Oehling, at (613) 992-4227 or by email at zresearchdata@sshrc.ca.

Sincerely,

Éric Bastien
Deputy Director
Research Grants and Partnerships Division

cc: Beverley Hunt, Research Data Centres Headquarters Operations

Encl.

Appendix B: Variables – Risk and Protective Factors

Material Risk Factors

Income

Total household income:
Variable Name: INCDHH
Concept: Total household income from all sources - (Derived)
Description: This variable is based on INC_21 (Total household income) which includes imputed values. The flag INCFIMP4 indicates whether the value in INC_21 was imputed, and if so, on what information the imputation was based.

Code	Content
1	NO INCOME
2	LESS THAN $5,000
3	$5,000 TO $9,999
4	$10,000 TO $14,999
5	$15,000 TO $19,999
6	$20,000 TO $29,999
7	$30,000 TO $39,999
8	$40,000 TO $49,999
9	$50,000 TO $59,999
10	$60,000 TO $79,999
11	$80,000 TO $99,999
12	$100,000 OR MORE

Income adequacy
Variable Name: INCDDIA4
Concept: Total household income – 4 categories - (Derived)
Description: This variable classifies the total household income into four categories based on total household income and the number of people living in the household.

Code	Content
1	LOWEST INCOME GROUPING
2	LOWER MIDDLE INCOME GROUPING
3	UPPER MIDDLE INCOME GROUPING
4	HIGHEST INCOME GROUPING

Education

Variable Name: INCDDIA4
Concept: Highest level of education - respondent, 4 levels - (Derived)
Description: This variable indicates the highest level of education acquired by each member of the household

Coding specifications: Categories 3 and 4 were combined to create a three category variable (low, medium, high) for educational attainment.

Code	Content
1	LOWEST INCOME GROUPING
2	LOWER MIDDLE INCOME GROUPING
3	UPPER MIDDLE INCOME GROUPING
4	HIGHEST INCOME GROUPING

Behavioural Risk Factors

Fruits and Vegetable consumption

Variable Name: GFVD17Y
Concept: Eats fruit - times per year - (Derived)
Description: The number of times per year the respondent eats fruit (fresh, frozen, canned).

Code	Content
0-5475	NUMBER OF TIMES
9999	NOT STATED

Variable Name: GFVD18Y
Concept: Eats tomatoes or tomato sauce - times per year - (Derived)
Description: The number of times per year the respondent eats tomatoes or tomato sauce (including salsa, tomato soup and spaghetti sauce but excluding tomato paste, ketchup or pizza sauce).

Code	Content
0-1460	NUMBER OF TIMES
9999	NOT STATED

Variable Name: GFVD19Y
Concept**:** Eats lettuce or green leafy salad - times per year - (Derived)
Description: The number of times per year the respondent eats lettuce or green leafy salad with or without other vegetables.

Code	Content
0-1825	NUMBER OF TIMES
9999	NOT STATED

Variable Name: GFVD20Y
Concept: Eats spinach, mustard greens/collards - times per year - (Derived)
Description: The number of times per year the respondent eats spinach, mustard greens or collards excluding kale.

Code	Content
0-730	NUMBER OF TIMES
9999	NOT STATED

Variable Name: GFVD23Y
Concept: Eats all other types of vegetables - times per year - (Derived)
Description: The number of times per year the respondent eats all other types of vegetables.

Code	Content
0-2190	NUMBER OF TIMES
9999	NOT STATED

Milk

Variable Name: MDCD11Y
Question: Name
Concept: Drinks milk - times per year - (Derived)
Description**:** The number of times per year the respondent drinks milk or enriched milk substitutes or uses them on cereal

Code	Content
0-3650	NUMBER OF TIMES
9999	NOT STATED

Variable Name: MDC_12G
Concept: Type of milk used - rice
Question: What kind of milk do you usually drink or use on cereal? - Rice

Code	Content
1	YES
2	NO
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Variable Name: MDC_12H
Concept: Type of milk used - soya
Question: What kind of milk do you usually drink or use on cereal? – Soya

Code	Content
1	YES
2	NO
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Variable Name: MDC_12I
Question: Name
Concept: Type of milk used - other

Question: What kind of milk do you usually drink or use on cereal? - Other

Code	Content
1	YES
2	NO
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

SSB

Variable Name: WSDD11Y
Concept: Drinks regular soft drinks - number of times per year
Description: The number of times per year the respondent drinks regular soft drinks.

Code	Content
0-2920	NUMBER OF TIMES
9999	NOT STATED

Variable Name: WSDD13Y
Concept: Drinks sport drinks - number of times per year
Description: The number of times per year the respondent drinks sport drinks.

