ANTHROPOMETRIC MARKERS OF HEALTH RISK

by

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A thesis submitted to the School of Kinesiology and Health Studies in conformity with the requirements for the degree of Doctor of Philosophy

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ABSTRACT

The objective of this thesis was to investigate the relationships between simple anthropometric measures and health risk towards a better characterization of the high-risk obesity phenotype. To this end, four studies were undertaken. The first study assessed the comparability of waist circumference (WC) data collected according to four commonly used measurement protocols in a sample of 520 community-dwelling men and women. This investigation quantified the influence of measurement site on the magnitude and reliability of WC and highlighted the impact of measurement site on prevalence estimates of abdominal obesity. To extend these findings, the second study examined the influence of WC measurement site on its association with cardiometabolic risk. Despite similar associations with risk factors including blood pressure, HDL-cholesterol, triglycerides, and blood glucose, prevalence estimates of metabolic syndrome differed depending on the anatomical site of WC measurement, particularly in women. In order to better understand the heterogeneity in human obesity and its sequelae, the third and fourth studies focused on the separate and combined influences of central and peripheral circumferences on health outcomes. Specifically, the third study used data from the Physical Activity Longitudinal Study (PALS) to demonstrate that after adjusting for BMI and WC, larger arm, calf, and thigh circumferences offer a protective effect against incident diabetes. The fourth study confirmed the opposing influences of central and peripheral circumferences on risk of all-cause mortality in a sample of 10,638 participants from the 1981 Canada Fitness Survey (CFS) with more than 12 y of follow-up. After adjustment for age, smoking status, alcohol consumption,
leisure-time physical activity and BMI, WC was positively associated with mortality whereas arm, thigh, and calf circumferences were significantly protective in men and arm and thigh circumferences were protective in women. Collectively, the results from these studies contribute to a better understanding of the role of body dimensions in determining health risk and have implications for the use of anthropometric measures in clinical and research settings.

**Keywords:** obesity, waist circumference, anthropometry, measurement, risk factors, diabetes, mortality, population, epidemiology
CO-AUTHORSHIP

The manuscripts presented in this thesis are the work of Caitlin Mason in collaboration with her co-authors. The co-authors include: Peter T. Katzmarzyk, PhD (Chapters 3, 4, 5, & 6), Lise Gauvin, PhD (Chapter 5) and Cora L. Craig (Chapters 5 and 6).
ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

AHA  American Heart Association
BMI  Body Mass Index
CFS  Canada Fitness Survey
C.I.  Confidence Interval
CMDB  Canadian Mortality Database
CSWB  Campbell’s Survey of Well-Being
CT  Computed Tomography
CVD  Cardiovascular Disease
DXA  Dual Energy X-Ray Absorptiometry
FEV$_1$  Forced Expiratory Volume in 1 second
HDL-C  High Density Lipoprotein Cholesterol
HR  Hazard Ratio
ICC  Intraclass Correlation Coefficient
IDF  International Diabetes Federation
LDL-C  Low Density Lipoprotein Cholesterol
MetS  Metabolic Syndrome
MRI  Magnetic Resonance Imaging
NHANES  National Health and Nutrition Examination Survey
NHLBI  National Heart, Lung, and Blood Institute
NIH  National Institutes of Health
OR  Odds Ratio
PALS  Physical Activity Longitudinal Study
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>PAR</td>
<td>Population Attributable Risk</td>
</tr>
<tr>
<td>ROC</td>
<td>Receiver Operating Characteristic</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>SEE</td>
<td>Standard Error of Estimate</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>WC</td>
<td>Waist Circumference</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WHR</td>
<td>Waist-to-Hip Ratio</td>
</tr>
<tr>
<td>WTA</td>
<td>Waist-to-Arm Ratio</td>
</tr>
<tr>
<td>WTC</td>
<td>Waist-to-Calf Ratio</td>
</tr>
<tr>
<td>WTH</td>
<td>Waist-to-Thigh Ratio</td>
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</tbody>
</table>
Obesity is an increasingly significant global health problem. Due to its major influence on the development and course of numerous chronic diseases including cardiovascular disease, type 2 diabetes and certain cancers, as well as on social functioning and quality of life (1); the rising prevalence of obesity represents a serious threat to public health in both developed and developing countries. In Canada, the prevalence of obesity has steadily increased in recent decades (2) and it is now estimated that 59% of the Canadian population is overweight (BMI ≥25 kg/m^2), including 23% of the population who are obese (BMI ≥30 kg/m^2) (3). Moreover, overweight and obesity among Canadian children and youth has reached an unprecedented high prevalence (26%) (4), having risen 2-3 fold in the past generation (5).

The dramatic increase in obesity prevalence underscores the importance of prevention strategies for reducing the consequent burden of chronic disease. Furthermore, the accurate characterization of obesity-related health risk has taken on new importance in efforts to create targeted intervention strategies and appropriately allocate health care resources.

Anthropometry involves the measurement of body dimensions for the purpose of understanding human physical variation. Although technological advancement has resulted in more accurate means of measuring human adipose tissue levels, anthropometric measures remain the preferred means of evaluating body fatness in settings where time-consuming and costly diagnostic tests are not feasible. Indeed,
obesity remains primarily diagnosed using the body mass index (BMI) – a ratio of weight to height (kg/m²) that is generally both easy to measure and interpret. Yet, despite the well-established association between BMI and health risk (6-12), overweight individuals exhibit favourable outcomes in some studies (13-15). BMI represents a useful measure of body composition in populations, but is simultaneously unreliable for individuals. This apparent paradox may reflect intrinsic limitations of BMI in differentiating lean and adipose tissues and in accounting for body fat distribution. These limitations are important given that the relevance of both the composition (i.e. fat and lean components) and localization of body mass in explaining health outcomes are increasingly recognized.

In this regard, it is now widely appreciated that body fat distribution is an important risk factor for both morbidity and mortality, above and beyond total excess body weight (12, 13, 16, 17). Consequently, current national and international guidelines advocate for the routine measurement of waist circumference (WC) in the assessment of obesity-related health risk (1, 6, 18). Additional anthropometric measures of body composition, including indicators of lean tissue or peripheral fat depots have also demonstrated the ability to help differentiate health risk above and beyond BMI (13, 19, 20); however, with the exception of the waist-to-hip ratio (WHR), these are less frequently used in clinical settings.

Since appropriate treatment and intervention strategies hinge on accurately discriminating health risk, efforts to improve the identification of obesity-related health
risks are ongoing. Recent studies have highlighted the complexity of this task by demonstrating simultaneously high prevalences of cardiometabolic risk among normal weight individuals, while a substantial proportion of overweight and obese individuals appear metabolically healthy (21, 22). Indeed, inherent in the concept of epidemiological risk is the realization that not all individuals exposed to a particular risk will develop disease, while some individuals without identifiable risk will be affected. While it is important to detect high risk patients, it is also important not to overextend risk criteria to non high-risk patients. This is aptly demonstrated in the case of obesity: opportunities to intervene early are more likely to be successful, yet, the arduous nature of weight loss limits its feasibility as a widespread intervention strategy in a population where the majority of adults are overweight.

Fractioning total cholesterol into its low- and high-density lipoprotein components significantly enhances its predictive value as a cardiovascular disease risk factor. Likewise, the ability to differentiate individuals with a preferential deposition of abdominal adipose tissue through the measurement of WC in addition to BMI represents an improved approach to risk stratification for obesity (16). Further refinement of WC measurement protocol and the simultaneous consideration of body components with protective as well as risk-associated effects have the potential to advance the descriptive and analytic epidemiology of obesity and improve clinical risk stratification for the growing number of individuals considered overweight or obese on the basis of BMI.
1.1 Purpose of Thesis

The primary focus of the four research studies undertaken for the purpose of this thesis was to evaluate the utility of various anthropometric measures for the assessment of health risk in clinical and research settings.

The first study addresses an important methodological question pertinent to the use of WC in clinical and research settings by assessing the comparability of data collected using four different measurement protocols in a sample of 520 community-dwelling men and women. This investigation quantified the systematic variation in the magnitude and reliability of WC across measurement sites and showed the impact of protocol on prevalence estimates of abdominal obesity. The second study extended these findings by examining whether variations in measurement protocol are differentially associated with cardiometabolic risk factors and the metabolic syndrome. A recent comprehensive review has indicated that the association between WC and health risks did not appear to differ depending on the measurement site; however, no single studies were identified that simultaneously compared different measurement sites in the same sample; rather the authors based their conclusion on comparisons across existing studies (23).

In order to better understand the heterogeneity in health outcomes associated with obesity, the third and fourth studies both investigate the independent role of peripheral body circumferences in determining health risk. Specifically, the third study used data from the Physical Activity Longitudinal Study (PALS) to examine the relationships between upper and lower-body circumference measures and incident
diabetes, independent of overall and abdominal adiposity. The fourth study examines the opposing influences of central and peripheral circumferences on the risk of all-cause mortality in a sample of 10,638 participants from the 1981 Canada Fitness Survey (CFS).

1.2 Main Hypotheses

Study 1

Hypothesis 1: The magnitude of WC will vary systematically according to the anatomical location of measurement. The magnitude of these differences will be greater in women than men.

Hypothesis 2: Inter- and intra-observer reliability of WC measures will vary according to sex and adiposity status. WC measurements will be less reliable in women than men and will decrease across increasing levels of adiposity (BMI).

Hypothesis 3: Inter- and intra-observer reliability of WC measures will not vary according to measurement site.

Study 2

Hypothesis 1: Irrespective of measurement site, WC will be positively associated with individual risk factors and with the presence of cardiometabolic risk factor clustering in men and women.

Hypothesis 2: The magnitude of the associations between WC and cardiovascular risk factors will not differ across four anatomical measurement sites.
Study 3

Hypothesis: For a given level of adiposity (BMI, WC), individuals with larger extremity circumferences (hip, thigh, arm) will have a lower incidence of diabetes.

Study 4

Hypothesis 1: For a given level of adiposity (BMI, WC), individuals with larger extremity circumferences (hip, thigh, calf, arm) will have a lower risk of mortality.

Hypothesis 2: The protective effect of larger extremity circumferences will be greater in women compared to men.
References


2.1 Obesity & Health Risk

Obesity is widely recognized as an important risk factor for cardiometabolic diseases such as hypertension, dyslipidemia, type 2 diabetes and coronary heart disease, as well as for certain cancers, orthopedic problems including osteoarthritis, and for premature mortality (1, 2). The prevalence of obesity is rising in most countries of the world and consequently, excess body weight has rapidly become a prominent health issue (3, 4). In Canada, estimates of population attributable risk (PAR) highlight this mounting public health burden by quantifying the proportion of specific health conditions that can be directly attributed to overweight and obesity (5) (Table 1).

Several leading health organizations, including the World Health Organization (6), the U.S. National Institutes of Health (1), and Health Canada (2) advocate a simple system for classifying obesity based on the Body Mass Index (BMI; kg/m$^2$) – a ratio of weight to height first developed by the Belgian statistician, Quetelet (7). BMI is directly correlated with the risk of medical complications and the sum of the evidence from a large body of epidemiologic studies generally shows a J-shaped or U-shaped relationship between BMI and risk of mortality (8-13). Based on these observed associations, men and women with a BMI $\geq$30 kg·m$^2$ are considered obese and generally have a higher risk than those classified as overweight (BMI 25.0-29.9 kg·m$^2$) who in turn have a greater risk than those who are normal weight (BMI 18.5-24.9 kg·m$^2$). BMI has the advantage of being easy to measure, reliable, and closely correlated ($r= 0.7-0.8$) with adult body fat.
and remains the most common method for identifying persons at increased risk of adverse obesity-related outcomes.

<table>
<thead>
<tr>
<th>Adverse Health Outcomes Associated with Obesity*</th>
<th>PAR %†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>34.0%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>---</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>---</td>
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<tr>
<td>Type II diabetes</td>
<td>28.6%</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>15.4%</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>---</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>25.5%</td>
</tr>
<tr>
<td>Orthopedic problems, including osteoarthritis</td>
<td>12.7%</td>
</tr>
<tr>
<td>Obstructive sleep apnea and respiratory</td>
<td>---</td>
</tr>
<tr>
<td>problems, including asthma</td>
<td></td>
</tr>
<tr>
<td>Cancer (breast, endometrial, colon, prostate,</td>
<td>6.2%</td>
</tr>
<tr>
<td>kidney, gallbladder)</td>
<td>(colon)</td>
</tr>
<tr>
<td></td>
<td>6.5%</td>
</tr>
<tr>
<td></td>
<td>(post-menopausal breast)</td>
</tr>
<tr>
<td>Complications of pregnancy</td>
<td>---</td>
</tr>
<tr>
<td>Psychological disorders, including depression</td>
<td>---</td>
</tr>
<tr>
<td>Social stigmatization</td>
<td>---</td>
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</tbody>
</table>

* Adapted from (1).
† Adapted from Katzmarzyk & Janssen (5), Table 3; PAR%=[P(RR-1)]/[1+ P(RR-1)]; P= prevalence of obesity in 2000-01 Canadian Community Health Survey; RR=summary relative risk derived from meta-analysis; (---) denotes conditions for which obesity-related PAR% in Canada has not been estimated.

Unfortunately, the use of BMI is plagued by several limitations; most notably, its inability to account for inter-individual differences in the relative proportions of body fat and lean tissue, and its inability to measure relative body fat distribution. Yet, both the relative contribution and distribution of body fat are important considerations in explaining the observed heterogeneity in obesity-related health outcomes.
2.2 Body Fat Distribution

A convincing body of accumulated evidence has demonstrated that many of the health risks associated with obesity are more closely related to the distribution of body fat than the total magnitude of excess adiposity (16, 17). The first published clinical observations of this phenomenon were made by Jean Vague in the late 1940s (18). Vague contended that irrespective of the magnitude of total obesity, it was the regional distribution of adipose tissue, determined by underlying neurohormonal mechanisms, that was responsible for an individual’s risk of specific clinical complications. In particular, it was a greater degree of fat localization on the upper body, as commonly seen among men, that was associated with a predisposition towards hypertension, atherosclerosis, and type 2 diabetes mellitus. In contrast, the accumulation of fat on the lower body, a pattern more frequently observed in women, was associated with certain mechanical complications but carried little additional risk of metabolic abnormalities (19). Despite the apparent sexual dimorphism in fat distribution, Vague noted significant variability within sexes and throughout the lifespan such that these phenotypes occurred on a continuum with a certain degree of overlap between the sexes.

In the 60 years since the publication of these observations, large-scale prospective cohort studies have confirmed Vague’s prescient observations that central rather than gluteofemoral adiposity is more strongly associated with health outcomes including ischemic heart disease, stroke, type 2 diabetes, and mortality (13, 16, 20-25). The specific nature of the relation between abdominal obesity and health outcomes is influenced by age, sex, race/ethnicity, physical activity, total adiposity and the particular
outcome(s) of interest (26). Nevertheless, the positive relation appears robust, having been consistently observed for a variety of outcomes across diverse populations (13, 16, 21, 26-36). In addition, results from clinical studies have demonstrated that decreases in abdominal adiposity and concomitant improvements in metabolic risk markers can be achieved through weight loss (37, 38), underscoring the viability of abdominal fat as a target for intervention.

The emergent use of imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) has made it possible to identify the accumulation of visceral adipose tissue in particular, as being most strongly associated with metabolic disturbances (39). The mechanism(s) through which visceral adipose tissue influences disease risk is not yet fully elucidated; however, it is hypothesized that cardiometabolic dysregulation may be caused by the release of free fatty acids, inflammatory cytokines, and select hormones directly into portal circulation by intraperitoneal adipose tissue (40-42), and/or that increased visceral fat may reflect a limited ability of subcutaneous adipose tissue to store excess energy resulting in an overflow of chemical energy to ectopic sites such as liver and skeletal muscle, and consequent dysfunction in those organs (43, 44).

2.3 Metabolic Syndrome

Most notably, visceral fat is implicated in the etiology of metabolic syndrome - a frequently observed clustering of central adiposity with insulin resistance, hypertension, and dyslipidemia (45) which is associated with increased odds of type 2 diabetes, CVD, and mortality (46). The exact origins of the metabolic syndrome are not fully
understood and the clinical implications have been subject to some debate (47, 48). Nevertheless, several national and international organizations have developed operational definitions intended to facilitate the identification of individuals with high atherogenic risk (49-51) (Table 2). Despite differences in these clinical criteria, waist circumference (WC) features prominently in several classification systems, underscoring the importance abdominal adiposity for identifying and managing high-risk individuals.

2.4 Anthropometric Assessment of Abdominal Obesity

2.4.1 Preferred measure(s) of abdominal obesity

Since the widespread use of imaging techniques is not yet feasible in most clinical settings or population studies, the use of anthropometry remains the most convenient and cost-effective alternative. Radiological imaging techniques have nevertheless contributed valuable information in this regard; by identifying WC as the best anthropometric predictor of visceral fat (38, 52, 53), and a better indicator of changes in abdominal fat over time than alternative measures such as the waist-to-hip ratio (38, 54).

2.4.2 Waist circumference thresholds

Using regression curves that identified the WC values associated with a BMI ≥30 kg·m² in primarily Caucasian men and women from North Glasgow, Scotland, Lean et al. (55) identified values above 102 cm (40 in) and 88 cm (35 in) as being indicative of increased risk for cardiometabolic disease in men and women, respectively. Although
Table 2. Clinical criteria for the metabolic syndrome according to the World Health Organization (WHO) (49), the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) (51), and the International Diabetes Federation (IDF) (50).

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>• Glucose Intolerance, IGT or diabetes and/or insulin resistance, Together with two or more of the following:</td>
<td>Three or more of the following:</td>
<td>• Elevated WC (according to ethnicity specific cutpoints) or BMI &gt;30 kg/m² Together with two or more of the following:</td>
</tr>
<tr>
<td>• Waist-to-hip ratio: &gt;0.9 (men); &gt;0.85 (women) and/or BMI &gt;30 kg/m²</td>
<td>• Elevated WC: ≥102 cm (men); ≥88 cm (women)</td>
<td>• Blood Pressure: ≥130 mmHg (systolic) or ≥85 mmHg (diastolic) or drug treatment for hypertension</td>
</tr>
<tr>
<td>• Blood Pressure: ≥140/90 mmHg</td>
<td>• Blood Pressure: ≥130 mmHg (systolic) or ≥85 mmHg (diastolic) or drug treatment for diagnosed hypertension</td>
<td>• Triglycerides (TG): ≥1.7 mmol/l or drug treatment for elevated TGs</td>
</tr>
<tr>
<td>• Triglycerides: ≥1.7 mmol/l and/or</td>
<td>• Triglycerides (TG): ≥1.7 mmol/l or drug treatment for elevated TGs</td>
<td>• HDL-cholesterol: &lt;1.03 mmol/l (men) &lt;1.29 mmol/l (women) or drug treatment for reduced HDL-C</td>
</tr>
<tr>
<td>• HDL-cholesterol: &lt;0.9 mmol/l (men) &lt;1.0 mmol/l (women)</td>
<td>• HDL-cholesterol: &lt;1.03 mmol/l (men) &lt;1.29 mmol/l (women) or drug treatment for reduced HDL-C</td>
<td>• Elevated fasting glucose: ≥100 mg/dL or drug treatment for elevated glucose</td>
</tr>
<tr>
<td>• Urinary albumin excretion rate ≥30 ug/min or albumin:creatinine ratio ≥220 mg/min</td>
<td>• Elevated fasting glucose: ≥100 mg/dL or drug treatment for elevated glucose</td>
<td>• Elevated fasting glucose: ≥5.6 mmol/l or diagnosed type 2 diabetes</td>
</tr>
</tbody>
</table>
these sex-specific thresholds were not developed based on the direct relationship between WC and health risk and therefore do not represent optimal thresholds, they continue to be the most widely advocated cut-points for classifying abdominal obesity in both clinical and research settings (1, 2, 6). Alternative thresholds have been proposed for non-Caucasian populations; however the practical utility of these cut-points in diverse populations such as Canada are unknown.

2.4.3 Joint assessment using BMI and waist circumference

Based on the strong evidence that increased BMI and centrally patterned obesity are both independently associated with cardiovascular and metabolic risk factors, leading national and international health agencies recommend the combined measurement of both BMI and WC for the assessment of obesity-related health risk (1, 2, 6) (Table 3). According to the widely adopted classification system, relative health risk is considered graded such that it increases when moving from normal weight to obese BMI categories, and is greater among individuals with high (women:>88 cm; men:>102 cm) compared to normal WC values within each BMI category.

Although WC has a demonstrated ability to discriminate risk across all levels of BMI (13, 35, 56-58), its use is advocated primarily in the range of BMI values of 25-35 kg/m$^2$, outside of which current thresholds have little ability to differentiate between individuals (57, 59-61). Thus, while the current classification system does indeed predict increased risk of morbidity and mortality within normal weight, overweight, and obese Class I BMI categories (60, 61); the use of BMI-specific WC cut-points may be able to achieve greater sensitivity and specificity (57).
2.5 Waist Circumference Measurement Issues

Despite the growing use of WC measurements, there remains no uniformly accepted measurement protocol. In fact, a review of the literature by Wang et al. (62) identified 14 different descriptions for the site of measurement. For example, the current U.S. clinical practice guidelines specify that WC be measured directly above the iliac crest (1), while the World Health Organization (WHO) and Health Canada instruct that measurements should be taken midway between the superior border of iliac crest and the lowest rib. The only operational definition of the metabolic syndrome to stipulate a specific anatomical location of WC measurement is that set out by the American Heart Association/ National Heart Lung, and Blood Institute (AHA/NHLBI), which is consistent with the National Institutes of Health (NIH) recommendation to measure WC superior to the iliac crest (51). Nevertheless, a survey of the published

<table>
<thead>
<tr>
<th>Category</th>
<th>Men &lt;102 cm</th>
<th>Men &gt;102 cm</th>
<th>Women &lt;88 cm</th>
<th>Women &gt;88 cm</th>
</tr>
</thead>
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<td></td>
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<tr>
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<td>Normal</td>
<td>Increased</td>
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<tr>
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<td>25-29.9</td>
<td>Increased</td>
<td>High</td>
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<td>Class I</td>
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<td>Very high</td>
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<td>Class II</td>
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<tr>
<td>Class III</td>
<td>≥40</td>
<td>Extremely high</td>
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</table>

*Based on U.S. National Institutes of Health (1) and Health Canada (4) guidelines.
literature indicates that this measurement protocol is not universally used; rather, a wide variety of measurement techniques are reported in clinical studies, including the minimal waist (33%), the umbilicus (27%), and the mid-point between the iliac crest and lowest rib (26%)(63).

To date, only a few studies have investigated the differences in WC measured at various anatomical locations (62-66). Based on a study of Danish men and women, Bigard et al. reported mean differences in technician-measured WC between the umbilicus and natural waist of +0.7 cm in men and +5.0 cm in women. Likewise, Houmard et al. (64) and Willis et al. (66) reported higher values at the umbilicus compared with the natural waist in middle-aged men and women. The magnitude of these differences varied between study populations, ranging from approximately 2 cm (64) in normal weight men to approximately 11 cm in overweight post-menopausal women (66). As a consequence of these differences, 54% more men and 68% more women met criteria for abdominal obesity (>102/88cm) when WC measurement was made at the umbilicus compared with the minimal waist. Furthermore, these measurement sites also differed in their association with cardiovascular risk factors, more so among women than men (66). In women, the minimal waist had higher correlation coefficients than the umbilicus with high density lipoprotein (HDL)—cholesterol, insulin sensitivity, and visceral adipose tissue mass. In men, differences in correlation coefficients did not prove to be statistically significant.

No studies in the published literature have compared differences in the association between measures from the iliac crest or midpoint on individual risk factors
or risk factor clustering. However, the above-mentioned findings highlight the potential importance of measurement site in clinical decision-making, even if the overall patterns of association with outcomes such as cardiovascular disease (CVD), type 2 diabetes, and mortality are not meaningfully impacted (63).

2.6 Waist Circumference, Visceral Fat, and Health Risk

Several studies have identified WC as a superior indicator of visceral fat than the waist-to-hip ratio (WHR), the sagittal diameter, or any other anthropometric measure of central fat deposition (52, 54, 67, 68). It could be hypothesized that the ability of one WC measurement site to predict visceral adipose tissue (VAT) more strongly than another may translate into a stronger association with cardiometabolic risk. If so, this would provide strong rationale for its uptake in clinical practice. However, no studies have compared multiple measures of WC in order to examine differences across measurement sites in regard to the ability to predict either visceral fat mass or cardiometabolic risk factors.

Using contiguous computed tomography (CT) images across the abdomen, Kuk et al. (69) recently compared the ability of VAT to predict metabolic syndrome across 8 measurement locations. The association was positive for all slice locations but the odds ratios were higher for VAT area measured in the upper abdomen (measured near L1-L2) than VAT measured at L4-L5. In contrast, Demerath et al. (70) reported a curvilinear relation between VAT area image location and the odds of metabolic syndrome, with higher odds in the mid-abdomen (L4-L5 + 9 cm in men; L4-L5 + 3 cm in women) than in the upper or lower abdomen. Overall, no single image was universally better correlated
with health risks than any other image for all risk factors. Rather, a range of single images provided equivalent correlations between VAT area and cardiometabolic risk factor levels; with the optimal range varying slightly according to sex and the particular risk factor being examined (70). Thus, the available evidence remains too limited to ascertain whether the anatomical location of WC measurement is likely to impact the prediction of VAT or influence its association with cardiometabolic risk in a manner of clinical significance.

2.7 Additional Anthropometric Measures: Beyond BMI and waist circumference

2.7.1 Associations with Morbidity

While the preferential accumulation of intra-abdominal fat confers an elevated risk of cardiovascular and metabolic dysfunction, other major body compartments have been associated with reduced odds of adverse health outcomes (71). In fact, while VAT has been identified as the abdominal fat depot most strongly associated with health risk and WC is the single best anthropometric indicator of visceral fat mass (52, 54, 67, 68), WC adjusted for hip circumference (WHR) demonstrates a better ability to predict health outcomes than WC alone in some studies (34, 72-74).

Several large epidemiologic studies have demonstrated larger hip and thigh circumferences to be inversely associated with CVD risk factors (67, 75-77), CVD outcomes including myocardial infarction (71, 72, 78), and type 2 diabetes (77-80), independent of overall and abdominal adiposity. For example, in the Quebec Family Study, associations between the WHR and cardiovascular risk factors including cholesterol (total, HDL-C, LDL-C), triglycerides, insulin, glucose, and blood pressure
tended to be stronger than they were with WC. However, when waist and hip circumference were entered into a regression model individually, they showed independent and opposing influences on cardiovascular risk, even after adjusting for BMI (67).

In an analysis of middle-aged Dutch adults, Snijder et al. (79) reported age-, BMI, and WC-adjusted odds ratios for type 2 diabetes of 0.55 (95% CI: 0.36-0.85) and 0.63 (95% CI: 0.42-0.94) per standard deviation (SD) of hip circumference for men and women, respectively. Corresponding odds ratios per 1 SD of thigh circumference were 0.79 (95% CI: 0.53-1.19) in men and 0.64 (95% CI: 0.46-0.93) in women. Similarly, cross-sectional analyses in a population-based sample of Australian adults ≥25 y of age revealed odds ratios for the presence of diabetes of 0.55 (95% CI: 0.41-0.73) in men and 0.42 (95% CI: 0.27-0.65) in women per SD of hip circumference, after adjustment for age, BMI, and WC (77).

2.7.2 Associations with Mortality

The protective nature of peripheral body circumferences have also been observed in several mortality studies. For example, findings from a representative sample of U.S. men from the National Health and Nutrition Examination Survey (NHANES) I and II Epidemiologic Follow-up Studies showed differential effects of upper arm circumference and BMI on mortality rates over 16 years of follow-up in men 25-75 y of age (81). In contrast, a parallel analysis of women from the same cohort showed inverse associations between anthropometric indicators of both fat and fat-free mass with mortality (82), a difference that was hypothesized to be associated with sex
differences in body fat distribution. In the Paris Study of middle-aged men, greater muscle mass (sum of mid-arm and mid-thigh circumferences adjusted for extremity skinfold thicknesses) was inversely associated with all-cause and cancer deaths, and low extremity subcutaneous fat was associated with greater cancer mortality (71), independent of abdominal fat (sagittal diameter adjusted for trunk skinfold thicknesses). In older men (61-79 y) from the British Regional Heart Study (83), mid-arm muscle circumference demonstrated a strong inverse association with mortality that persisted after adjustment for multiple indicators of ill health including FEV$_1$ (forced expiratory volume in one second), albumin, self-reported poor health, preexisting cancer, diabetes or CVD. Moreover, the adverse consequences of low arm circumference in that sample were observed irrespective of BMI and WC, and in active as well as inactive men.

Recently, published findings by Wannamethee et al. (83) reported a decreasing risk of all-cause mortality across increasing quintiles of mid-arm muscle circumference in older men (60-79 y of age), independent of abdominal adiposity, leading these authors to suggest that the simultaneous assessment of central and extremity circumferences may more accurately characterize particular body shape phenotypes than either measure alone.

It is hypothesized that the apparent health “protective” effect of larger upper and lower-body extremity circumferences for a given level of adiposity may be explained by a greater accumulation of subcutaneous adipose tissue, higher lean muscle mass, or a combination of both factors (75, 84, 85). Indeed, mounting evidence suggests that specific characteristics of muscle tissue and peripheral fat depots may
represent important protective influences against morbidity and premature mortality (86, 87). The specific characteristics of these tissues which, in turn, contribute to the observed variation in anthropometric circumferences are influenced by both genetic and behavioural characteristics (88, 89). Aging, for instance, is associated with steady increases in visceral fat and an eventual decrease in subcutaneous fat and peripheral muscle mass (90). Differences in the obesity phenotype related to lean mass have also been proposed as one mechanism through which physical activity may decrease health risk, even among overweight and obese individuals (91).

2.8 Differentiating Fat and Lean Tissue

It is difficult to distinguish distinct aspects of body composition using solely anthropometric circumference measures. However, select studies have used anthropometry and imaging technologies simultaneously in order to discern the relative contribution fat and lean tissue compartments to anthropometric variation and health outcomes. In the Hoorn Study, hip circumference was positively associated with DXA (dual energy x-ray absorptiometry)-measured leg fat and leg lean mass in both men and women (75). Further, the accumulation of both leg fat and leg lean mass (in men only) were independently associated with lower post-load glucose levels. By comparison, the use of computed tomography (CT) in elderly (70-79 y) participants of the Health, Aging and Body Composition Study revealed that thigh circumference was equally dependent on fat and muscle components in men, while the fat component was the primary contributor in women (76). In that study, subcutaneous thigh fat was favorably
associated with fasting glucose levels; however, this association was only statistically significant among men, but not women.

Using whole-body magnetic resonance imaging (MRI), Kuk et al. (92) recently reported that when WC is held constant, men and women with larger hip and thigh circumferences have greater quantities of total, lower-body, and abdominal subcutaneous adipose tissue, greater skeletal muscle mass, and less visceral adipose tissue. Therefore, it is possible that a low amount of subcutaneous adipose tissue or a low muscle mass in the extremities represents a phenotypic companion to visceral adipose tissue accumulation that further explains health risk – a scenario which would help explain why the WHR maintains a good ability to predict metabolic dysfunction and clinical outcomes (72, 93-95) despite the fact that it is inferior to WC as an indicator of visceral fat accumulation (54).
References


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Variability in Waist Circumference Measurements According to Anatomic Measurement Site
Abstract

The measurement of waist circumference (WC) is widely advocated as a simple anthropometric marker of health risk; yet there remains no uniformly accepted measurement protocol. The purpose of this study was to determine whether the magnitude of WC differs across four measurement sites, and to quantify the influence of measurement site on the apparent prevalence of abdominal obesity. The predominantly Caucasian sample consisted of 223 men and 319 women (20 to 67 y). WC was measured using a non-stretching tape at the following anatomical locations: superior border of the iliac crest, midpoint between the iliac crest and lowest rib, umbilicus, and minimal waist. Differences in mean WC at each site were tested using repeated measures analysis of variance, adjusted for multiple comparisons. Inter- and intra-observer reliabilities across measurement sites were estimated using intraclass correlation coefficients. In women, the mean WC for all measurement sites were significantly different from each other, with the exception of the iliac crest and midpoint. In contrast, no significant differences between sites were found in men. Measurement site had a substantial influence on the apparent prevalence of abdominal obesity (>88/102 cm), ranging from 23% to 34% in men and 31% to 55% in women. The reproducibility of WC was high at all measurement sites and was comparable across levels of BMI. In conclusion, the magnitude of WC is influenced by measurement site, particularly in women. Small differences in this regard are amplified when dichotomous cut-points rather than a continuum are used to define abdominal obesity.
Consequently, the choice of measurement protocol may bias research findings and influence clinical decision-making. Adopting of a standard measurement protocol will facilitate the interpretation and clinical utility of WC measures for obesity-related risk stratification.

**Keywords:** obesity, anthropometry, reliability, measurement
Introduction

The measurement of waist circumference (WC) is now widely advocated as a simple anthropometric indicator of metabolic and cardiovascular disease risk. WC is a key diagnostic criterion for the metabolic syndrome according to the U.S. National Cholesterol Education Program (1) and the International Diabetes Federation (2), and has been incorporated into clinical practice guidelines for the identification and treatment of overweight and obesity in several countries, including the U.S. (3), Canada (4), and Australia (5). For practical reasons, single sex-specific thresholds (M: >102 cm, >F: 88 cm) are most commonly used to denote elevated risk associated with abdominal obesity in clinical settings (6), although alternate cut-points have been proposed for specific racial/ethnic groups (4, 7) and different BMI categories (8).

Despite the widespread use of WC measurements, there remains no uniformly accepted measurement protocol, resulting in a variety of techniques employed throughout the published literature. For example, current U.S. National Institutes of Health (NIH) guidelines specify that waist circumference be measured directly above the superior border of the iliac crest (3), while the World Health Organization (WHO) (9) and Health Canada (10) recommend measurement at the mid-point between the superior border of the iliac crest and the lowest rib. Measurements made at the umbilicus and at the minimal waist are also commonly used in clinical and research settings (11). Even subtle differences in the anatomical location of measurement could potentially affect the utility of waist measures for risk assessment, particularly when risk stratification depends on dichotomous thresholds. Yet, the degree to which the choice of
measurement site influences the reliability of waist measurements or apparent prevalence estimates of abdominal obesity has not been extensively investigated.

To date, the most comprehensive study to examine the difference in magnitude of waist measurements taken using different protocols was published by Wang et al. (12). However, their sample was relatively small (n=111) and included a broad age range (7-83 years) which is problematic given changes in anthropometric indicators of body composition during childhood and in the elderly (13-15). Therefore, the purpose of the current investigation was to determine whether the magnitude of WC measurement differs systematically across four commonly used sites of measurement in adult men and women, and to quantify the influence of measurement site on prevalence estimates of abdominal obesity and on the reproducibility of the measures.

Methods & Procedures

Sample

Healthy volunteers (223 men; 319 women) 20-67 y of age were recruited using local posters and advertisements. Pregnant women and persons currently undergoing treatment for any systemic illness which may have had an impact on waist measurements were excluded from participation. The study protocol was approved by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. All participants provided written informed consent prior to participation.
**Measures**

Height was measured to the nearest mm and body mass was measured to the nearest 0.1 kg using a stadiometer and standard digital scale (Tanita HD-351), respectively. For these measurements, participants wore light clothing and no shoes.

WC was measured using a flexible, tension-sensitive, non-stretching tape measure (Gulick II) placed directly on the skin. Participants stood relaxed, with arms folded comfortably across the chest so multiple WC measurements could more easily be made. Measures were made at the end of normal expiration with special attention paid to ensure the tape was positioned perpendicular to the long axis of the body and parallel to the floor. A series of four measurements were taken on the right side at the following anatomical locations by a single, trained researcher: 1) superior border of the iliac crest, 2) midpoint between the iliac crest and the lowest rib, 3) umbilicus, and 4) minimal waist.

Inter- and intra-observer reliability were assessed in smaller subsamples (n=43 and n=45, respectively) of weight stable (< ±1.5 kg) participants measured by one of four other experienced observers on a separate occasion within one week of the initial measurement.

**Statistical Analysis**

Pearson correlations between age and WC measures made at each anatomical site of measurement were computed. Significant differences in mean WC values across anatomical sites were tested using a repeated measures analysis of variance, with Bonferroni adjustment for multiple comparisons. This analysis was also repeated after
stratifying the sample according to BMI classification (normal weight, overweight, and obese). The influence of age on the mean differences between measurement sites was examined using linear regression to model the mean difference in each pair of measurements. In all cases, separate analyses were performed for men and women.

The degree of reproducibility of measurement at each site was assessed using intraclass correlation coefficients. Potential heterogeneity in the reliability of WC measures according to age or BMI was examined by correlating age and BMI with the difference in WC measurements within and between observers.

Data management and analysis was conducted using SAS software and procedures version 9.1 (SAS Institute Inc., Cary, NC.). SPSS version 16.0 was used to calculate intraclass correlation coefficients.

Results

The age and BMI characteristics of the participants are presented in Table 1. The sample was predominantly white (95%) but with a range in age (20-67 y) and BMI (18.5-52.0 kg·m⁻²). The prevalence of obesity (BMI ≥30 kg·m⁻²) was 29.2% in men and 18.2% in women. The subsample used to evaluate the reproducibility of measurements at each site was slightly older (women: 51.3 y (p=0.0007); men: 45.2 y (NS)) than the overall sample. Male participants used in the subsample had a higher mean BMI (30.0 kg·m⁻²) compared with the overall sample (28.2 kg·m⁻², p=0.01).

WC measurements made at all anatomic sites were highly correlated with each other in both men and women (Table 2), and there was a significant, moderately positive correlation between age and WC in men as well as women. In both sexes, the
highest mean values were measured at the umbilicus and the smallest at the narrowest waist, with a mean range of 2.5 cm and 8.6 cm across these sites in men and women, respectively. In women, the overall mean for each measurement site was significantly different from all other individual site means, with the exception of measures taken at the iliac crest and midpoint. In contrast, no significant differences in the magnitude of waist circumference between anatomical sites were found in men (Table 3). However, the site of measurement did result in different estimates of abdominal obesity when cut-points of >88 cm (women) and >102 cm (men) were applied to the sample. The magnitude of the differences between WC sites in men and women were consistent across categories of BMI (Figure 1). Age did not influence the magnitude of the differences in women; however, among men, the differences became smaller with advancing age (results not shown).