Code	Content
0-1460	NUMBER OF TIMES
9999	NOT STATED

Variable Name: WSDD13Y
Concept: Drinks fruit flavoured drinks - number of times per year
Description: The number of times per year the respondent drinks fruit flavoured drinks.

Code	Content
0-2190	NUMBER OF TIMES
9999	NOT STATED

Alcohol

Variable Name: ALCDTYP
Concept: Type of drinker - (Derived)
Description: This variable indicates the type of drinker the respondent is based on his/her drinking habits.

Code	Content
1	REGULAR DRINKER
2	OCCASIONAL DRINKER
3	FORMER DRINKER
4	NEVER DRANK
6	NOT APPLICABLE

9	NOT STATED

Variable Name: ALCDWKY
Concept: Weekly consumption - (Derived)
Description: This variable indicates the total number of drinks consumed in the week prior to the

Code	Content
0-168	NUMBER OF DRINKS
996	NOT APPLICABLE
999	NOT STATED

Smoking

Variable Name: SMKDSTY
Concept: Type of smoker - (Derived)
Description: This variable indicates the type of smoker the respondent is, based on his/her smoking habits.

Code	Content
1	DAILY SMOKER
2	OCCASIONAL SMOKER (FORMER DAILY SMOKER)
3	ALWAYS AN OCCASIONAL SMOKER
4	FORMER DAILY SMOKER
5	FORMER OCCASIONAL SMOKER
6	NEVER SMOKED
96	NOT APPLICABLE
99	NOT STATED

Variable Name: SMK_31
Concept: Number of cigarettes smoked per day (daily smoker)
Question: How many cigarettes do you smoke each day now?

Code	Content
0-60	NUMBER OF CIGARETTES
96	NOT APPLICABLE
99	NOT STATED

Physical Inactivity

Variable Name: PACDPAI
Concept: Physical Activity Index - (Derived)
Question: This variable categorizes respondents as being "active", "moderate", or "inactive" based on the total daily Energy Expenditure

Code	Content
1	ACTIVE
2	MODERATELY ACTIVE
3	INACTIVE
6	NOT APPLICABLE
9	NOT STATED

Screen time

Variable Name: SAC_11
Concept: Number of hours/typical week - on a computer - past 3 months
Question: In a typical week in the past 3 months, how much time did you usually spend on a computer, including using the Internet, playing computer games, e-mailing or chatting on-line?

Code	Content
0.0 - 95.5	NUMBER OF HOURS
99.6	NOT APPLICABLE
99.9	NOT STATED

Variable Name: SAC_12
Concept: Number of hours/typical week - video games - past 3 months
Question: In a typical week in the past 3 months, how much time did you usually spend playing video games, such as XBOX, Nintendo and Playstation?

Code	Content
0.0 - 50.0	NUMBER OF HOURS
99.6	NOT APPLICABLE
99.9	NOT STATED

Variable Name: SAC_13
Concept: Hours/typical week - television/DVD/videos - past 3 months
Question: (In a typical week in the past 3 months, how much time did you usually spend:) ... watching television,

Code	Content
0.0 - 95.0	NUMBER OF HOURS
96	NOT APPLICABLE
99	NOT STATED

Sleep

Variable Name: SLP_11
Concept: Hours spent sleeping in 24 hour period
Question: How many hours do you usually spend sleeping in a 24 hour period, excluding time spent resting?

Code	Content
1.5-20.0	NUMBER OF HOURS
99.7	DON'T KNOW

Psychosocial Risk Factors

Stress

Variable Name: GEN_15
Concept: Self-perceived stress
Question: Thinking about the amount of stress in your life, would you say that most days are: (not at all stressful, not very stressful, a bit stressful, quite a bit stressful, or extremely stressful)?

Code	Content
1	NOT AT ALL STRESSFUL
2	NOT VERY STRESSFUL
3	A BIT STRESSFUL
4	QUITE A BIT STRESSFUL
5	EXTREMELY STRESSFUL
6	NOT APPLICABLE
7	DON'T KNOW
8	REFUSAL

Job Stress

Employment status
Variable Name: GEN_16
Concept: Worked at job or business
Question: Have you worked at a job or business at any time in the past 12 months?

Code	Content
1	YES
2	NO
3	NOT APPLICABLE
4	NOT STATED

Work Stress
Variable Name: GEN_17
Concept: Self-perceived work stress
Question: The next Question: is about your main job or business in the past 12 months. Would you say that most days at work were: (not at all stressful, not very stressful, a bit stressful, quite a bit stressful, or extremely stressful)?