The reproducibility of WC measurements was very high across all 4 anatomical sites (Table 4). The intraclass correlation coefficients (ICCs) for intra-observer reliability at the iliac crest, midpoint, umbilicus, and minimal waist were 0.993, 0.991, 0.992 and 0.989, respectively. Corresponding ICCs for inter-observer reliability were: 0.987, 0.987, 0.979, and 0.989. Sex-specific correlation coefficients are presented in Table 4. Overall, the ICCs were marginally stronger in men compared to women. There was no evidence that the reproducibility of WC measurements was influenced by either age or BMI. The correlations between age and the difference in WC measurements within and between observers ranged from $r=-0.283$ to $r=0.066$ (all $p>0.05$). Similarly, the correlations with BMI ranged from $r=-0.155$ to $r=0.244$ (all $p>0.05$).
Discussion

The findings from the present study indicate that choice of measurement protocol significantly influences the magnitude of WC measurements and the proportion of individuals considered at elevated health risk, particularly in women. Our findings are consistent with previous investigations suggesting that WC measurements made using different protocols are not all comparable. For example, absolute differences in the magnitude of WC measured at the umbilicus compared with the natural waist have been reported in middle-aged men and women (16, 17). The magnitude of these differences varied between study populations, ranging from approximately 2 cm (16) in normal weight men to approximately 11 cm in overweight post-menopausal women (17). Wang et al. (12) also compared measurements taken at four sites similar to those in the present study. In their sample of 111 subjects, significant differences between all measurement sites were detected among women (minimal waist < immediately below the lowest rib < midpoint between lowest rib and iliac crest < immediately above iliac crest; all p<0.05), while only the minimal waist was significantly different from the others among men.

The variability in between-site differences reported across diverse populations suggests that these differences may themselves vary according to characteristics of the sample including age, sex, race/ethnicity, and level of adiposity. In the primarily Caucasian sample of the present study, BMI classification (normal weight, overweight, obese class I, obese class II or III) did not significantly alter the magnitude of differences between WC measurement sites, while age had a minor impact in men only.
In a comprehensive review and meta-analysis, Ross et al. (11) recently concluded that differences in measurement protocol do not appear to meaningfully influence the relationship between WC and major disease end-points such as diabetes and cardiovascular mortality. Yet, differences in the magnitude of WC measurements between sites are not trivial in clinical settings where treatment recommendations commonly hinge on dichotomous cut-points. For example, Willis et al. (17) reported that 54% more men and 68% more women met the National Cholesterol Education Program (NCEP) criteria for metabolic syndrome when waist measurement was made at the umbilicus compared with the minimal waist. Likewise, prevalence estimates of abdominal obesity (>88/102 cm) ranged dramatically according to measurement site in the present study. In women, measures taken at the minimal waist resulted in the lowest prevalence (31%), while measures from the umbilicus resulted in the highest (55%). Even the small mean difference (2.5 cm) in the magnitude of WC across these sites in men resulted in a nearly 50% higher prevalence of abdominal obesity at the umbilicus (34%) compared to the minimal waist (23%). Consequently, the measurement protocol may have particularly important implications in population studies and the interpretation of epidemiological data. Adopting of a standard approach to WC measurement would therefore add to the utility of WC measures for obesity-related risk stratification. In order to facilitate the comparison of data collected using different protocols, we have included regression equations derived from this sample as an appendix (Appendix 1).
Subjective accounts of the technical issues related to the measurement of WC have been noted elsewhere (11, 12). Similarly, advantages and disadvantages unique to each measurement site were noted by the trained observers in the present study. While external landmarks (i.e. minimal waist and umbilicus) were generally easy to identify in both men and women, the identification of a single ‘narrowest’ point was sometimes difficult in cases of extreme thinness or when large deposits of subcutaneous fat prohibited the tape from lying flat against the skin. Furthermore, proper positioning of the tape can be complicated when the umbilicus is located below the level of the iliac crest, as can be the case in markedly obese individuals. The identification of bony landmarks required more training and experience to locate consistently but had the distinct advantage of being identifiable in virtually all participants. Due to the sharply curved skin surface superior to the iliac crest in many women, it was often more difficult to stabilize the tape measure at this site relative to others. Because it required the identification of two landmarks, the midpoint was more time-consuming than the other measures. Nevertheless, protocols using bony (internal) landmarks have the distinct advantage of being more promising indicators of change in clinical settings since they remain unaffected by changing levels of adiposity.

In the absence of a specific scientific rationale favoring the use of one particular measurement site over another, the relative superiority of any particular protocol is best discriminated on the basis of its ease and acceptability to clinicians as well as patients, and to the reproducibility of the measures achieved. Although a few previous investigations have reported estimates of reliability associated with the measurement of
WC, to our knowledge, this is the first study to measure both intra- and inter-observer reliability across four measurement sites. In this regard, the reliability coefficients for WC measured at each of the four anatomical locations indicated a high degree of reproducibility. Indeed, the intraclass correlation coefficients (ICCs) for intra-observer reliability exceeded 0.988 at all four sites (range: 0.989-0.993), while the ICCs for inter-observer reliability ranged from 0.979 to 0.989. The least reproducible inter-observer measurements were taken at the umbilicus (ICC=0.979), the most reproducible at the minimal waist (0.989). Contrary to expectations, measures of intra- and inter-observer reproducibility were virtually identical between measures taken at the iliac crest and mid-point, despite the identification of an additional landmark required by the latter.

Similarly high estimates of reliability have been reported elsewhere. For example, Wang et al. (11) reported high intraclass correlations (>0.996) for multiple sites when measurements were taken on a single occasion. Chen et al. (18) reported intra- and inter-observer ICCs of 0.987 (95% CI: 0.983-0.990) and 0.988 (95% CI: 0.982-0.993), respectively for WC measures made at the narrowest waist in a sample of 218 adults, and Sebo et al. (19) reported good inter-observer reliability (R=0.97) in measurement taken at the midpoint between 12 primary care physicians after one hour of training. Thus, with appropriate instruction and practice, WC is a highly reproducible measure of abdominal obesity, irrespective of measurement site.

In light of evidence that abdominal fat distribution and appropriate WC thresholds may vary according to race/ethnicity (2, 4, 20), the primarily Caucasian sample used for this analysis represents a limitation of this study. Replicating this work
in more diverse populations will be an important area of future investigation and will facilitate global comparisons of WC data.

In summary, the magnitude of WC is influenced by its anatomic location of measurement, particularly in women. Small differences in this regard are amplified when dichotomous cut-points are used to define abdominal obesity. Consequently, the choice of measurement protocol may bias research findings and influence clinical decision-making. Until a uniform approach to the measurement of WC is widely adopted, the location of measurement should be an important consideration in the interpretation of WC measurements.
Acknowledgements

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Disclosure

The authors declare no conflict of interest.
References


Table 1. Age and BMI characteristics of the participant sample

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<td></td>
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<td>Mean (SD)</td>
<td>%</td>
<td>%</td>
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<tr>
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</tr>
<tr>
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<td>45.3</td>
<td>29.2</td>
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<td>19.5-52.0</td>
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<tr>
<td>Women</td>
<td>319</td>
<td>45.1 (11.6)</td>
<td>26.4 (5.2)</td>
<td>32.6</td>
<td>18.2</td>
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<td></td>
<td>20-67</td>
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<td>18.6-48.2</td>
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Table 2. Correlations between age and waist circumference measurements made at 4 anatomical locations in men (unshaded) and women (shaded).

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Umbilicus</th>
<th>Iliac</th>
<th>Midpoint</th>
<th>Minimal</th>
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<tr>
<td>Age</td>
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<td>0.362</td>
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<td>0.960</td>
<td>0.956</td>
<td>0.948</td>
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<td>Iliac</td>
<td>0.303</td>
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<td>Midpoint</td>
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<td>0.348</td>
<td>0.973</td>
<td>0.979</td>
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All correlations significant at p<0.0001
**Table 3.** Mean waist circumference measurements and related prevalence of abdominal obesity obtained at 4 sites in men and women.

<table>
<thead>
<tr>
<th>Measurement site</th>
<th>Mean (SD)</th>
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<th>Mean</th>
<th>&gt;88cm/35 in (%)</th>
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</thead>
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<tr>
<td>Umbilicus</td>
<td>98.3 (12.6)</td>
<td>34.1</td>
<td>91.9 (13.4)(^{a,b,d})</td>
<td>55.2</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>97.8 (12.8)</td>
<td>31.8</td>
<td>89.1 (12.8)(^{c,d})</td>
<td>47.0</td>
</tr>
<tr>
<td>Midpoint</td>
<td>97.5 (13.2)</td>
<td>32.7</td>
<td>87.0 (13.1)(^{c,d})</td>
<td>41.1</td>
</tr>
<tr>
<td>Minimal</td>
<td>95.7 (12.5)</td>
<td>23.3</td>
<td>83.3 (12.9)(^{a,b,c})</td>
<td>30.7</td>
</tr>
<tr>
<td>Any WC site(^{†})</td>
<td>-</td>
<td>35</td>
<td>-</td>
<td>57.1</td>
</tr>
</tbody>
</table>

Superscript letters represent significant differences (p<0.008) between sites: a) superior border of the iliac crest; b) midpoint between the superior border of the iliac crest and the lowest rib; c) the umbilicus; d) the minimal waist

\(^{†}\)Any WC site refers to the proportion of individuals with WC >102/88 cm at any one or more of the measured anatomical sites.
Table 4. Reproducibility of waist circumference according to measurement site

<table>
<thead>
<tr>
<th></th>
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<th>Interobserver reliability</th>
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</tr>
<tr>
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<tr>
<td>Umbilicus</td>
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<td>0.988-0.998</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>0.989</td>
<td>0.974-0.996</td>
</tr>
<tr>
<td>Midpoint</td>
<td>0.984</td>
<td>0.962-0.994</td>
</tr>
<tr>
<td>Minimal</td>
<td>0.980</td>
<td>0.975-0.996</td>
</tr>
<tr>
<td><strong>Men</strong></td>
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<td></td>
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<tr>
<td>Umbilicus</td>
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<td>0.945-0.995</td>
</tr>
<tr>
<td>Iliac Crest</td>
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<td>0.990-0.998</td>
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<tr>
<td>Minimal</td>
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<td>0.982-0.996</td>
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Figure Legends

Figure 1. Differences in mean waist circumference across measurement sites, according to BMI in women (panel a) and men (panel b).

Figure 2. Scatterplot of waist circumference measurements taken by the same observer on two separate days, according to measurement site.

Figure 3. Scatterplots of waist circumference measurements taken by different observers, according to measurement site. Each pair of observers is represented by a different symbol.
Appendix 1. Regression equations predicting waist circumference based on measurement site.

<table>
<thead>
<tr>
<th>WOMEN</th>
<th></th>
<th>MEN</th>
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<tbody>
<tr>
<td><strong>Equation</strong></td>
<td><strong>r^2</strong></td>
<td><strong>SEE</strong></td>
<td><strong>Equation</strong></td>
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<tr>
<td>Iliac = 5.12519 - 0.00230(Age) + 0.96628(Midpoint)</td>
<td>0.9726</td>
<td>2.13144</td>
<td>Iliac = 3.87870 - 0.03092(Age) + 0.97692(Midpoint)</td>
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<tr>
<td>Iliac = 4.44034 + 0.00748(Age) + 0.91676(Umbilicus)</td>
<td>0.9217</td>
<td>3.60570</td>
<td>Iliac = -1.80499 + 0.03300(Age) + 0.99961(Umbilicus)</td>
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<tr>
<td>Iliac = 9.36758 - 0.00105(Age) + 0.95692(Minimal)</td>
<td>0.923</td>
<td>3.57423</td>
<td>Iliac = 2.71298 - 0.05107(Age) + 1.01647(Minimal)</td>
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<tr>
<td>Midpoint = -2.99438 + 0.01479(Age) + 1.00269(Iliac)</td>
<td>0.9728</td>
<td>2.17123</td>
<td>Midpoint = -3.17294 + 0.13505(Age) + 1.01397(Iliac)</td>
</tr>
<tr>
<td>Midpoint = 0.69541 + 0.01801(Age) + 0.01717(Umbilicus)</td>
<td>0.9148</td>
<td>3.84001</td>
<td>Midpoint = -0.539163 + 0.06704(Age) + 1.01818(Umbilicus)</td>
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<td>Midpoint = 4.74124 + 0.00347(Age) + 0.98493(Minimal)</td>
<td>0.9401</td>
<td>3.21928</td>
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<tr>
<td>Umbilicus = 2.12320 + 0.02927(Age) + 0.99364(Iliac)</td>
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<td>Umbilicus = 6.46787 + 0.02263(Age) + 0.97198(Midpoint)</td>
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<td>3.92451</td>
<td>Umbilicus = 6.91192 - 0.05797(Age) + 1.06210(Midpoint)</td>
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<td>Umbilicus = 9.47241 + 0.01609(Age) + 0.98090(Minimal)</td>
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<td>4.2727</td>
<td>Umbilicus = 5.371236 - 0.07808(Age) + 1.00169(Minimal)</td>
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<tr>
<td>Minimal = -3.23098 + 0.03632(Age) + 0.95356(Iliac)</td>
<td>0.924</td>
<td>3.56796</td>
<td>Minimal = 0.91851 + 0.06556(Age) + 0.94039(Iliac)</td>
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<tr>
<td>Minimal = -0.02699 + 0.02433(Age) + 0.94584(Midpoint)</td>
<td>0.9406</td>
<td>3.15474</td>
<td>Minimal = 3.92086 + 0.03237(Age) + 0.92918(Midpoint)</td>
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<tr>
<td>Minimal = -1.02517 + 0.03207(Age) + 0.90184(Umbilicus)</td>
<td>0.8997</td>
<td>4.09690</td>
<td>Minimal = -1.19141 + 0.09503(Age) + 0.94491(Umbilicus)</td>
</tr>
</tbody>
</table>
This manuscript was prepared for publication in the American Journal of Cardiology. Dr. Peter T. Katzmarzyk is a coauthor on this paper. Wendy Stephen, Travis Saunders and Jennifer Kuk aided with data collection. Financial support for this study was provided through an ancillary grant from the Canadian Heart Health Surveys Follow-Up Study.
Effect of the Site of Measurement on the Prevalence of the Metabolic Syndrome
Abstract

Waist circumference (WC) is widely advocated as a marker of health risk and is a key diagnostic criterion for the metabolic syndrome (MetS); yet, there remains no uniformly accepted measurement protocol. The purpose of this study was to determine whether WC is differentially associated with cardiometabolic risk factors according to its anatomical measurement site, and to quantify the impact of measurement site on prevalence of the MetS. The sample included 520 community-dwelling adults (208 men, 312 women). WC was measured at 4 common sites: the superior border of the iliac crest, midpoint between the iliac crest and the lowest rib, umbilicus, and minimal waist. Resting blood pressure was measured, and fasting blood samples were analyzed for concentrations of HDL-cholesterol, triglycerides, and glucose. The MetS was diagnosed according to the criteria of the AHA/NHLBI. Overall, the patterns of association between WC and cardiometabolic risk factors were similar across anatomical locations of measurement. In men, the prevalence of the MetS was the same when WC was measured at the iliac crest, the midpoint, or the umbilicus (21.2%), but was lower (18.3%) using the minimal waist. In women, the prevalence of the MetS was 15.1%, 14.4%, 14.1%, and 13.1% using the umbilicus, iliac crest, midpoint and minimal waist, respectively. The prevalence of the MetS is modestly influenced by the anatomical site of WC measurement. Efforts should be made to standardize the protocol for the measurement of WC given its potential to influence research findings and clinical decision-making.
Keywords: obesity, risk factors, anthropometry, measurement
Introduction

In the absence of a universally accepted approach to waist circumference (WC) measurement, a variety of protocols are used to assess abdominal adiposity in clinical and research settings. The purpose of this study is to determine whether WC is differentially associated with cardiometabolic risk factors according to its anatomical site of measurement, and to assess the impact of measurement site on prevalence estimates of the MetS in adult men and women.

Methods

Healthy volunteers (208 men; 312 women) 20 to 66 years of age were recruited from the local community. Pregnant women and persons undergoing treatment for any systemic illness were excluded. The study protocol was approved by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. All participants provided written informed consent prior to participation.

Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg using a stadiometer and standard digital scale (Tanita HD-351), respectively. Participants wore light clothing and no shoes. WC was measured using a flexible, tension-sensitive, non-elastic tape measure (Gulick II) placed directly on the skin. Participants stood relaxed with legs parallel and shoulder-width apart; arms were folded comfortably across the chest. Measurements were made at the end of normal expiration with special attention paid to ensure the tape lay perpendicular to the long axis of the body and parallel to the floor. A series of 4 measurements were taken at the following anatomical locations by a single, trained researcher: immediately above the
superior border of the iliac crest, midpoint between the superior border of iliac crest and the lowest rib, the umbilicus, and the minimal waist.

Resting blood pressure was measured using an automated monitor (BpTRU model BPM-100; VSM MedTech Ltd., Vancouver, BC, Canada). After 5 minutes of rest, 6 serial measurements were taken at 1-minute intervals. The last 5 readings were averaged and recorded. Blood samples were taken in the morning after an overnight fast of approximately 12 hours. Samples were drawn using a single capillary finger-stick sample and analyzed (Cholestech LDX, Hayward, CA) for concentrations of HDL-cholesterol, triglycerides, and glucose. The Cholestech LDX system has been validated against reference laboratories, and performed well (1, 2). Due to a non-normal distribution, plasma triglyceride values were log transformed prior to further analysis.

The MetS was operationally defined according to American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria (3) of three or more of: high WC (M: ≥102 cm; F: ≥88 cm), high blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg or drug treatment for hypertension), elevated plasma triglycerides (≥1.7 mmol/L or drug treatment for elevated triglycerides), low HDL-cholesterol (M: <1.03 mmol/L; F: <1.3 mmol/L; or drug treatment for reduced HDL-cholesterol), and elevated fasting blood glucose (≥5.6 mmol/L or drug treatment for type 2 diabetes or high glucose). Since WC was the primary subject of the present analysis, risk factor clustering was defined by the presence of two or more (≥2) of: high blood pressure, elevated triglycerides, low HDL-cholesterol, or elevated fasting blood glucose. Information about the use of medications was collected via self-administered
questionnaire. Participants were asked to bring a list of physician prescribed medications at the time of data collection and to indicate if they were being treated for high blood pressure, dyslipidemia or type 2 diabetes/high blood glucose. Individuals being treated for hypertension or high blood glucose were coded accordingly. As stipulated in the MetS criteria set out by the AHA/NHLBI, individuals taking fibrates or nicotinic acid were presumed to have both elevated triglycerides and low HDL-cholesterol.

Differences in mean WC values across anatomical sites were tested using a repeated measures analysis of variance, with Bonferroni adjustment for multiple comparisons. Pearson correlation coefficients were used to summarize the relationships between WC and cardiometabolic risk factors for each WC measurement site. Significant differences in the strength of these associations across WC sites were tested as suggested by Meng et al. (4) In cases where significant heterogeneity in the correlations was detected, pair-wise comparisons were performed for each pair of WC measurements, adjusting for multiple comparisons.