Code	Content
1	NOT AT ALL STRESSFUL
2	NOT VERY STRESSFUL
3	A BIT STRESSFUL
4	QUITE A BIT STRESSFUL
5	EXTREMELY STRESSFUL
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Mood Disorder

Variable Name: CCC_83

Concept: Has a mood disorder

Question: Do you have a mood disorder such as depression, bipolar disorder, mania or dysthymia?

Code	Content
1	YES
2	NO
3	DON'T KNOW

Life Satisfaction

Variable Name: GEN_13

Concept: Satisfaction with life in general

Question: How satisfied are you with your life in general?

Code	Content
1	VERY SATISFIED
2	SATISFIED
3	NEITHER SATISFIED NOR DISSATISFIED
4	SOMEWHAT DISSATISFIED
5	VERY DISSATISFIED
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Self-perceived quality of Life

Variable Name: GEN_19

Concept: Self-perceived quality of life

Question: Would you rate your quality of life as: (excellent, very good, good, fair or poor)?

Code	Content
1	EXCELLENT
2	VERY GOOD
3	GOOD
4	FAIR
5	POOR
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Limited sense of community

Variable Name: GEN_18

Concept: Sense of belonging to local community

Question: How would you describe your sense of belonging to your local community? Would you say it is: (very strong, somewhat strong, somewhat weak, or very weak)?

Code	Content
1	VERY STRONG
2	SOMEWHAT STRONG
3	SOMEWHAT WEAK
4	VERY WEAK
6	NOT APPLICABLE
7	DON'T KNOW
9	NOT STATED

Appendix C: Variables - Metabolic Syndrome

Note: Medication coding is presented using the ATC (Anatomical Therapeutic Chemical classification system) coding used in the Canadian Health Measures Survey

Waist Circumference

Anthropometric Measure

Variable Name: HWM_14CM
Concept: Waist circumference (centimetres) - WHO protocol

Code	Content
40.4 – 229.3	WAIST CIRCUMFERENCE IN CENTIMETRES
6	NOT APPLICABLE
7	DON'T KNOW
8	REFUSAL
9	NOT STATED

Triglycerides

Laboratory Measure

Variable Name: LAB_TRIG
Concept: Triglycerides (mmol/L)

Code	Content
0.31 - 10.90	WAIST CIRCUMFERENCE IN CENTIMETRES
6	NOT APPLICABLE
7	DON'T KNOW
8	REFUSAL
9	NOT STATED

Medication information

Recorded Medications

ATC code	Common Name
C10AB	Simvastatin

Blood Pressure

Laboratory Measures

Variable Name: BPMDPBPS
Concept: Final prevalence average. systolic blood pressure (mmHg) - (Derived)

Code	Content
69 - 209	SYSTOLIC BLOOD PRESSURE
996	NOT APPLICABLE
999	NOT STATED

Variable Name: BPMDPBPD
Concept: Final prevalence avg. diastolic blood pressure (mmHg) - (Derived)

Code	Content
42 - 122 5	DIASTOLIC BLOOD PRESSURE
996	NOT APPLICABLE
999	NOT STATED

Medication information

Self-reported

Variable Name: CCC_32
Concept: Medication – High blood pressure – past month
Question: Question In the past month have you taken any medicine for high blood pressure?

Code	Content
1	YES
2	NO
6	NOT APPLICABLE
7	DON'T KNOW

Recorded Medications

ATC code	Common Name
C02AC01	Clonidine
C02CA01	Prazosin
C02CA04	Doxazosin
C02DB02	Hydralazine
C02LA01	Reserpine and diuretics
C03AA03	Hydrochlorothiazide
C03BA04	Chlortalidone
C03BA08	Metolazone
C03BA11	Indapamide
C03DA01	Spironolactone
C03EA01	Hydrochlorothiazide and potassium-sparing agents
C07AA05	Propranolol
C07AA07	Sotalol
C07AA12	Nadolol
C07AB02	Metoprolol
C07AB03	Atenolol
C07AB04	Acebutolol
C07AB07	Bisoprolol
C07AG01	Labetalol
C07AG02	Carvedilol
C07BA12	Nadolol and thiazides
C07CB03	Atenolol and other diuretics
C08CA01	Amlodipine
C08CA02	Felodipine
C08CA05	Nifedipine
C08DA01	Verapamil
C08DB01	Diltiazem