A series of sex-specific logistic regression models was used to predict the odds of high blood pressure, elevated triglycerides, elevated fasting glucose, low HDL-cholesterol, and cardiometabolic risk clustering (≥2 risk factors) from WC at each measurement site, adjusted for age. Initially, WC was included as a continuous variable. In subsequent models, WC was dichotomized according to sex-specific cut-points (≥102/88 cm) to facilitate interpretation. The sensitivity and specificity of these cut-
points for detecting abnormal risk factor levels was calculated for each of the 4 locations of WC measurement.

Data management and analysis was conducted using SAS software and procedures version 9.1 (SAS Institute Inc., Cary, NC.).

Results

Baseline characteristics (mean, SD) of the sample are presented in Table 1. The sample was predominantly white (95%) but ranged in age (20-66 y) and BMI (18.6-49.2 kg·m\(^{-2}\)). Excluding participants who self-reported a race/ethnicity other than white did not significantly alter any of the findings. In both sexes, the highest mean WC values were measured at the umbilicus and the smallest at the minimal waist, with a mean range of 2.5 cm and 8.6 cm across sites in men and women, respectively. Consequently, the prevalence of abdominal obesity (≥102/88 cm) ranged from 22.1%-33.2% in men and from 30.1%-55.5% in women, depending on the site of measurement.

WC measurements made at all 4 sites were highly correlated with each other in both men and women (all p<0.001). The magnitude of the correlations between cardiometabolic risk factors and WC at each site are illustrated separately for men and women in Figure 1. WC was inversely associated with HDL-cholesterol and positively correlated with all other risk variables. Overall, the magnitude and direction of the associations were similar across all WC measurement sites. Only the minimal waist emerged as a significantly better correlate of diastolic blood pressure and HDL-cholesterol in women compared to measurements at the iliac crest, midpoint, or umbilicus (p<0.0001).
The odds of abnormal risk factor levels and risk factor clustering (≥2 risk factors) associated with abdominal obesity were also similar across all WC sites. The odds ratios (95% C.I.) and corresponding sensitivity and specificity are presented in Table 2 (women) and Table 3 (men). Despite odds ratios of comparable magnitude, the sensitivity and specificity of high WC varied substantially across measurement sites. In general, high WC demonstrated greater sensitivity but less specificity for detecting risk in women compared to men. Prevalence estimates of the MetS also varied according to which WC site was used to define abdominal obesity, particularly in women (Table 4), although no statistical differences were detected.

Discussion

The findings from this study indicate that the nature of the associations between WC and cardiometabolic risk are similar across 4 common sites of measurement. Yet, the choice of measurement protocol will influence the sensitivity and specificity of WC as an indicator of cardiometabolic risk and prevalence estimates of the MetS, particularly in women. Consequently, measurement site is an important consideration in the interpretation of WC data.

To our knowledge, this study is the largest in size and scope to evaluate potential differences in the associations between WC and cardiometabolic risk factors according to measurement site. Although subtle differences were detected between sites in the strength of the associations with specific variables, the lack of any statistical difference or a clear pattern across all risk factors prevents the identification of a single superior WC measurement protocol based on stronger associations with
cardiometabolic risk. Rather, our results suggest that the associations between WC and cardiometabolic risk factors are similar in magnitude and direction, irrespective of measurement site.

These findings are consistent with those of Houmard et al. (5) who reported that both umbilical and minimal WC measurements correlated similarly with metabolic risk variables in 46 non-obese, middle to older aged men (mean age = 52.8 y). In contrast, WC measures at the minimal WC were consistently more highly correlated with cardiovascular disease risk factors than umbilical WC measurements in a sample of 266 middle-aged, overweight or obese men and women (6); however, none of these differences reached statistical significance. In that sample, the mean differences across the two sites were 10.6 cm and 4.5 cm in women and men, respectively (compared with 8.5 and 2.5 cm in the present study); therefore the subtle differences in the strength of the associations observed could presumably be attributed to the greater specificity of minimal WC measures relative to those taken at the umbilicus. Based on our estimates of sensitivity and specificity, WC thresholds of ≥102/88 cm are most sensitive but also least specific for predicting cardiometabolic risk clustering at the umbilicus compared to other measurement sites. Measurements taken at the iliac crest or midpoint may offer a superior compromise between sensitivity and specificity than either the umbilicus or minimal waist. It could be hypothesized that the ability of one WC measurement site to predict visceral adipose tissue (VAT) more strongly than another may translate into a stronger association with cardiometabolic risk. However, to our knowledge, no studies
have compared the association between WC and VAT using different WC measurement protocols.

The consistency of the observed associations between WC and cardiometabolic risk factors observed in the present analysis supports the sum of the evidence from prospective studies that WC measurement protocol has no substantial influence on its association with health outcomes such as cardiovascular events and all-cause mortality (7). Nevertheless, the choice of measurement site does influence the diagnosis of the MetS in women, and to a lesser degree in men. The differences observed in this regard are owed almost exclusively to the variation in abdominal obesity when dichotomous cut-points are applied to WC at different sites of measurement. In this sample, 50% more men and 84% more women met the criteria for abdominal obesity when WC was measured at the umbilicus compared with the minimal waist. These findings are similar to those previously reported by Willis et al. (6) in a sample of overweight adults 45-60 years of age where 54% more men and 68% more women were classified as abdominally obese at the umbilicus compared to the minimal waist. These discrepancies could lead to substantially different utilization of health resources since the use of WC measurements at the minimal waist may underestimate prevalence of the MetS relative to other measurement sites in both sexes, while the umbilicus will yield a modestly higher prevalence in women relative to intermediate estimates using measurements at the iliac crest or midpoint.

The overall prevalence of metabolic risk factors in this sample was similar to the most recent population estimates for Canada. Based on data from the Canada Heart
Health Surveys (1986-92), it has previously been estimated that 17% of Canadian men and 13.2% of Canadian women have the MetS (8), compared with 18-22% of men and 13-15% of women in the current study, depending on measurement site. Unfortunately, no current population-level data on measured risk factors are available in Canada for direct comparison; therefore, it is difficult to estimate to what degree the contemporary sample used in this analysis may have been affected by a ‘healthy subject’ bias. In addition, the prevalence of abnormal cardiometabolic risk factors and risk factor clustering reported here were likely influenced by the reliance on self-reported physician-prescribed medications and the use of serial automated blood pressure measurements that have been shown to result in lower measurements (8/7mmHg) as compared to ausculatory methods (9), but are generally similar to mean awake 24-hour ambulatory blood pressure readings (10).

The relationship between abdominal fat distribution and health risk is influenced by race/ethnicity (11-14) and alternative WC cut-points have been proposed for specific racial/ethnic groups (15). Thus, the primarily Caucasian sample used for this analysis represents a limitation of the study. Replicating this analysis in diverse populations will be an important area for future investigation. Moreover, since the choice of measurement protocol may ultimately influence clinical decision making when risk classification hinges on dichotomous cut-points, the standardization of measurement site should be an important consideration in the development of any future clinical WC thresholds or in refining the diagnosis of the MetS. Subjective accounts of the technical
issues related to the measurement of WC have been noted elsewhere (7, 16) but these issues also merit further study.
Acknowledgements

We would like to gratefully acknowledge the participants of this study as well as Wendy Stephen, Auburn Larose, Travis Saunders and Jennifer Kuk for their assistance with data collection. CM was responsible for all parts of this study. PK assisted with the data analysis and interpretation, and in the preparation of the final manuscript. CM is funded by a CIHR Canada Graduate Scholarship. PTK is supported, in part, through the Louisiana Public Facilities Authority Endowed Chair in Nutrition. The authors declare no conflict of interest.
References


Table 1. Physical and biological characteristics of study sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men n=208</th>
<th>Women n=312</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.1 (10.7)</td>
<td>44.6 (11.3)</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>27.9 (4.7)</td>
<td>26.3 (5.2)</td>
</tr>
<tr>
<td>25-29.9</td>
<td>45.2%</td>
<td>32.1%</td>
</tr>
<tr>
<td>≥30</td>
<td>27.4%</td>
<td>18.0%</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>&gt;102 cm</td>
<td>&gt;88 cm</td>
</tr>
<tr>
<td>Umbilicus</td>
<td>97.5 (12.2)</td>
<td>91.7 (13.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a,b,d</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>97.1 (12.4)</td>
<td>88.8 (12.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c,d</td>
</tr>
<tr>
<td>Midpoint</td>
<td>96.7 (12.8)</td>
<td>86.7 (13.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c,d</td>
</tr>
<tr>
<td>Narrowest Waist</td>
<td>95.0 (12.2)</td>
<td>83.1 (12.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a,b,c</td>
</tr>
<tr>
<td>Risk Factors</td>
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<td>Blood Pressure</td>
<td>113/73 mmHg</td>
<td>106/68 mmHg</td>
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<td>Triglycerides</td>
<td>1.44 (0.93) mmol/L</td>
<td>1.27 (0.73) mmol/L</td>
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<tr>
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<td>127.5 (82.4) mg/dL</td>
<td>112.5 (64.7) mg/dL</td>
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<tr>
<td>HDL_C</td>
<td>1.21 (0.34) mmol/L</td>
<td>1.59 (0.42) mmol/L</td>
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<td>46.8 (13.1) mg/dL</td>
<td>61.5 (16.2) mg/dL</td>
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<tr>
<td>Fasting Glucose</td>
<td>5.36 (0.72) mmol/L</td>
<td>5.06 (1.04) mmol/L</td>
</tr>
<tr>
<td></td>
<td>97.5 (13.1) mg/dL</td>
<td>92.0 (18.9) mg/dL</td>
</tr>
</tbody>
</table>

Superscript letters represent significant differences (p<0.008) between sites: a) the superior border of the iliac crest; b) midpoint between the superior border of the iliac crest and the lowest rib; c) the umbilicus; d) the narrowest waist

†Elevated risk according to AHA/NHLBI: high blood pressure (systolic: ≥130 mmHg or diastolic: ≥85 mmHg), high plasma triglycerides (≥1.7 mmol/L), low high-density lipoprotein cholesterol (M: <1.03 mmol/L; F: <1.3 mmol/L), and high blood glucose (≥5.6 mmol/L). Individuals being prescribed medication for hypertension, dyslipidemia or type 2 diabetes were considered to be meeting the corresponding risk criteria.
Table 2. Sensitivity, specificity and odds ratios (95% C.I.) of elevated cardiometabolic risk factors* associated with WC ≥88 cm across measurement sites in women

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Sensitivity/Specificity</th>
<th>UMBILICUS</th>
<th>ILIAC CREST</th>
<th>MIDPOINT</th>
<th>MINIMAL</th>
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</thead>
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<td><strong>High Blood Pressure</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Sensitivity/Specificity</td>
<td>87.8/50.6</td>
<td>87.8/59.8</td>
<td>82.9/65.1</td>
<td>70.7/76.0</td>
<td></td>
</tr>
<tr>
<td>OR¹</td>
<td>3.99 (1.91-8.30)</td>
<td>5.08 (2.46-10.52)</td>
<td>4.38 (2.37-8.09)</td>
<td>3.88 (2.38-6.34)</td>
<td></td>
</tr>
<tr>
<td>OR²</td>
<td>2.81 (1.33-5.93)</td>
<td>3.78 (1.81-7.89)</td>
<td>3.33 (1.77-6.25)</td>
<td>3.25 (1.94-5.46)</td>
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<tr>
<td><strong>Elevated Triglycerides</strong></td>
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<td></td>
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</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>80.0/51.0</td>
<td>65.5/57.6</td>
<td>65.5/65.0</td>
<td>63.6/77.0</td>
<td></td>
</tr>
<tr>
<td>OR¹</td>
<td>3.60 (1.98-6.53)</td>
<td>2.29 (1.49-3.53)</td>
<td>2.81 (1.82-4.34)</td>
<td>2.81 (1.92-4.12)</td>
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<tr>
<td>OR²</td>
<td>3.60 (1.93-6.74)</td>
<td>2.24 (1.41-3.55)</td>
<td>2.87 (1.80-4.58)</td>
<td>2.88 (1.92-4.32)</td>
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<td><strong>Low HDL-cholesterol</strong></td>
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</tr>
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<td>Sensitivity/Specificity</td>
<td>68.4/51.6</td>
<td>63.2/60.8</td>
<td>57.9/67.3</td>
<td>50.5/78.8</td>
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<tr>
<td>OR¹</td>
<td>1.78 (1.25-2.52)</td>
<td>1.80 (1.31-2.60)</td>
<td>1.92 (1.41-2.61)</td>
<td>2.20 (1.64-2.95)</td>
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<tr>
<td>OR²</td>
<td>1.77 (1.22-2.57)</td>
<td>1.82 (1.30-2.57)</td>
<td>1.98 (1.41-2.77)</td>
<td>2.32 (1.68-3.21)</td>
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<td><strong>Elevated Glucose</strong></td>
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<td>Sensitivity/Specificity</td>
<td>73.3/48.7</td>
<td>68.9/57.3</td>
<td>62.2/63.3</td>
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<tr>
<td>OR¹</td>
<td>2.07 (1.23-3.46)</td>
<td>2.10 (1.33-3.34)</td>
<td>2.00 (1.30-3.03)</td>
<td>2.31 (2.06-3.43)</td>
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<tr>
<td>OR²</td>
<td>1.86 (1.09-3.20)</td>
<td>1.94 (1.19-3.16)</td>
<td>1.84 (1.17-2.88)</td>
<td>2.21 (1.46-3.36)</td>
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<tr>
<td><strong>≥2 risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sensitivity/Specificity</td>
<td>84.5/54.4</td>
<td>77.5/62.7</td>
<td>73.2/69.3</td>
<td>67.6/80.9</td>
<td></td>
</tr>
<tr>
<td>OR¹</td>
<td>4.60 (2.57-8.24)</td>
<td>3.97 (2.46-6.41)</td>
<td>3.82 (2.48-5.90)</td>
<td>4.19 (2.85-6.18)</td>
<td></td>
</tr>
<tr>
<td>OR²</td>
<td>3.57 (1.97-6.47)</td>
<td>3.17 (1.94-5.18)</td>
<td>3.12 (1.99-4.89)</td>
<td>3.67 (2.45-5.50)</td>
<td></td>
</tr>
</tbody>
</table>

OR¹ derived from separate models; represent unadjusted odds associated with WC ≥88 cm
OR² derived from separate models; represent odds associated with WC ≥88 cm, adjusted for age

* Elevated risk according to AHA/NHLBI (1): elevated blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg or drug treatment for hypertension); elevated plasma triglycerides (≥1.7 mmol/L or drug treatment for elevated triglycerides), low high-density lipoprotein (HDL) cholesterol (<1.3 mmol/L or drug treatment for reduced HDL-cholesterol), elevated blood glucose (≥5.6 mmol/L or drug treatment for elevated glucose).
Table 3. Sensitivity, specificity, and odds ratios (95% C.I.) of elevated cardiometabolic risk factors* associated with WC ≥102 cm across measurement sites in men

<table>
<thead>
<tr>
<th><em>Elevated cardiometabolic risk factors</em></th>
<th>UMBILICUS</th>
<th>ILIAC CREST</th>
<th>MIDPOINT</th>
<th>MINIMAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Blood Pressure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>57.1/71.6</td>
<td>57.1/74.0</td>
<td>60.0/74.0</td>
<td>45.7/82.7</td>
</tr>
<tr>
<td>OR¹</td>
<td>2.55 (1.56-4.16)</td>
<td>2.58 (1.59-4.18)</td>
<td>2.71 (1.66-4.40)</td>
<td>2.61 (1.63-4.21)</td>
</tr>
<tr>
<td>OR²</td>
<td>2.26 (1.32-3.87)</td>
<td>2.26 (1.34-3.80)</td>
<td>2.38 (1.40-4.04)</td>
<td>2.21 (1.33-3.68)</td>
</tr>
<tr>
<td><strong>Elevated Triglycerides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>53.8/73.7</td>
<td>51.9/75.6</td>
<td>51.9/75.0</td>
<td>42.3/84.6</td>
</tr>
<tr>
<td>OR¹</td>
<td>2.30 (1.54-3.45)</td>
<td>2.40 (1.60-3.59)</td>
<td>2.37 (1.59-3.54)</td>
<td>2.46 (1.63-3.71)</td>
</tr>
<tr>
<td>OR²</td>
<td>2.39 (1.57-3.62)</td>
<td>2.50 (1.65-3.80)</td>
<td>2.48 (1.64-3.75)</td>
<td>2.60 (1.69-3.99)</td>
</tr>
<tr>
<td><strong>Low HDL-cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>48.0/75.2</td>
<td>46.7/77.4</td>
<td>48.0/77.4</td>
<td>34.7/85.0</td>
</tr>
<tr>
<td>OR¹</td>
<td>2.10 (1.47-2.99)</td>
<td>2.25 (1.58-3.22)</td>
<td>2.30 (1.61-3.29)</td>
<td>2.17 (1.50-3.14)</td>
</tr>
<tr>
<td>OR²</td>
<td>1.94 (1.34-2.80)</td>
<td>2.09 (1.45-3.02)</td>
<td>2.14 (1.48-3.09)</td>
<td>1.99 (1.35-2.92)</td>
</tr>
<tr>
<td><strong>Elevated Glucose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>46.2/71.2</td>
<td>44.2/73.1</td>
<td>46.2/73.1</td>
<td>32.7/81.4</td>
</tr>
<tr>
<td>OR¹</td>
<td>1.88 (1.27-2.77)</td>
<td>1.82 (1.24-2.66)</td>
<td>1.73 (1.19-2.53)</td>
<td>1.69 (1.14-2.51)</td>
</tr>
<tr>
<td>OR²</td>
<td>1.68 (1.12-2.52)</td>
<td>1.61 (1.08-2.41)</td>
<td>1.53 (1.03-2.28)</td>
<td>1.47 (0.97-2.22)</td>
</tr>
<tr>
<td><strong>≥2 risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity/Specificity</td>
<td>53.7/80.2</td>
<td>53.7/83.3</td>
<td>54.9/83.3</td>
<td>40.2/89.7</td>
</tr>
<tr>
<td>OR¹</td>
<td>3.12 (2.13-4.56)</td>
<td>3.29 (2.24-4.83)</td>
<td>3.35 (2.29-4.91)</td>
<td>3.19 (2.14-4.75)</td>
</tr>
<tr>
<td>OR²</td>
<td>2.80 (1.94-4.24)</td>
<td>3.03 (2.04-4.48)</td>
<td>3.08 (2.08-4.57)</td>
<td>2.88 (1.92-4.33)</td>
</tr>
</tbody>
</table>

OR¹ derived from separate models; represent unadjusted odds associated with WC ≥102 cm
OR² derived from separate models; represent odds associated with WC ≥102 cm, adjusted for age
*Elevated risk according to AHA/NHLBI (1): elevated blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg or drug treatment for hypertension); elevated plasma triglycerides (≥1.7 mmol/L or drug treatment for elevated triglycerides), low high-density lipoprotein (HDL) cholesterol (<1.03 mmol/L or drug treatment for reduced HDL-cholesterol), elevated blood glucose (≥5.6 mmol/L or drug treatment for elevated glucose).
Table 4. Prevalence of the metabolic syndrome as defined by the American Heart Association/National Heart, Lung, and Blood Institute (1), according to waist circumference measurement site in men and women.