C09AA01	Captopril
C09AA02	Enalapril
C09AA03	Lisinopril
C09AA04	Perindopril
C09AA05	Ramipril
C09AA06	Quinapril
C09AA07	Benazepril
C09AA08	Cilazapril
C09AA09	Fosinopril
C09AA10	Trandolapril
C09BA02	Enalapril and diuretics
C09BA03	Lisinopril and diuretics
C09BA04	Perindopril and diuretics
C09BA05	Ramipril and diuretics
C09BA06	Quinapril and diuretics
C09BB05	Ramipril and felodipine
C09CA01	Losartan
C09CA02	Eprosartan
C09CA03	Valsartan
C09CA04	Irbesartan
C09CA06	Candesartan
C09CA07	Telmisartan
C09DA01	Losartan and diuretics
C09DA02	Eprosartan and diuretics
C09DA03	Valsartan and diuretics
C09DA04	Irbesartan and diuretics
C09DA06	Candesartan and diuretics
C09DA07	Telmisartan and diuretics

High Density Lipoprotein Cholesterol

Laboratory Measure

Variable Name: LAB_HDL

Concept: High-density lipoprotein cholesterol (HDL) (mmol/L)

Code	Content
0.45 - 3.78	LAB RESULT
9.96	NOT APPLICABLE
9.99	NOT STATED

Medication information

Recorded Medications

ATC code	Common Name
C10AC	Nicotinic Acid

Fasting Glucose

Laboratory Measure

Variable Name: LAB_GLUP (cycle 1), LAB_GLUS (cycle 2)

Concept: Glucose (mmol/L)

Code	Content
2.3 - 28.9	LAB RESULT
9.96	NOT APPLICABLE
9.99	NOT STATED

Medication information

Recorded Medications

ATC code	Common Name
A10A	Insulins and Analogs
A10BA	Biguanides
A10BB.	Sulfonamides, urea deriv
A10BG	Thiazolidinediones
A10BX02	Repaglinide
A10BF01	Acarbose

Appendix D: Variables - Accelerometer Data

Activity Monitor Data

AMSDHR-Average wear time (hours)

Average daily wear time was calculated by summing the total wear time on all valid days, and dividing by the number of valid days. Wear time is the amount of time the activity monitor was worn by a person for a given day. Wear time was defined by subtracting nonwear time from 24 hours. Nonwear time was defined as a period of a least 60 consecutive minutes of zero counts, with allowance for 1 to 2 minutes of counts between 0 and 100.

AMSDMVA- Average daily moderate-to-vigorous physical activity (minutes per day)

Average time spent in moderate-to-vigorous physical activity was calculated by summing time spent in moderate-to-vigorous physical activity on all valid days, and dividing by the number of valid days. Time spent in moderate-to-vigorous physical activity is derived using an intensity cut-point and is theoretically equivalent to > 3 METs. The metabolic equivalent (MET) is a value of metabolic energy cost expressed as a multiple of the resting metabolic rate. For example, an activity of 4 METs requires four times the amount of energy as compared to when the body is at rest. The number of minutes that were accumulated above the moderate cut-point were counted as moderate-to-vigorous physical activity and summed across all valid days.

Note: There was no bout requirement in this summation of moderate-to-vigorous physical activity. In other words, all minutes above the cut-point were counted. The moderate cut-point used for preschool children aged 3-5 years (2,860cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Pfeiffer et al., 2006). The preschool cut-point was developed for 15- sec epochs therefore that value (715 counts per 15-sec) was multiplied by 4 to get a cut-point that is appropriate for use in data collected in 60-sec epochs. The moderate cut-point used for children aged 6-19 years (1,500 cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Puyau, Adolph et al., 2004). The moderate intensity cut-point used for adults aged 20-79 years (1,535 cpm) was obtained from a calibration study conducted internally at Statistics Canada (Colley and Tremblay, 2011).

AMSDMA-Average daily moderate physical activity (minutes per day)

Average daily moderate physical activity was calculated by summing time spent in moderate physical activity on all valid days, and dividing by the number of valid days. Time spent in moderate physical activity is derived using an intensity cut-point and is theoretically equivalent to > 3 and < 6 METs. The metabolic equivalent (MET) is a value of metabolic energy cost expressed as a multiple of the resting metabolic rate. For example, an activity of 4 METs requires four times the amount of energy as