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilicus</td>
<td>15.1</td>
<td>21.2</td>
</tr>
<tr>
<td>Iliac Crest</td>
<td>14.4</td>
<td>21.2</td>
</tr>
<tr>
<td>Midpoint</td>
<td>14.1</td>
<td>21.2</td>
</tr>
<tr>
<td>Narrowest Waist</td>
<td>13.1</td>
<td>18.3</td>
</tr>
<tr>
<td>Any WC site</td>
<td>15.4</td>
<td>21.2</td>
</tr>
</tbody>
</table>
**Figure Legend**

Figure 1. Pearson correlation coefficients between cardiometabolic risk factors and waist circumference at 4 anatomical measurement sites among men (panel a) and women (panel b). The direction of the correlations for HDL-C have been reversed to allow comparisons with the other risk factors. The asterix (*) denotes statistical difference in the strength of the correlation between minimal waist and each of the other WC measurement sites (all p<0.0083). Participants receiving drug treatment for high blood pressure, elevated triglycerides, reduced HDL-C or elevated blood glucose were excluded from correlations with those variables.
CHAPTER 5 MANUSCRIPT 3

This manuscript was prepared in accordance with the requirements for publication in the Canadian Journal of Diabetes. Cora L. Craig, Dr. Lise Gauvin, and Dr. Peter T. Katzmarzyk are coauthors on this paper.
Opposing Effects of Waist and Extremity Circumferences on the Risk of Incident Type 2 Diabetes
Abstract

Objective: To investigate the relationship between anthropometric circumferences and incident type 2 diabetes in Canadian adults. Methods: The sample included 516 men and 579 women from the Physical Activity Longitudinal Study. Waist, hip, thigh, and upper arm circumferences were used to predict incident diabetes over 15.5 y of follow-up. The odds of developing diabetes associated with 1 standard deviation of each anthropometric measure was calculated using sex-specific logistic regression, adjusted for age and parental history of diabetes. Results: There were 56 new cases of diabetes, yielding a 15.5 y cumulative incidence of 5.1%. With the exception of arm and thigh circumferences in men, all of the anthropometric variables were positive predictors of diabetes. However, after adjustment for BMI and waist circumference, the nature of the associations between hip, thigh and arm circumferences and diabetes reversed, such that they became inversely associated with diabetes development. The positive association between waist circumference and incident diabetes was independent of all other circumference measures but was attenuated by BMI. Conclusions: Larger extremity circumferences are associated with a lower risk of incident diabetes after adjustment for overall and abdominal adiposity, highlighting the potential value of these measures above and beyond the routine measurement of BMI and waist circumference.

MeSH Keywords: physical activity longitudinal study, anthropometry, adiposity, cohort study, BMI, waist-to-hip ratio.
Introduction

It is now well established that obesity and body fat distribution are associated with an increased risk of type 2 diabetes (1-4). Consequently, waist circumference is increasingly being used in population studies and clinical settings as a simple marker of metabolic and cardiovascular risk. Generally, the positive association between waist circumference and health risk appears quite robust and persists after statistical adjustment for a variety of other anthropometric measures, including the body mass index (BMI), hip circumference, and thigh circumference (5-9). In contrast, the nature of the associations between BMI and hip or thigh circumferences and health risk changes from positive to negative after adjustment for waist circumference (6, 8-12). For example, greater hip and/or thigh circumferences have been associated with better glucose metabolism (8) and with a lower prevalence of dyslipidemia and diabetes (9, 10), once adjusted for overall and abdominal adiposity.

It is postulated that the apparent health “protective” effect of greater BMI, hip circumference, or thigh circumference for a given waist circumference may be explained by a greater accumulation of extremity subcutaneous adipose tissue, higher lower-body lean muscle mass, or a combination of both factors (13, 14). Yet, despite the potential importance of extremity body composition in promoting healthy metabolic functioning, the degree to which anthropometric circumferences, particularly of the upper body, exert independent influences on diabetes risk has not been widely investigated. Therefore, the purpose of this investigation was to examine the independent and
shared influences of hip and extremity circumferences and adiposity on the incidence of diabetes in a diverse cohort of Canadians from a large, population-based sample.

Methods

Sample

The Physical Activity Longitudinal Study (PALS) is a cohort study of individuals aged 15 y and older who are members of a family that originally participated in the nationally representative 1981 Canada Fitness Survey (CFS) and/or the 1988 Campbell’s Survey of Well-Being in Canada (CSWB) (15). Participants were traced and sent a follow-up, self-administered questionnaire pertaining to a variety of health-related topics between September 2002 and April 2004. Since no information was collected on diabetes in the 1981 CFS, the 1988 CSWB was used as the baseline for the present analysis.

Of the approximately 4900 eligible PALS participants, 10% were lost to follow-up and 19.8% refused to participate. Of those remaining, 2511 completed questionnaires while the remainder were either deceased (n=899) or unable to participate for health reasons (n=32) (15). The sample used for the present analysis was limited to 1095 adults (516 men, 579 women) 20-69 years of age who were free of diabetes in 1988 (baseline) and had measurements of waist circumference and at least one other circumference (hip, thigh, or arm). Sample sizes vary between measures due to missing values for some participants (Table 1). PALS was approved by the Faculty of Medicine’s Ethics Review Board of the Université de Montréal and informed consent was obtained from participants in both 1988 and 2002-04.
Baseline Measures

Anthropometric dimensions were taken according to the standardized procedures of the CFS (16) during household visits in 1988, and a quality assurance program was conducted to ensure ongoing precision and accuracy of measurement. Briefly, stature was measured with a Harpenden tape to the nearest 0.1 cm and body mass was measured to the nearest 0.1 kg using a standing beam balance scale (Seca Corporation, Columbia, MD). Body mass index (BMI) was calculated as weight (kg)/height (m)^2. Circumference measurements were made to the nearest mm using a flexible anthropometric tape. Upper arm circumference was measured at the widest girth on the right arm while it was flexed (contracted muscle) in a comfortable raised position. Thigh circumference was measured on the right thigh, one centimeter below the gluteal line. Waist circumference was measured at the point of noticeable waist narrowing. In cases of indeterminant waist narrowing, waist circumference was measured at the estimated lower level of the twelfth or lower floating rib. Finally, hip circumference was measured at the level of the symphysis pubis and the greatest gluteal protuberance. The waist-to-hip ratio (WHR) was calculated as waist circumference divided by hip circumference. For comparison, a waist-to-thigh (WTH) and waist-to-arm (WTA) ratio were similarly calculated.

Covariates

Age and parental history of diabetes were collected by questionnaire at baseline and included as covariates in all analyses. Age was determined from birth and observation dates and coded as a continuous variable. Parental history of diabetes (‘Did
your mother or father ever have non-insulin dependent diabetes?’) was coded as a
categorical variable (yes, no).

Ascertainment of Incident Diabetes

The presence of diabetes was assessed via questionnaire during the 1988 and
2002-04 surveys. Participants were asked to provide information concerning health
conditions that had lasted or were expected to last a minimum of 6 months and that
had been diagnosed by a health professional. Participants were considered as having
diabetes if they answered ‘yes’ to either of the questions: ‘Do you suffer from diabetes?’
or ‘Do you currently take insulin?’. Given that existing cases of diabetes were screened
out at baseline, and that participants were initially aged 20 y or older, these cases were
assumed to be cases of type 2 diabetes. Moreover, since the incidence rate of type 1 by
comparison to type 2 diabetes among adults is low, any potential misclassification
would have only a minimal impact on the results.

Statistical Analysis

All data management and analyses were conducted using SAS software version
9.1 (SAS Inc, Cary, NC). Differences in baseline characteristics between men and women
were tested by Student’s t-test for continuous variables and by chi-square test for
proportions. Partial correlations between all of the anthropometric variables were
computed, adjusting for age. To examine the association between baseline
anthropometric measurements and incident diabetes, the odds of developing diabetes
over the follow-up period was calculated from separate sex-specific logistic regression
models, adjusted for age and parental history of diabetes. For ease of interpretation,
the odds of diabetes are expressed per standard deviation of each measure. Logistic regression was also used to examine the influence of hip, thigh and arm circumferences, independent of BMI, waist circumference, age, and parental history of diabetes. In addition, potential effect modification by sex was also evaluated by adding product terms to combined regression models.

Results

The descriptive characteristics of men and women at baseline are presented in Table 1. Men and women were of the same age, but differed significantly with respect to all anthropometric variables except hip circumference. Women had lower BMI, waist circumference, WHR, and arm circumference values, but higher thigh circumferences compared with men. The age-adjusted partial correlation coefficients between anthropometric variables in men and women are shown in Table 2. All anthropometric variables exhibited positive correlations with the other variables. In general, WHR had the lowest correlations with other indicators in both men and women, with the exception of waist circumference.

During the 15.5 y follow-up period there were 30 new cases of diabetes among men and 26 cases among women, yielding a cumulative incidence rate of 5.1%. With the exception of arm and thigh circumferences in men, all of the anthropometric variables were positive predictors of diabetes in both sexes after adjusting for age and parental history of diabetes (Table 3). In men, the risk of diabetes per SD of BMI was of a greater magnitude than for a SD of any other anthropometric variable. However, waist circumference, WHR, and WTH ratios were also associated with high and nearly
identical odds ratios. In women, a single SD increase in waist circumference was associated with the greatest increase in diabetes risk in comparison to the other measures. In all cases, the magnitude of the risk associated with a given anthropometric measure was higher among women than men; however, sex was not a significant effect modifier of any of the associations.

After adjustment for BMI and waist circumference, the nature of the associations between hip, thigh, and arm circumferences reversed, such that they became inversely associated with the development of diabetes (Figure 1). For a given BMI and waist circumference in men, a single SD elevation in hip, thigh, or arm circumference were each associated with an approximate 50% risk reduction in incident diabetes. Although a similar pattern of results was observed for women, only the effect of hip circumference was statistically significant, independent of BMI and waist circumference (OR: 0.34, 95% CI: 0.15-0.78). Waist circumference initially exhibited a strong association with incident diabetes independent of extremity circumference measures in men and women; however, in all cases this association was attenuated to non-significance once the effects of BMI were included in the regression models.

Discussion

The results of the present study confirm previous findings that, after adjusting for BMI and waist circumference, greater hip and thigh circumferences are associated with lower odds of developing diabetes (5, 9, 10). Although the inverse associations did not reach statistical significance in all cases, the overall pattern of findings suggests that this is true for both adult men and women. Previously, Snijder et al. (10) reported waist
circumference-, BMI-, and age-adjusted odds ratios of 0.55 (95% CI: 0.36-0.85) and 0.63 (0.42-0.94) per SD of hip circumference for men and women, respectively, who participated in the Hoorn Study - a population based study of 50-75 y old adults living in the Dutch city of Hoorn. Corresponding odds ratios per 1 SD of thigh circumference were 0.79 (0.53-1.19) in men and 0.64 (0.46-0.93) in women. Similarly, cross-sectional analyses from the AusDiab study revealed odds ratios for the presence of diabetes of 0.55 (0.41-0.73) in men and 0.42 (0.27-0.65) in women per SD of hip circumference, after adjustment for age, BMI, and waist circumference in a population-based sample of Australian adults ≥25 y of age (9). These risk estimates are of similar magnitude to those from the present study, underscoring the robustness of these relationships across populations.

The present study also extends these previous findings to include arm circumference, and the results suggest that the protective nature of larger extremities may not be limited only to the lower body. For a given waist circumference, a higher mid-upper arm circumference also appears to impart a modest beneficial effect against the development of diabetes. Further investigations will be required to determine the consistency of this observation for diabetes and for other health outcomes. Recently published findings by Wannamethee et al. (17) found a decreasing risk of all-cause mortality across quartiles of mid-arm muscle circumference (arm circumference adjusted for skinfold thickness) in men 60-79 y of age (p-trend=0.0003). In contrast, the association between waist circumference and mortality was weak in this population (p-trend=0.30) and became significantly positive only after adjustment for arm
circumference (17). Therefore, the simultaneous assessment of central and extremity circumferences may more accurately characterize particular body shape phenotypes and help improve risk stratification.

The use of a longitudinal cohort based on a representative sample of the Canadian population at baseline, with direct measures of several anthropometric markers, and a considerable follow-up period are major strengths of this study. However, despite the longitudinal design, the data collected for the purposes of the PALS are limited by the lack of interim measures throughout the follow-up period and at the time of diabetes diagnosis. Anthropometric measurements may not be stable over time, and the degree to which any changes in these measures were responsible for the development of diabetes cannot be known. Furthermore, it was not possible to obtain measurements of fasting glucose or to confirm the self-reported diagnosis of diabetes at baseline or at follow-up. A previous analysis of data from the population-based Manitoba Heart Health Survey indicated that undiagnosed diabetes cases accounted for about one third of all diabetes cases (18). Thus, the reliance on self-reported physician-diagnosed diabetes as the outcome measure in the present study likely resulted in an underestimate of the true incidence of diabetes in this sample. Unfortunately no specific data describing race/ethnicity were collected in the PALS, its role as a potential confounder could not be examined in the present analysis. Further investigations into the role of race/ethnicity in this regard are warranted.
Although waist circumference is a well-accepted surrogate measure of abdominal adiposity, it is difficult to determine the degree to which larger hip and extremity circumferences represent greater volumes of subcutaneous fat or higher muscle mass, and the relative impact of these tissues on the risk of disease. Unfortunately, the PALS did not include imaging measures; thus, the degree to which circumference measures reflect variation in bone structure, muscle mass, and subcutaneous fat distribution could not be determined. In the Hoorn Study, hip circumference was positively associated with DXA (dual x-ray absorbitometry)-measured leg fat and leg lean mass in both men and women (13). Further, both leg fat and leg lean mass (in men only) were independently associated with lower post-load glucose levels. By comparison, the use of computed tomography in elderly (70-79 y) participants of the Health, Aging and Body Composition Study revealed that thigh circumference was equally dependent on fat and muscle components in men, while the fat component was the primary contributor in women (11). In that study, subcutaneous thigh fat was inversely associated with both fasting and 2-hr postload glucose levels; however, these associations were only statistically significant among men, but not women.

Using whole-body magnetic resonance imaging (MRI), Kuk et al. (14) recently reported that when waist circumference is held constant, men and women with greater hip and thigh circumferences have greater quantities of total, lower-body, and abdominal subcutaneous adipose tissue, greater skeletal muscle mass, and lower visceral adipose tissue. Therefore, it is possible that a low amount of subcutaneous
adipose tissue or a low muscle mass in the extremities represents a phenotypic companion to visceral adipose tissue accumulation that further explains diabetes risk. Indeed, this could help explain why the waist-to-hip ratio maintains a good ability to predict metabolic dysfunction and diabetes risk (3, 19, 20), despite the fact that it is inferior to waist circumference as an indicator of visceral fat accumulation (21). The predictive nature of WTH and WTA in this study lends some further support for this hypothesis. Nonetheless, further investigation is required to more specifically characterize phenotypic variation in body composition and to distinguish the independent influences of subcutaneous adipose tissue and skeletal muscle mass on the attenuation of diabetes risk observed with larger extremity circumferences for a given level of waist circumference. Moreover, it is not clear whether it is the volume of muscle tissue or its quality that is more important for healthy metabolic functioning. Low muscular strength and endurance have been associated with metabolic disorders including metabolic syndrome (22) and incident diabetes (23). As well, skeletal fiber composition has been shown to be related to body fat distribution and insulin sensitivity (24, 25). Mechanistic research and the use imaging technology to accurately characterize body composition in future prospective studies will be valuable in unraveling the interrelationships between anthropometry, body composition and diabetes risk.

Current clinical guidelines advocate the combined use of BMI and waist circumference for the stratification of obesity-related health risk based on evidence of additive influences of overall and abdominal adiposity on the development of adverse
health outcomes including diabetes. The results of this study suggest that hip and extremity circumferences also exert an independent influence on the risk of diabetes and may offer additional means of assessing diabetes risk and improving risk stratification towards the prevention and treatment of this mounting public health burden.
Author Contributions and Disclosure

The authors’ responsibilities were as follows: PK, CC, LG: obtained grant funding; CM & PK: study design and first draft of manuscript; CM: statistical analysis; CC: data collection and management. All authors contributed to the interpretation of results and to the review of the final manuscript. No authors have conflicts of interest.
References


Table 1. Baseline (1988) characteristics of men and women in the Physical Activity Longitudinal Study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men</th>
<th></th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (SD)</td>
<td>n</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>516</td>
<td>38.3 (11.6)</td>
<td>579</td>
<td>38.9 (11.7)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>515</td>
<td>25.6 (3.3)</td>
<td>577</td>
<td>24.3 (4.3)*</td>
<td></td>
</tr>
<tr>
<td>WC (cm)</td>
<td>516</td>
<td>88.4 (9.6)</td>
<td>576</td>
<td>75.9 (10.1)*</td>
<td></td>
</tr>
<tr>
<td>HIP (cm)</td>
<td>515</td>
<td>99.9 (6.2)</td>
<td>577</td>
<td>100.0 (8.8)</td>
<td></td>
</tr>
<tr>
<td>WHR</td>
<td>515</td>
<td>0.88 (0.06)</td>
<td>576</td>
<td>0.76 (0.06)*</td>
<td></td>
</tr>
<tr>
<td>THIGH (cm)</td>
<td>509</td>
<td>56.0 (4.3)</td>
<td>564</td>
<td>57.7 (5.4)*</td>
<td></td>
</tr>
<tr>
<td>ARM (cm)</td>
<td>511</td>
<td>31.7 (2.9)</td>
<td>572</td>
<td>28.4 (3.7)*</td>
<td></td>
</tr>
<tr>
<td>Parental history of diabetes (%)</td>
<td>516</td>
<td>11.1%</td>
<td>579</td>
<td>13.1%</td>
<td></td>
</tr>
</tbody>
</table>

*significantly different from men, p<0.05
BMI=body mass index; WC=waist circumference; HIP=hip circumference; WHR=waist-to-hip ratio; THIGH=thigh circumference, ARM= arm circumference.
**Table 2.** Partial correlation coefficients between baseline (1988) anthropometric measures among male (shaded) and female (non-shaded) PALS participants, adjusted for baseline age.

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>WHR</th>
<th>WC</th>
<th>HIP</th>
<th>THIGH</th>
<th>ARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHR</td>
<td>0.44*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC</td>
<td>0.89*</td>
<td>0.72*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIP</td>
<td>0.88*</td>
<td>0.16*</td>
<td>0.80*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THIGH</td>
<td>0.77*</td>
<td>0.09†</td>
<td>0.63*</td>
<td>0.85*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARM</td>
<td>0.85*</td>
<td>0.34*</td>
<td>0.76*</td>
<td>0.80*</td>
<td>0.73*</td>
<td></td>
</tr>
</tbody>
</table>

**p<0.001, †p<0.01**

BMI=body mass index; WHR=waist-to-hip ratio; WC=waist circumference; HIP=hip circumference; THIGH=thigh circumference, ARM= arm circumference.
Table 3. Odds of incident diabetes associated with various anthropometric markers over 15.5 y of follow-up in the Physical Activity Longitudinal Study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>OR[^] [95% CI]</td>
</tr>
<tr>
<td>BMI</td>
<td>515</td>
<td>2.08 [1.47-2.97]</td>
</tr>
<tr>
<td>WC</td>
<td>516</td>
<td>1.94 [1.35-2.79]</td>
</tr>
<tr>
<td>HIP</td>
<td>515</td>
<td>1.50 [1.05-2.12]</td>
</tr>
<tr>
<td>THIGH</td>
<td>509</td>
<td>1.13 [0.76-1.68]</td>
</tr>
<tr>
<td>ARM</td>
<td>511</td>
<td>1.46 [1.00-2.14]</td>
</tr>
<tr>
<td>WHR</td>
<td>515</td>
<td>1.95 [1.31-2.90]</td>
</tr>
<tr>
<td>WTH</td>
<td>509</td>
<td>1.96 [1.36-2.91]</td>
</tr>
<tr>
<td>WTA</td>
<td>511</td>
<td>1.67 [1.12-2.46]</td>
</tr>
</tbody>
</table>

[^]Results for each measure are derived from a separate model and expressed per standard deviation of the variable; adjusted for age & parental history of diabetes.

BMI=body mass index; WC=waist circumference; HIP=hip circumference; THIGH=thigh circumference, ARM= arm circumference; WHR=waist-to-hip ratio; WTH=waist-to-thigh ratio; WTA=waist-to-arm ratio.
Figure Legend

Figure. Odds of incident diabetes per 1 SD of hip (panel a), thigh (panel b), and arm (panel c) circumferences in men and women. The results for each panel are from a separate model that includes both waist and the extremity circumference, as well as age, BMI, and parental history of diabetes as covariates. Error bars denote 95% confidence intervals and are statistically significant effects where error bars do not cross 1.0.
This manuscript was published in the journal Obesity (2008; 16(12):2690–2695). Cora L. Craig and Dr. Peter T. Katzmarzyk are coauthors on this paper. Funding for the record linkage at Statistics Canada was provided by Health Canada.
Influence of Central and Extremity Circumferences on All-Cause Mortality in Men and Women
Abstract

Background: For a given level of adiposity, larger lower body circumferences appear to exert a protective effect on several disease outcomes including cardiovascular disease and diabetes; however, the independent associations between extremity circumferences and mortality have not been widely investigated. The purpose of this study was to determine the independent and shared influences of upper- and lower-body circumferences on the risk of mortality in a large, population-based sample of adults. Methods: The sample included 10,638 adults 20-69 y of age (5012 men; 5626 women) from the nationally representative 1981 Canada Fitness Survey, who were monitored for mortality over 13 y of follow-up. Body mass index (BMI) was calculated from measured height and weight. Waist, hip, thigh, calf and upper arm circumferences were measured using a flexible, non-elastic anthropometric tape. Sex-specific proportional hazards regression models were used to evaluate the relationship between standardized values (Z-scores) of extremity circumference measures, waist circumference (WC) and mortality. Age, smoking status, alcohol consumption, and leisure-time physical activity were collected by questionnaire and were included as covariates. Results: During 131,563 person-y of follow-up, there were 340 deaths in men and 231 in women. After mutual adjustment, WC was positively associated with mortality while arm, thigh and calf circumferences were significantly protective in men and arm and thigh circumference were protective in women. Conclusion: Waist and extremity circumferences appear to have opposite, independent effects on mortality in
this sample of Canadians. Independent of level of BMI and WC, men and women with larger extremity circumferences had a lower risk of mortality.

**Keywords:** body composition, obesity, cohort study, Canada Fitness Survey
Introduction

Obesity is a major risk factor for a multitude of chronic conditions as well as for premature mortality (1). Thus, as the prevalence of obesity increases around the world, so does its relative importance as a modifiable risk factor for improving public health. An international classification system based on the body mass index (BMI) is now widely used to identify individuals with elevated obesity-related health risks. Yet, the BMI is not without its limitations. For example, the BMI cannot differentiate between lean and fat mass, nor can it account for differences in relative fat distribution. These are important limitations given that the localization of fat mass in the abdomen is an independent predictor of premature death (2), and that fat and lean mass have previously been shown to have differential effects on the risk of mortality (3-5).

Achieving a more accurate characterization of health risk using anthropometry will advance the descriptive and analytic epidemiology of obesity and consequently improve clinical risk stratification among the growing number of individuals classified as overweight or obese on the basis of BMI. While elevated waist circumference (WC) confers additional health risk at any level of BMI (6), smaller hip and thigh circumferences have been identified as significant predictors of cardiovascular disease risk factors (7-9) and type 2 diabetes mellitus (8, 10, 11). Moreover, hip circumference has been shown to independently influence longevity among participants of the Gothenburg Women’s Health Study (12) and in older adults (50-70 y) enrolled in the prospective study of ‘Diet, Cancer, and Health’ (13). Yet, to date, few studies have
examined the independent influence of additional upper- and lower-body circumferences on mortality rates, particularly in the general population.

Recently published findings by Wannamethee et al. (14) reported a decreasing risk of all-cause mortality across increasing quintiles of mid-arm muscle circumference in older men (60-79 y of age), independent of adiposity. Similarly, findings based on a representative samples of men and women from the NHANES I and II Epidemiologic Follow-up Studies also showed differential effects of arm circumference and BMI on mortality rates (4, 15). The purpose of this investigation was to examine the influence of upper and lower-body circumferences on the risk of mortality, independent of BMI and waist circumference in a large, population-based sample of Canadian adults.

**Methods & Procedures**

**Sample**

The 1981 Canada Fitness Survey (CFS) was based on a representative sample of the Canadian population, including individuals from urban and rural areas of every Canadian province (16). Approximately 3% of the total population was excluded, including Aboriginal people living on reserves, students living in school dormitories, armed forces personnel living on bases, and residents of the Territories and remote areas. A total of 23,400 people between the ages of 7 and 97 y participated in the survey in one way or another. The overall sample considered here includes 10,638 adults (5012 men; 5626 women) 20-69 years of age; however sample sizes vary from measure to measure due to missing values for some participants. Participants were
given an explanation of the testing protocol and informed consent was obtained before participation.

**Exposure Variables**

Anthropometric dimensions were taken according to the standardized procedures of the CFS during household visits in 1981 (17), and a quality assurance program was conducted to ensure ongoing precision and accuracy of measurement. Briefly, stature was measured with a Harpenden tape to the nearest 0.1 cm and body mass was measured to the nearest 0.1 kg using a standing beam balance scale (Seca Corporation, Columbia, MD). Body mass index (BMI) was calculated as weight (kg)/height (m)². Circumference measurements were taken on participants in the standing position and were made to the nearest 0.1 cm using a flexible, non-elastic anthropometric tape. Waist circumference (WC) was measured at the point of noticeable waist narrowing. In cases of indeterminant waist narrowing, WC was measured at the estimated lower level of the twelfth or lower floating rib. Hip circumference was measured at the level of the symphysis pubis and the greatest gluteal protuberance. The waist-to-hip ratio (WHR) was calculated as WC divided by hip circumference. Thigh circumference was measured on the right thigh, one centimeter below the gluteal line. Calf circumference was measured on the lower right leg at the point of maximal circumference. Finally, the upper arm circumference was measured as the right arm was flexed in a comfortable raised position. The measurement was taken at the widest girth while the muscle was contracted. Arm, thigh, and calf circumference
measures were also used to derive ratio measures (waist-to-arm, WTA; waist-to-thigh, WTH; waist-to-calf, WTC) in a manner similar to the WHR.

**Covariates**

Age, smoking status, alcohol consumption, and leisure-time physical activity were collected by questionnaire at baseline and considered as covariates. Age was determined from birth and observation dates and coded as a continuous variable. The smoking status of participants was coded as non-smokers, ex-smokers, or current smokers. Alcohol consumption was categorized according to average intake and frequency of consumption (abstainer; <10 drinks/month; 10-50 drinks/month; >50 drink/month) and included in the regression models as a series of dummy variables.

Leisure-time physical activity levels were assessed using a questionnaire modeled after the Minnesota Leisure Time Physical Activity Questionnaire (18) that collected information about physical activities performed over the preceding 12 months. A list of physical activities was provided and respondents indicated the number of occasions and the average duration of the activity bouts. Average daily leisure-time activity energy expenditure (AEE) was calculated as follows:

\[
AEE \text{ (kcal kg}^{-1}\text{.day}^{-1}) = \Sigma [N_i x D_i x METS_i]/365
\]

where \(N_i\) is the number of times the activity was performed, \(D_i\) was the average duration in hours of the activity, and \(METs_i\) was the estimated energy cost of the activity (kcal kg\(^{-1}\) hr\(^{-1}\)). Due to significant skewness of the original AEE variable, the natural logarithm of (AEE + 1) was used in all regression analyses (with one added to obtain only non-
negative values). For ease of interpretation, descriptive data are presented in original units.

**Ascertainment of Mortality**

The CFS database was linked to the Canadian Mortality Database (CMDB) at Statistics Canada. The CMDB contains all recorded deaths in Canada since 1950, and is regularly updated using death registrations supplied by every province and territory. Record linkage was performed using computerized probabilistic techniques, and the potential for death linkages to be missed using the method employed by Statistics Canada is quite small (19, 20). All deaths occurring from the end of CFS data collection (1981) through December 31st, 1993 were included in the present analysis. A total of 571 deaths occurred during 131,563 person-years of follow-up (mean: 12.4 y).

**Statistical Analysis**

All data management and analyses were conducted using SAS software version 9.1 (SAS Inc, Cary, NC). Differences in baseline characteristics between men and women were tested by Student’s t-tests for continuous variables and by chi-square tests for proportions. Partial correlations between all of the anthropometric variables were computed, adjusting for age. Sex-specific proportional hazards regression models were used to evaluate the relationship between standardized values (Z-scores) of BMI, WC, hip and extremity circumferences (thigh, calf, and arm) with all-cause mortality rates. Initially, all models included age as a covariate and subsequent models included the effects of BMI, smoking status, alcohol consumption, and leisure-time physical activity. Second order polynomial terms were systematically tested in order to evaluate non-
linear relationships between anthropometric measures and mortality. Only the squared term for hip circumference reached statistical significance among women ($p=0.027$); therefore, these terms were not retained in the final models. Potential effect modification by sex was also evaluated by adding appropriate product terms to general regression models that included the entire sample. In order to investigate the effect of eliminating disease assumed to be present at baseline, the primary analyses were subsequently repeated after exclusion of individuals who died within the first two years of follow-up ($n=61$).

**Results**

Table 1 provides the baseline characteristics of the sample. Women were significantly older than men (mean age: 38.5 y vs. 38.0 y) at baseline. Men and women also differed significantly with respect to all anthropometric variables. Women had lower BMI, WC, hip circumference, calf circumference, and arm circumference values, but higher thigh circumferences compared with men. Ratio measures (WHR, WTH, WTA and WTC) were also lower among women than men. Women were less likely to be current smokers or heavy drinkers at baseline and reported significantly lower levels of leisure-time physical activity compared with men. All of the anthropometric variables exhibited significant positive correlations with each other in both men and women and the partial correlation coefficients (adjusted for age) are shown in Table 2. The derived ratio scores generally had the weakest correlations with other variables, with the exception of the relationship between WHR and WC (data not shown).
After 13 y of follow-up, there were 340 deaths (132 CVD, 114 cancer, 94 other causes) in men and 231 deaths (49 CVD, 114 cancer, 68 other causes) in women. Table 3 summarizes the age-adjusted hazard ratios derived from Cox regression analysis for each of the anthropometric measures in relation to total mortality. After adjusting for all covariates, BMI, WC, and the WHR were significant positive predictors of all-cause mortality in women but not men. In contrast, thigh, calf and arm circumference were inversely associated with mortality in men but not women. Hip circumference was not a significant predictor of mortality in either sex. Waist to-thigh (WTH), WTC, and WTA ratios were each a strong positive predictor of mortality in men and women. Sex was a significant (p<0.05) effect modifier of the associations between both arm and calf circumference and all-cause mortality, but not for any other variables. For the sake of comparison, risk ratios were also calculated for cardiovascular and cancer related deaths. In both cases, the direction of the associations were as the same as for all-cause mortality; and the magnitude of the protective effect associated with hip, thigh, calf, and arm circumferences was surprisingly robust. However, some of these associations failed to reach statistical significance.

After adjustment for WC, arm, hip, thigh and calf circumferences were inversely associated with all-cause mortality in men and in women, independent of BMI and the other covariates (Figure 1). For a given WC, each standard deviation in arm circumference was associated with a significantly lower risk of mortality of the same magnitude in both men (HR: 0.75, 95% CI: 0.62-0.90) and women (HR: 0.75, 95% CI: 0.59-0.95). Likewise, the risk reduction associated with each standard deviation of thigh
circumference was also of a similar magnitude in both sexes (M: 0.79, 95% CI: 0.67-0.93; F: 0.81, 95% CI: 0.67-0.98). By comparison, the hazard ratio associated with each standard deviation of hip and calf circumferences were 0.98 (95%CI: 0.79-1.20) and 0.78 (95% CI: 0.66-0.92) in men and 0.81 (95% CI: 0.63-1.04) and 0.86 (95% CI: 0.73-1.02) in women, respectively (Figure 1). No significant association was apparent between BMI and mortality in models that included waist circumference in addition to any one or more of the upper or lower-body circumferences.

The exclusion of deaths occurring within the first 2 y of follow-up (n=61) had no meaningful effects on the results reported above. With the exception of thigh circumference in women (p=0.0656), arm, calf, and thigh (in men) circumferences remained significantly predictive of all-cause mortality in models that included WC, BMI and all other covariates.

Discussion

The purpose of this study was to examine the independent effects of waist circumference and multiple upper- and lower-body circumferences on mortality rates in a large, representative sample of adults. Despite the positive associations between all of the circumferences and mortality when considered separately, the mutually adjusted associations of waist and these additional circumferences occurred in opposing directions. Therefore, the results confirm the elevated risk of premature mortality associated with abdominal adiposity reported elsewhere (5, 21) but also indicate a substantial protective effect of larger extremity circumferences, particularly thigh, calf, and arm, independent of BMI.
The observed protective health effects associated with larger upper and lower-body circumferences in this study are consistent with a limited number of previous reports. In particular, it has been shown that a larger hip circumference for a given WC is inversely associated with cardiovascular and metabolic morbidities (7, 9-11, 22), as well as with mortality (12, 13). Similarly, an inverse association between upper arm circumference and mortality, independent of BMI, has previously been shown in female (15) and male (4) participants of NHANES I and II. In older men (61-79 y) from the British Regional Heart Study (14), mid-arm muscle circumference demonstrated a strong inverse association with mortality that persisted after adjustment for multiple indicators of ill health including FEV\textsubscript{1}, albumin, self-reported poor health, preexisting cancer, diabetes or cardiovascular disease. Moreover, the adverse consequences of low arm circumference in that sample were observed irrespective of BMI and WC, and in active as well as inactive men. To our knowledge, the current investigation is the first to demonstrate a protective effect of multiple upper- and lower-body circumferences on mortality in a single population-based sample. It is postulated that these inverse associations between upper- and lower-body circumferences and health risk may be owed to a greater accumulation of subcutaneous adipose tissue, greater lean-body mass, or a combination of these factors in the periphery (23-26). Attempts to estimate the muscle cross-sectional area in the arm and lower leg by correcting for skinfold thickness (27) among participants of the CFS did not yield hazard ratios that were meaningfully different from those of the simple circumferences. However, major body mass compartments have been previously shown to have differential effects on
mortality in select populations (3-5). For example, higher abdominal fat (sagittal diameter adjusted for trunk skinfold thicknesses) was a significant predictor of all-cause, cardiac and cancer deaths in the Paris Prospective Study of middle-aged men, while greater muscle mass (sum of midarm and midthigh circumferences adjusted for extremity skinfold thicknesses) was inversely associated with all-cause and cancer deaths, and low extremity subcutaneous fat was associated with greater cancer mortality (5).

Since the CFS did not employ imaging technology, it is difficult to accurately discern the degree to which the effects of larger extremity circumferences observed in this study reflect variation in bone structure, muscle mass, and/or subcutaneous fat mass. Using whole-body MRI, Kuk et al. (26) recently reported that for a given WC, men and women with larger hip and thigh circumferences have higher quantities of total, lower body, and abdominal subcutaneous adipose tissue, greater skeletal muscle mass, and less visceral adipose tissue. The authors suggested that smaller lower-body circumferences may therefore represent a phenotypic companion to visceral adipose tissue accumulation, further contributing to a body shape phenotype at high risk of cardiometabolic complications.

Owing to sample size limitations, an in-depth analysis of disease-specific causes of death was not possible in this investigation. However, the direction of the associations and the magnitude of effect associated with larger extremity circumferences for a given BMI and WC appeared consistent for cardiovascular and cancer related deaths in supplemental calculations. Thus, while dominant anti-
atherogenic properties of peripheral subcutaneous adipose tissue, particularly of the lower-body, have been previously highlighted in elderly women (24), the protective effects of larger extremity circumferences may not be mediated solely through cardiometabolic pathways. Indeed, results from the Paris Prospective Study Prospective study demonstrated elevated risk of cancer mortality associated with low muscle mass and with low subcutaneous fat in the arm and thigh region of native-born Frenchmen (5). More focused efforts to elucidate the mechanistic link(s) through which extremity circumferences exert their influence on mortality are therefore warranted and will be an important area for future study. Further investigations in this area may also help to clarify potential differences in the relative importance of body composition in the upper compared with lower limbs with respect to specific health outcomes.

There are several strengths and weaknesses of the current investigation that warrant discussion. The large, representative sample of Canadian men and women and the prospective design are marked strengths, as is the direct measurement of all anthropometric indicators. Unfortunately, no data are available with respect to changes in anthropometric markers over the follow-up period, which would have allowed the analyses to be refined further. Since excluding participants who died within the first 2 years of follow-up did not appreciably change the results; it appears that the observed relationships were not confounded by changes in body composition secondary to undiagnosed disease present at baseline. Moreover, since CFS participants underwent conservative screening procedures intended to identify health conditions that would preclude participation in a test of aerobic fitness, potential bias attributable to cases of
lower-leg edema potentially associated with certain cardiovascular conditions is unlikely.

The measurement protocols employed in the CFS used measurements of proximal thigh circumference which may have been uncomfortable for some individuals, resulting in missing data for approximately 2% of participants. Alternative protocols for thigh circumference take measurements at the mid-thigh (mid-way between the inguinal crease and the proximal border of the patella) (28) which may be more culturally acceptable in many cases. Based on our results, we suspect that the observed association between thigh circumference and mortality would be comparable between these anatomical locations of thigh measurement.

The relevance of both the composition (i.e. fat and lean components) and localization of body mass in explaining health outcomes are increasingly recognized. This study adds important new information regarding the influences of extremity circumferences on the risk of mortality, above and beyond that captured by overall and central adiposity as measured by BMI and WC. It also adds to the growing discussion with regards to the characterization of high-risk phenotypes and the value of anthropometric measurements for clinical risk stratification. The strong inverse associations between extremity circumferences and mortality observed in this study suggest that extremity circumferences taken in conjunction with WC may serve some utility in research and clinical settings.