compared to when the body is at rest. The number of minutes that were accumulated above the moderate cut-point and below the vigorous cut-point were counted as moderate physical activity and summed for each valid day.
Note: There was no bout requirement in this summation of moderate physical activity. In other words, all minutes between the two cut-points were counted. The moderate cut-point used for preschool children aged 3-5 years (2,860cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Pfeiffer et al., 2006). The preschool cut-point was developed for 15- sec epochs therefore that value (715 counts per 15-sec) was multiplied by 4 to get a cut-point that is appropriate for use in data collected in 60-sec epochs. The moderate cut-point used for children aged 6-19 years (1,500 cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Puyau, Adolph et al., 2004). The moderate intensity cut-point used for adults aged 20-79 years (1,535 cpm) was obtained from a calibration study conducted internally at Statistics Canada (Colley and Tremblay, 2011). The vigorous cut-point used for preschool children aged 3-5 years (5,644cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Pfeiffer et al., 2006). The preschool cut-point was developed for 15- sec epochs therefore that value (1411 counts per 15-sec) was multiplied by 4 to get a cut-point that is appropriate for use in data collected in 60-sec epochs. The vigorous cut-point used for children aged 6-19 years (6,500 cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Puyau, Adolph et al., 2004). The vigorous intensity cut-point used for adults aged 20-79 years (3,962 cpm) was obtained from a calibration study conducted internally at Statistics Canada (Colley and Tremblay, 2011).

AMSDVA-Average daily vigorous physical activity (minutes per day)

Average time spent in vigorous physical activity was calculated by summing time spent in vigorous physical activity on all valid days, and dividing by the number of valid days. Time spent in vigorous physical activity is derived using an intensity cut-point and is theoretically equivalent to > 6 METs. The metabolic equivalent (MET) is a value of metabolic energy cost expressed as a multiple of the resting metabolic rate. For example, an activity of 4 METs requires four times the amount of energy as compared to when the body is at rest. The number of minutes that were accumulated above the vigorous cut-point were counted as vigorous physical activity and summed across all valid days.
Note: There was no bout requirement in this summation of vigorous physical activity. In other words, all minutes above the cutpoint were counted. The vigorous cut-point used for preschool children aged 3-5 years (5,644cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Pfeiffer et al., 2006). The preschool cut-point was developed for 15- sec epochs therefore that value (1411 counts per 15-sec) was multiplied by 4 to get a cut-point that is appropriate for use in data collected in 60-sec epochs. The vigorous cut-point used for children aged 6-19 years (6,500 cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Puyau, Adolph et al., 2004). The vigorous intensity cut-point used for adults aged 20-79 years (3,962 cpm) was obtained from a calibration study conducted internally at Statistics Canada (Colley and Tremblay, 2011).

AMSDLA-Average daily light physical activity (minutes per day)

Average daily time spent in light physical activity was calculated by summing time spent in light physical activity on all valid days, and dividing by the number of valid days. Total light physical activity is derived using an intensity cut-point and is theoretically equivalent to 2-3 METs. The metabolic equivalent (MET) is a value of metabolic energy cost expressed as a multiple of the resting metabolic rate. For example, an activity of 4 METs requires four times the amount of energy as compared to when the body is at rest. The number of minutes where counts were greater than or equal to the sedentary cut-point (100 cpm) but less than the moderate physical activity cutpoint were counted as light physical activity and summed for each valid day. The cut-point to differentiate between sedentary and light activity (100 cpm for both children and adults) was based on a preliminary examination of CHMS data which used low step counts as a way of determining an appropriate count value to associate with sedentary behaviour (Wong, Colley et al., 2011). The moderate cut-point used for preschool children aged 3-5 years (2,860cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Pfeiffer et al., 2006). The preschool cut-point was developed for 15- sec epochs therefore that value (715 counts per 15-sec) was multiplied by 4 to get a cut-point that is appropriate for use in data collected in 60-sec epochs. The moderate cut-point used for children aged 6-19 years (1,500 cpm) was obtained from a calibration study that related Actical counts to measured energy expenditure (Puyau, Adolph et al., 2004). The moderate intensity cut-point used for adults aged 20-79 years (1,535 cpm) was obtained from a calibration study conducted internally at Statistics Canada (Colley and Tremblay, 2011).

AMSDXSA-Average daily sedentary physical activity (minutes per day)

Average daily sedentary time was calculated by summing time spent sedentary on all valid days, and dividing by the number of valid days. Total sedentary time is derived using an intensity cut-point and is theoretically equivalent to < 2 METs. The metabolic equivalent (MET) is a value of metabolic energy cost expressed as a multiple of the resting metabolic rate. For example, an activity of 4 METs requires four times the amount of energy as compared to when the body is at rest. The number of weartime minutes where counts were greater than or equal to zero but less than the sedentary cut-point (100 cpm) were counted as sedentary and summed for each valid day. The cut-point to differentiate between sedentary and light intensity was based on a preliminary examination of CHMS data which used low step counts as a way of determining an appropriate count value to associate with sedentary behaviour (Wong, Colley et al., 2011).