A better understanding of the associations observed in this study and the physiological mechanism(s) underlying them will require concurrent assessment using
anthropometry in conjunction with sophisticated imaging techniques that will allow specific types of tissues to be accurately differentiated. Moreover, there is some evidence that muscle morphology, rather than muscle mass alone, may be of greater consequence for health outcomes (29, 30). Potential differences in this regard also merit further investigation. Despite practical challenges, studies to carefully assess regional body composition may yield novel and useful insights into the relationship between body composition and mortality.
Acknowledgements

Funding for the record linkage at Statistics Canada was provided by Health Canada. CM is supported by a Canada Graduate Scholarship from the Canadian Institutes of Health Research. PK is supported, in part, by the Louisiana Public Facilities Authority Endowed Chair in Nutrition.

Disclosure

The authors have no conflict of interest to declare.
References


Table 1. Baseline characteristics of men and women 20-69 y of age from the Canada Fitness Survey.

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<th>Variable</th>
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<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>5012</td>
<td>38.0 (13.2)</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>4992</td>
<td>25.2 (3.5)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>5012</td>
<td>88.0 (10.0)</td>
</tr>
<tr>
<td>HIP (cm)</td>
<td>4928</td>
<td>98.0 (6.9)</td>
</tr>
<tr>
<td>THIGH (cm)</td>
<td>4925</td>
<td>54.6 (5.0)</td>
</tr>
<tr>
<td>CALF (cm)</td>
<td>4988</td>
<td>36.6 (2.9)</td>
</tr>
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<td>5009</td>
<td>31.3 (3.1)</td>
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</tr>
<tr>
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<td>WTA</td>
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<td>Smoking status (%)</td>
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<td>Former</td>
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<tr>
<td>Current</td>
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<tr>
<td>&lt;10 drinks/mo</td>
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</tr>
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<td>10-50 drinks/mo</td>
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<td>31.2</td>
</tr>
<tr>
<td>&gt;50 drinks/mo</td>
<td>988</td>
<td>20.5</td>
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<tr>
<td>Physical Activity (kcal·kg⁻¹·day⁻¹)</td>
<td>4854</td>
<td>2.39 (3.52)</td>
</tr>
</tbody>
</table>

*significantly different from men, p<0.05

BMI=body mass index; WC=waist circumference; HIP=hip circumference; THIGH=thigh circumference; CALF= calf circumference; ARM= arm circumference; WHR=waist-to-hip ratio; WTH=waist-to-thigh ratio; WTC=waist-to-calf ratio; WTA=waist-to-arm ratio.
Table 2. Partial correlation coefficients between baseline anthropometric measures among men (shaded) and women (non-shaded) in the CFS, adjusted for age.

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>WC</th>
<th>HIP</th>
<th>THIGH</th>
<th>CALF</th>
<th>ARM</th>
</tr>
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<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC</td>
<td>0.73</td>
<td></td>
<td>0.79</td>
<td>0.63</td>
<td>0.58</td>
<td>0.70</td>
</tr>
<tr>
<td>HIP</td>
<td>0.72</td>
<td>0.60</td>
<td></td>
<td>0.73</td>
<td>0.67</td>
<td>0.69</td>
</tr>
<tr>
<td>THIGH</td>
<td>0.63</td>
<td>0.44</td>
<td>0.73</td>
<td></td>
<td>0.64</td>
<td>0.67</td>
</tr>
<tr>
<td>CALF</td>
<td>0.59</td>
<td>0.38</td>
<td>0.61</td>
<td>0.58</td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td>ARM</td>
<td>0.72</td>
<td>0.59</td>
<td>0.62</td>
<td>0.59</td>
<td>0.51</td>
<td></td>
</tr>
</tbody>
</table>

*All of the correlations between anthropometric variables are significant at p<0.001
BMI=body mass index; WC=waist circumference; HIP=hip circumference; THIGH=thigh circumference; CALF= calf circumference; ARM= arm circumference; WHR=waist-to-hip ratio; WTH=waist-to-thigh ratio; WTC=waist-to-calf ratio; WTA=waist-to-arm ratio.
Table 3. Hazard Ratios for all-cause mortality associated with anthropometric markers over 13 y follow-up of participants in the 1981 Canada Fitness Survey.

<table>
<thead>
<tr>
<th>Variable</th>
<th>MEN OR[^a][ 95% CI]</th>
<th>OR[^b][ 95% CI]</th>
<th>WOMEN OR[^a][ 95% CI]</th>
<th>OR[^b][ 95% CI]</th>
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<tbody>
<tr>
<td>BMI</td>
<td>0.93 [0.84-1.03]</td>
<td>0.95 [0.85-1.05]</td>
<td>1.15 [1.02-1.30]</td>
<td>1.15 [1.02-1.29]</td>
</tr>
<tr>
<td>WC</td>
<td>0.99 [0.88-1.11]</td>
<td>0.99 [0.88-1.11]</td>
<td>1.21 [1.07-1.36]</td>
<td>1.17 [1.04-1.33]</td>
</tr>
<tr>
<td>HIP</td>
<td>0.95 [0.85-1.07]</td>
<td>0.98 [0.87-1.09]</td>
<td>1.07 [0.95-1.21]</td>
<td>1.07 [0.95-1.21]</td>
</tr>
<tr>
<td>THIGH</td>
<td>0.81 [0.72-0.92]</td>
<td>0.84 [0.75-0.95]</td>
<td>0.91 [0.79-1.04]</td>
<td>0.95 [0.83-1.08]</td>
</tr>
<tr>
<td>CALF</td>
<td>0.83 [0.75-0.93]</td>
<td>0.86 [0.76-0.96]</td>
<td>0.98 [0.86-1.10]</td>
<td>1.00 [0.88-1.14]</td>
</tr>
<tr>
<td>ARM</td>
<td>0.84 [0.75-0.94]</td>
<td>0.87 [0.75-0.95]</td>
<td>1.04 [0.91-1.19]</td>
<td>1.03 [0.91-1.18]</td>
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<tr>
<td>WHR</td>
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<td>1.04 [0.90-1.19]</td>
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<td>1.18 [1.06-1.31]</td>
<td>1.14 [1.02-1.28]</td>
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<td>1.21 [1.08-1.36]</td>
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<tr>
<td>WTC</td>
<td>1.19 [1.06-1.34]</td>
<td>1.16 [1.02-1.31]</td>
<td>1.25 [1.13-1.39]</td>
<td>1.21 [1.08-1.35]</td>
</tr>
<tr>
<td>WTA</td>
<td>1.23 [1.12-1.36]</td>
<td>1.19 [1.07-1.32]</td>
<td>1.20 [1.09-1.31]</td>
<td>1.17 [1.06-1.29]</td>
</tr>
</tbody>
</table>

[^a]: Results for each measure are derived from a separate model and expressed per standard deviation of the variable; adjusted for age.

[^b]: Results for each measure are derived from a separate model and expressed per standard deviation of the variable; adjusted for age, smoking status, alcohol consumption, and leisure-time physical activity.

BMI=body mass index; WC=waist circumference; HIP=hip circumference; THIGH=thigh circumference; CALF=calf circumference; ARM=arm circumference; WHR=waist-to-hip ratio; WTH=waist-to-thigh ratio; WTC=waist-to-calf ratio; WTA=waist-to-arm ratio.
Figure Legend

**Figure.** Hazard Ratios for all-cause mortality per 1 SD of hip (panel a), thigh (panel b), calf (panel c) and arm (panel d) circumferences in men and women. The results for each panel are from a separate model. All models included age, BMI, smoking status, alcohol consumption and leisure-time physical activity as covariates. The error bars denote 95% confidence intervals.
The studies contained in this thesis explore the relationships between anthropometric measures and a range of outcomes from individual cardiometabolic risk factors to all-cause mortality. The results confirm the positive association between waist circumference (WC) and cardiometabolic risk, type 2 diabetes, and mortality, but highlight the need for WC measurement to be standardized in order to facilitate its interpretation and maximize its clinical utility. Using upper- and lower-body anthropometric measures in conjunction with BMI and WC may also offer added means of discriminating health risk. The inverse associations observed between extremity circumferences and incident type 2 diabetes and mortality, independent of BMI and WC, suggest that extremity circumferences taken in conjunction with WC may enhance risk stratification. Although larger lower body circumferences have previously been associated with attenuated health risk (1-7), it appears this effect may not be exclusive to lower body extremities. Pursuing lines of research aimed at better understanding the underlying mechanisms through which body composition influences disease risk and the degree to which clinical risk stratification can be improved using anthropometric measures continues to be warranted.

Several important issues that deserve further discussion with respect to the studies presented in this thesis are addressed below:
7.1 Strengths and Limitations

Studies 1 and 2 surpass in both size and scope any previous investigations examining the influence of measurement protocol on the magnitude of WC and its association with other risk factors, providing more definitive answers to important practical questions pertaining to the use of WC in clinical and research settings. The sample of community-dwelling volunteers used in both studies 1 and 2 was primarily Caucasian and likely suffered some degree of healthy subject bias since the majority of participants were university educated and the overall prevalence of obesity was somewhat lower than the prevalence among adults in the general Canadian population (8). Depending on the WC measurement site used, 18-22% of men and 13-15% of women in this sample had metabolic syndrome, compared with 17% of men and 13.2% of women from the Canada Heart Health Surveys (1986-92)(9). Unfortunately, no contemporary estimates of cardiometabolic risk factors in the Canadian population are available for comparison; results from the upcoming Canadian Health Measures Survey will be of great interest in this regard. Nevertheless, the correlations between WC and cardiometabolic risk factors in this sample are similar to what has been reported in previous population-based samples (Table 1). Therefore, the sample selection is unlikely to have compromised the internal validity of these studies.
Table 1. Correlations between waist circumference and cardiometabolic risk factors in participants of studies 1 and 2 by comparison to population-based samples.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Umbilicus</th>
<th>Iliac Crest</th>
<th>Midpoint</th>
<th>Narrowest</th>
<th>CCHS&lt;sup&gt;a&lt;/sup&gt;</th>
<th>NHANES III&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WOMEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>0.39</td>
<td>0.40</td>
<td>0.40</td>
<td>0.41</td>
<td>0.46</td>
<td>0.32</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>0.46</td>
<td>0.47</td>
<td>0.48</td>
<td>0.50</td>
<td>0.44</td>
<td>0.31</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.44</td>
<td>0.45</td>
<td>0.45</td>
<td>0.45</td>
<td>0.44</td>
<td>-</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>0.25</td>
<td>0.28</td>
<td>0.27</td>
<td>0.25</td>
<td>0.30</td>
<td>-</td>
</tr>
<tr>
<td>LDL_C (mmol/L)</td>
<td>0.25</td>
<td>0.27</td>
<td>0.28</td>
<td>0.28</td>
<td>0.31</td>
<td>0.22</td>
</tr>
<tr>
<td>HDL_C (mmol/L)</td>
<td>-0.38</td>
<td>-0.38</td>
<td>-0.38</td>
<td>-0.37</td>
<td>-0.29</td>
<td>-0.27</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>0.22</td>
<td>0.22</td>
<td>0.23</td>
<td>0.24</td>
<td>-</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>MEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>0.45</td>
<td>0.46</td>
<td>0.45</td>
<td>0.47</td>
<td>0.42</td>
<td>0.27</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>0.29</td>
<td>0.29</td>
<td>0.29</td>
<td>0.31</td>
<td>0.37</td>
<td>0.31</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.35</td>
<td>0.36</td>
<td>0.37</td>
<td>0.37</td>
<td>0.41</td>
<td>-</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>0.19</td>
<td>0.18</td>
<td>0.19</td>
<td>0.19</td>
<td>0.31</td>
<td>-</td>
</tr>
<tr>
<td>LDL_C (mmol/L)</td>
<td>0.22</td>
<td>0.20</td>
<td>0.21</td>
<td>0.20</td>
<td>0.28</td>
<td>0.13</td>
</tr>
<tr>
<td>HDL_C (mmol/L)</td>
<td>-0.28</td>
<td>-0.29</td>
<td>-0.30</td>
<td>-0.36</td>
<td>0.29</td>
<td>-0.28</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>0.37</td>
<td>0.39</td>
<td>0.39</td>
<td>0.40</td>
<td>-</td>
<td>0.21</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data from the Canadian Heart Health Surveys (1986-92), from Reeder <i>et al.</i> (10)

<sup>b</sup>Data from the third National Health and Examination Survey (NHANES III, 1988-94), from Zhu <i>et al.</i> (11)

The cross-sectional nature of studies 1 and 2 also limits the conclusions that can be drawn about the relationship between WC measurement site and health risk. Abdominal obesity has been implicated in the etiology of metabolic dysregulation but the temporal sequence of this relationship is not yet clear (12); it is also possible that metabolic dysregulation contributes to abdominal obesity. Study 2 was unable to examine whether one WC measurement site serves as a better predictor of incident disease or long-term health outcomes; however previous comparisons across different
studies suggests that meaningful differences are unlikely to exist (13). Furthermore, it was not possible to assess whether one measurement site is more sensitive to changes in WC as a result of weight loss. Studies that examine changes in WC across different sites in response to lifestyle interventions and weight loss would be of clinical interest.

In contrast, studies 3 and 4 were based on large, population-based surveys of the Canadian population which adds to their generalizability and is a marked strength. Furthermore, the direct measures of multiple body circumferences and their prospective design with considerable follow-up periods provide compelling evidence for the independent role of upper and lower-body circumferences in determining health risk.

The primary limitation to these studies lies in the lack of interim measures throughout the follow-up periods. Anthropometric measurements and the underlying tissues they capture are unlikely to be stable over time (14-16), therefore, the timing and degree to which any changes in anthropometric measures influenced the development of type 2 diabetes or risk of death cannot be known. The reliance on self-reported cases of diabetes as the outcome in study 3 may have resulted in the misclassification of some individuals. Since undiagnosed diabetes may represent up to one third of all cases (17), any misclassification would have likely biased the results towards non-significance and may have led to an underestimate of the strength of the association between peripheral circumferences and incident diabetes.
Finally, questions pertaining to the impact of race/ethnicity on the relationship between anthropometric markers and health risk could not be adequately addressed in the four studies included in this thesis. Clear evidence demonstrates that the relationship between abdominal fat distribution and health risk is influenced by race/ethnicity (18-22) and alternative WC thresholds have been proposed for certain populations (23). It is therefore possible that both the magnitude of WC and its relationship with cardiometabolic risk factors are differentially affected by measurement site in non-Caucasian populations. Unfortunately, this issue could not be investigated given the primarily Caucasian sample used in studies 1 and 2. Furthermore, no specific data describing race/ethnicity were collected as part of either the CFS or PALS and therefore its role in moderating the separate and combined effects of central and extremity circumferences on health risk also require further investigation. Given the truly global nature of the current obesity epidemic (24, 25) these are particularly important research questions.

7.2 Clinical Implications

The differences in the magnitude of WC achieved using different measurement protocols are widely underappreciated. Yet, this issue has clinical relevance given that the impact of relatively small measurement differences are amplified when dichotomous cut-points are used to define abdominal obesity and classify the metabolic syndrome. Indeed, the choice of measurement protocol could influence clinical decision-making in cases where WC thresholds are of critical importance to risk stratification systems such as those advocated in current clinical practice guidelines (26).
The results presented in studies 1 and 2 do not justify the selection of one measurement protocol over the others based on stronger associations with cardiometabolic risk factors or the ability to achieve more reliable measurements. However, the smallest absolute differences existed between WC measurements taken at the iliac crest and the midpoint; measurements made at these locations also offered the best compromise between sensitivity and specificity when using thresholds of \( \geq 102/88 \) cm for predicting cardiometabolic risk clustering.

Subjective accounts of the technical issues related to the measurement of WC have been noted previously (13, 27) and each measurement protocol has distinct advantages and disadvantages. In the absence of a strong scientific rationale favoring the use of one measurement site over another, the selection of any particular protocol is likely best made on the basis of its ease and acceptability to clinicians as well as patients. Yet, given that measurement protocols which rely on the identification of internal (skeletal) landmarks are less likely to change as result of weight gain or loss, the superior border of the iliac crest or the midpoint between the iliac crest and lowest rib may indeed be practically superior to the minimal waist or umbilicus.

The results of studies 3 and 4 provide compelling evidence that the measurement of extremity circumferences may offer additional means of characterizing obesity phenotypes and improving risk stratification beyond what is captured by BMI and WC. However, the clinical implications of these findings are not yet clear. While WC is a well-accepted surrogate measure of abdominal adiposity, the interpretation of
upper and lower body circumferences is complicated by the fact that these measurements may reflect variation in bone structure, muscle mass and/or subcutaneous fat. Since many anthropometric variables are highly correlated, it is difficult to establish to what degree they are measuring distinct aspects of body composition and the relative impact of these tissues on health outcomes. Further investigations are needed to discern whether predictive models for disease based on BMI and WC can be meaningfully improved with the addition of upper or lower-body circumferences and, if so, whether clinicians are willing to adopt these measurements in their assessment of obesity-related health risk.

7.3 Future Research

Central fat distribution characterized by an elevated WC was recognized as a risk factor for adverse health outcomes long before technology enabled visceral fat to be quantified or the underlying physiological mechanisms were understood (28). Therefore, continuing to unravel the interrelationships between anthropometry, body composition and disease risk stands to serve as a fruitful area for future research. Moreover, given the simplicity and cost-effectiveness of anthropometric measures, their use in discriminating obesity-related health risk may be of particular importance in settings where more sophisticated measures of body composition or cardiometabolic risk factors are not readily available or feasible.

In particular, there are three areas of future research that warrant attention:
7.3.1 Waist circumference thresholds and protocol

It is well recognized that current WC thresholds do not represent optimal thresholds for the prediction of health risk since they were not developed based on a direct relationship between WC and health risk but rather as an alternative to identifying individuals on the basis on BMI (29). These particular cut-points were developed using WC measurements taken midway between the iliac crest and lowest rib, yet the same thresholds are advocated in guidelines that promote WC measurements superior to the iliac crest (26, 30). Alternative WC thresholds have been proposed but not yet widely considered (31, 32). Given the potential influence of measurement site, technical issues relating to the measurement of WC should be a primary consideration in the development of future thresholds and will contribute to a more accurate and uniform approach to the assessment of obesity-related risk. Further research is also needed to elucidate how anthropometric measurements can most effectively be used in combination with other clinical risk assessment tools, such as the Framingham index (33).

7.3.2 Influence of race/ethnicity

It is increasingly apparent that the associations between anthropometry, body composition and health risk differ between people of varying racial/ethnic origin (19, 23, 34, 35). Examining the influence of race/ethnicity using stratified analysis and replicating studies relating anthropometry to health outcomes in diverse populations ought to be a research priority moving forward.
Specifically, the variation in WC according to measurement site may not be the same in non-Caucasian populations and the impact of potential differences for defining abdominal obesity and classifying the metabolic syndrome, particularly when race/ethnic specific WC thresholds are applied, will be of interest not only in Canada but other countries around the world.

It is perhaps even more likely that there are important differences in the effect of upper- and lower-body circumferences on health outcomes according to race/ethnicity (36-38). Comparative studies may lead to a better understanding of different obesity phenotypes and help explain observed racial/ethnic differences in obesity-related outcomes (19, 39, 40).

**7.3.3 Relative contributions of lean mass vs. fat mass**

The major limitation of anthropometry is its inability to differentiate variation in bone structure, muscle mass and fat mass. Thus, while examining the independent influence of upper- and lower-body circumferences on additional outcomes including cardiovascular events and cause-specific mortality may help in discerning the mechanisms through which larger peripheral circumferences appear to attenuate the health risk associated with a given level of BMI and WC, a more complete understanding of these relationships will require using anthropometry in conjunction with sophisticated imaging techniques to accurately differentiate specific tissues. Ultimately, emerging technology will be critical for understanding how changes in peripheral muscle mass, subcutaneous fat mass, and visceral fat interact to determine health risk. Further investigations in this area may also help to clarify differences in the relative importance
of body composition in the upper compared with lower limbs with respect to specific health outcomes.
References


8.1 Summary

The overall objective of this thesis was to evaluate the utility of various anthropometric measures for the assessment of health risk in clinical and research settings. Together, the four studies that comprise this thesis add to the descriptive epidemiology of obesity and its associated health risk and provide insight towards a better characterization of the high-risk obesity phenotype.

The first study addressed an important methodological question pertinent to the use of waist circumference (WC) in clinical and research settings by assessing the comparability of data collected using four different measurement protocols in a sample of 520 community-dwelling men and women. This investigation quantified the influence of measurement site on the magnitude and reliability of WC and highlighted the impact of measurement site on prevalence estimates of abdominal obesity. The findings indicate that the choice of measurement protocol influences the magnitude of WC measurements, particularly in women. The implications of even small differences in WC measurement are amplified when dichotomous thresholds are used to define abdominal obesity. In general, measures taken at the minimal waist resulted in the lowest prevalence, while measures from the umbilicus resulted in the highest. The least reproducible inter-observer measurements were taken at the umbilicus (ICC=0.979), the most reproducible at the minimal waist (ICC=0.989). Contrary to expectations, measures of intra- and inter-observer reproducibility were virtually identical between
measures taken at the iliac crest and mid-point despite the identification of an additional landmark required by the latter.

The second study extended these findings by examining whether variations in measurement protocol are differentially associated with cardiometabolic risk factors and the metabolic syndrome. As the first study to simultaneously compare four different WC measurement sites in the same sample, this study provided strong evidence in support of previous conclusions based on comparisons between existing studies that the association between WC and health risk does not meaningfully differ according to measurement site. Yet, despite similar associations with risk factors including blood pressure, HDL-cholesterol, triglycerides and blood glucose, the choice of measurement protocol will influence the sensitivity and specificity of WC as an indicator of cardiometabolic risk and prevalence estimates of metabolic syndrome, particularly in women. Estimates of sensitivity and specificity revealed that WC thresholds of ≥102/88 cm are most sensitive but also least specific for predicting cardiometabolic risk clustering at the umbilicus compared to other measurement sites. Measurements taken at the iliac crest or midpoint may offer a superior compromise between sensitivity and specificity than either the umbilicus or minimal waist. Consequently, WC measurement site should be an important consideration in the interpretation of WC data.

The third and fourth studies investigated the independent influences of upper- and lower-body circumferences on health risk in large, population based cohorts. Specifically, the third study used data from the Physical Activity Longitudinal Study
(PALS) to demonstrate that after adjusting for BMI and WC, larger arm, calf, and thigh circumferences offer a protective effect against incident type 2 diabetes. The fourth study confirmed the opposing influences of central and peripheral circumferences on risk of all-cause mortality among participants of the 1981 Canada Fitness Survey (CFS). After adjustment for age, smoking status, alcohol consumption, leisure-time physical activity and BMI, WC was positively associated with mortality whereas arm, thigh, and calf circumferences were significantly protective in men and arm and thigh circumferences were protective in women.

Overall, the findings confirm the utility of WC in predicting cardiometabolic risk, diabetes and mortality. However, they highlight the fact that commonly used measurement protocols cannot be considered interchangeable and consequently measurement site ought to be an important consideration in the interpretation of WC data. Efforts to standardize the anatomical location of WC measurement in clinical practice as well as research settings will facilitate the comparison of results and should be a priority in moving towards a universal approach to the assessment of cardiometabolic risk. Further improvements in risk stratification may be possible using additional anthropometric measurements such as hip, thigh, calf, and arm circumferences. However, further research is needed to discern the clinical utility of these measurements.
8.2 Conclusions

The high prevalence of obesity among Canadian adults (1) and children (2) suggests that the adverse health consequences of obesity will remain a major public health issue for the foreseeable future. With the majority of Canadians classified as overweight or obese, the accurate characterization of obesity-related health risk has particular importance for creating targeted intervention strategies and appropriately allocating health care resources. Yet, this task is complex and maximizing the utility of anthropometric measurements for the characterization of obesity-related health risk remains a challenge: many normal weight individuals demonstrate substantial cardiometabolic risk while some overweight and obese individuals appear metabolically healthy (3, 4).

Although sophisticated means of measuring body composition are likely to become more widely accessible in the future, by and large, the use of anthropometry continues to be the preferred means of assessing body composition and evaluating health risk in many clinical and population-based research settings. Collectively, the contents of this thesis help to answer important practical questions about the use and interpretation of anthropometric measurements for characterizing obesity-related health risk and provide an impetus for ongoing research to better understand the relevance of both the localization of body mass and its composition (i.e. fat and lean components) in explaining health outcomes.
References


APPENDIX A:

Ethics
Study protocols for the research involving primary data collection (Manuscripts 1 & 2) underwent expedited review and were approved by the Queen’s University Research Ethics Board on September 11th, 2006.

Studies 3 and 4 involved secondary analysis of data previously collected in government-funded studies. The official position of the Queen’s University Research Ethics Board (adopted from the Tri-Council Policy Statement on Study in Humans\textsuperscript{1} states that ethics review is not required for research that is “based entirely on publicly available information, documents, records, works, performances, or archival materials” (Article 1.1). Data from the Canada Fitness Survey and the Physical Activity Longitudinal Study were available to Dr. Katzmarzyk on a collaborative basis with co-investigators at the Canadian Fitness and Lifestyle Research Institute (Ottawa, ON). In both cases, the study protocols were subject to institutional review at the primary investigators’ university prior to study onset.

September 1, 2006

Dr. Peter T. Katzmarzyk
School of Kinesiology and Health Studies
Queen's University

Re: "Waist circumference and cardiovascular risk: Is measurement site important?"

Dear Dr. Katzmarzyk,

I am writing to acknowledge receipt of your recent ethics submission for the above-named study. I have reviewed the materials and do not feel that it is necessary for the study to undergo a full REB review. I have therefore given the study an expedited review and an approval sheet is appended for your records. I would ask that the area codes be added to the contact telephone numbers on the consent form. This study will be reported to the Research Ethics Board.

Yours sincerely,

[Signature]

Albert Clark, Ph.D.
Chair
Research Ethics Board

AFC/kr

c.c.: Ms. Caitlin Mason, School of Kinesiology and Health Studies
May 23, 2008

Dr. Peter Katzmarzyk
School of Kinesiology and Health Studies
Physical Education Centre
Queen's University

Re: "Waist circumference and cardiovascular risk: Is measurement site important?" PHE-069-06

Dear Dr. Katzmarzyk,

I am writing to acknowledge receipt of your letter dated May 14, 2008 which included the following:

- Notification that The Upper Canada District School Board is interested in having their employees participate in the study
- Notification that the School Board would like to receive a report back on the aggregate data of subjects recruited from their employee base
- Provision of a revised information/consent form to request consent from the employees to report aggregate data back to the school board

I have reviewed this amendment and the revised consent form and hereby give my approval. Receipt of this amendment will be reported to the Research Ethics Board.

Yours sincerely,

Albert Clark, Ph.D.
Chair
Research Ethics Board

AFC/kr
**Facility of Health Sciences and Affiliated Teaching Hospitals Data Sheet**

For research involving human subjects

To be completed only if the research involves the use of human subjects

Attach to Office of Research Services, Research Data Summary, and Signature Sheet

**Project Title:** Waist circumference and cardiovascular risk: Is measurement site important?

1. Human subjects will be required to participate: NO [ ] YES [ X ]

2. The protocol has been submitted for ethics review: NO [ ] YES [ X ]

3. If answer to 1 is "YES" and 2 is "NO", please explain:

4. Does this research require the participation of hospital patients? NO [ X ] YES [ ]

   Circle hospital(s) concerned: KGH HDH SMOL KPH Other (specify)

5. Will hospital facilities be required for research involving human subjects? NO [ X ] YES [ ]

   Circle hospital(s) concerned: KGH HDH SMOL KPH Other (specify)

6. Will patients be selected from department other than your department of primary affiliation?
   If yes, your signature below indicates that you have received written consent from the
   Head(s) of hospital department(s)

5. NO [ X ] YES [ ]

7. Do all research personnel having contact with patients have appropriate hospital
   Department appointments (i.e. staff, residents, departmental assistants)? NO [- ] YES [ ]

8. Will research involve the use of hospital facilities over and above those required
   for normal patient care? NO [ X ] YES [ ]

   If "YES", indicate department: Cost Costs confirmed with (name of person)

   Laboratory
   Nursing
   Pharmacy
   Radiology
   Other [please specify]
   TOTAL

   Are these costs included in the budget of the grant application? NO [- ] YES [ ]

   If not, how will they be paid for?

   [Signatures]

   Investigator: Aug 25/06
   Department Head: 25 Aug 06
   Chair, Research Ethics Board

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Queen’s University, in accordance with the “Tri-Council Policy Statement, 1998” prepared by the Medical Research Council, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada requires that research projects involving human subjects be reviewed annually to determine their acceptability on ethical grounds.

A Research Ethics Board composed of:

Dr. A.F. Clark
Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen’s University (Chair)

Dr. S. Burke
Emeritus Professor, School of Nursing, Queen’s University

Rev. T. Deline
Community Member

Dr. M. Evans
Community Member

Mr. C. Kenny
Community Member

Dr. J. Low
Emeritus Professor, Department of Obstetrics and Gynaecology, Queen’s University and Kingston General Hospital

Dr. W. Racz
Emeritus Professor, Department of Pharmacology & Toxicology, Queen’s

Dr. H. Richardson
Assistant Professor, Department of Community Health & Epidemiology Project Coordinator, NCIC CTG, Queen’s University

Dr. B. Simchison
Assistant Professor, Department of Anesthesiology, Queen’s University

Dr. A.N. Singh
WHO Professor in Psychosomatic Medicine and Psychopharmacology Professor of Psychiatry and Pharmacology Chair and Head, Division of Psychopharmacology, Queen’s University Director & Chief of Psychiatry, Academic Unit, Quinte Health Care, Belleville General Hospital

Dr. M. Sommerfeld
Physician and Assistant Professor, Department of Family Medicine, Queen’s University

Ms. K. Weisbaum
LL.B. and Adjunct Instructor, Department of Family Medicine (Bioethics)

has examined the protocol and consent form for the project entitled "Waist circumference and cardiovascular risk: Is measurement site important?" as proposed by Dr. Peter Katzmarzyk and Ms. Caitlin Mason of the School of Kinesiology and Health Studies at Queen’s University and considers it to be ethically acceptable. This approval is valid for one year. If there are any amendments or changes to the protocol affecting the subjects in this study, it is the responsibility of the principal investigator to notify the Research Ethics Board. Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information."

Chair, Research Ethics Board
Date

PHE-069-06
EX
APPENDIX B:

Study Forms
B.1  CONSENT FORM
CONSENT FORM FOR A RESEARCH STUDY
INVESTIGATING WAIST SIZE AND
CARDIOVASCULAR HEALTH

PURPOSE OF THE STUDY

You are being invited to participate in a research study that will assess whether the site at which waist circumference is measured is important in determining its relationship with various risk factors for cardiovascular disease such as high blood pressure, high cholesterol, and diabetes. It is important to identify these relationships as they will have direct implications for the use of waist circumference in clinical and research settings.

This study is being conducted by Caitlin Mason and Dr. Peter Katzmarzyk of the Department of Kinesiology and Health Studies at Queen’s University. One of the study researchers will review this consent form with you, describe the procedures in detail and answer any questions you may have. This study has been reviewed for ethical compliance by Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

PROCEDURES AND MEASUREMENTS

If you agree to participate in the study, the measurement session will last approximately 25-30 minutes. During this time you will be asked to complete a brief questionnaire about your general health. Once completed, your blood pressure will be measured by wearing an inflatable cuff around the upper left arm which will automatically inflate and then slowly deflate over a period of approximately 5 minutes. During inflation, the cuff will tighten around the arm and may be briefly uncomfortable but should not cause any pain. Next, your height, weight, and waist circumference will be measured. You will be asked to wear light clothing with no shoes for these measurements. Your waist will be measured with a plastic tape measure at four different places ranging from directly above the hip bone to below the lowest rib. Finally, a small blood sample (<1/4 teaspoon) will be taken from one fingertip using a very small spring loaded needle. This blood sample will be analyzed immediately for levels of cholesterol, blood lipids and blood sugar.

RISKS

An important part of this study is the collection of blood samples. A small volume of blood (<1/4 teaspoon) will be drawn from one fingertip using a very small spring-loaded needle. This procedure may be associated with minimal risks but could cause brief discomfort at the fingertip, bruising, or temporary light-headedness. Measurement personnel are trained to deal with any potential problems and precautions will be taken to avoid all potential difficulties.

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**BENEFITS**

From participation in this study, you will be provided with free risk screening of your blood pressure, lipid profile, and blood sugar level. You will also be provided with information about the recommended ranges for each of these measures. If your test results indicate potentially elevated risk you will be referred to your physician who can review your results in detail, conduct further testing and discuss possible treatment options if required.

**EXCLUSIONS**

In order to obtain reliable measures, you will be asked to avoid food or drink (except water) within 10-12 hours of your participation and to inform us of any prescription medications you are currently taking. You will be excluded from participating in this study if you have had food or drink within 10-12 hours of your measurement session, are not between the ages of 20 and 65 years, or if you are pregnant.

**CONFIDENTIALITY**

All information obtained during the course of the study is strictly confidential and your anonymity will be protected at all times. None of your personal data will be released to your employer or any other parties. No names will be used in the data or published work; instead, you will be identified by a subject number only.

The data will be kept in locked files that are only accessible to Dr. Katzmarzyk and his trained students and assistants. There is a possibility that your data file, including identifying information, may be inspected by officials from the Health Protection Branch in Canada in the course of carrying out regular governmental functions. The study results will be used as anonymous data for scientific publications and presentations. You will not be identified in any publication or reports.

**FREEDOM TO WITHDRAW FROM THE STUDY**

Your participation in this study is strictly voluntary. You may withdraw from this study at any time.

**PAYMENT**

You will not be compensated for your participation in this study.

**COMPENSATION FOR INJURY**

In the event that you are injured as a result of the study procedures, medical care will be provided until resolution of the medical problem. By signing this form, you do not waive
your legal rights nor release the investigator(s) from their legal and professional responsibilities.

**SUBJECT STATEMENT AND SIGNATURE SECTION**

I have read and understand the consent form for this study. I have had the purposes, procedures and technical language of this study explained to me. I have been given sufficient time to consider the above information and to seek advice if I choose to do so. I have had the opportunity to ask questions which have been answered to my satisfaction. I am voluntarily signing this form. I will receive a copy of this consent form for my information.

If at any time I have further questions, problems or adverse events, I will contact:

Jean Cote, PhD at 613-533-6601
Director, School of Kinesiology & Health Studies
Queen's University, Kingston, ON, K7L 3N6

If I have questions concerning research subject's rights, I will contact:

Dr. Albert F. Clark, Chair, at 613-533-6081
Office of Research Services
Fleming Hall, Jemmett Wing 301,
Queen's University, Kingston, ON, K7L 3N6

**By signing this consent form, I am indicating that I agree to participate in this study.**

__________________________________  ______________________________
Subject Name (Please Print)              Name of Witness (Please Print)

__________________________________  ______________________________
Permanent Address of Subject            Signature of Witness

__________________________________  ______________________________
Signature of Subject                   Date
STATEMENT OF INVESTIGATOR

I, or one of my colleagues, have carefully explained to the subject the nature of the above research studies. I certify that, to the best of my knowledge, the subject understands clearly the nature of the study and demands, benefits, and risks involved to participants in this study.

____________________________________  ______________________
Peter T. Katzmarzyk, PhD  Date

(Principal Investigator)
B.2 DEMOGRAPHIC & LIFESTYLE QUESTIONNAIRE
Instructions: Please answer the following questions as honestly and completely as possible. If you have any questions or need clarification, please ask the study investigator. All information provided will be kept strictly confidential.

Sex:  M / F

Age: __________

Birthdate: _____/_____/______

m          d           y

Height: _________ feet/inches / cm

circle one

Weight: _________ lbs / kg

circle one

People living in Canada are from many different cultural and racial backgrounds. Are you… (please mark one):

_____ White     _____ Chinese     _____ Filipino     _____ Latin American     _____ Arab

_____ Black     _____ Japanese     _____ Korean     _____ West Asian (e.g. Afghan, Iranian, etc.)

_____ South Asian (e.g. East Indian, Pakistani, Sri Lankan, etc.)

_____ Southeast Asian (e.g. Cambodian, Indonesian, Laotian, Vietnamese, etc.)

_____ Aboriginal People of North America (North American Indian, Métis, Inuit/Eskimo)

_____ Other     Please specify: ___________________________

What is the highest level of education you have completed (please mark one):

_____ less than high school diploma     _____ Undergraduate university degree (3 or 4 y)

_____ high school diploma             _____ Graduate University degree

_____ college or trade school diploma
Which of the following describes how often you smoke cigarettes? (please mark one):

- Regular smoker
- Occasional smoker
- Former smoker
- Never

Approximately how many cigarettes/day

Approximately how many cigarettes/month

How many years ago did you quit?____

How often do you usually drink alcohol? (please mark one):

- More than once a day
- 1 to 3 times a month
- 4 to 7 times a week
- Less than once a month
- 1 to 3 times a week
- I don’t drink alcohol

How many drinks (bottle of beer, glass of wine, 1 ½ oz. shot of liquor) do you usually have at a time? (please mark one):

- One
- 4 or 5
- 8 or more
- 2 or 3
- 6 or 7
- Not Applicable

During a typical 7-Day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time (write on each line the appropriate number):

a) Strenuous Exercise (heart beats rapidly)
   (e.g., running, jogging, hockey, soccer, squash, basketball, cross country skiing, judo, vigorous swimming, vigorous long distance cycling)

b) Moderate Exercise (not exhausting)
   (e.g., fast walking, baseball, tennis, bicycling, volleyball, badminton, easy swimming, dancing)

c) Mild Exercise (minimal effort)
   (e.g., easy walking, yoga, bowling, horseshoes, snow-mobiling)
During a typical 7-Day period (a week), in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

_____ often     ____ sometimes  _____ never/rarely

What is your usual level of physical activity at work?

_____ I don’t work regularly outside my home

_____ Sedentary (e.g. desk/computer work, etc)

_____ Standing (e.g. hairdresser, teacher, shop assistant, security guard)

_____ Physical work (e.g. plumber, cleaner, nurse, etc.)

_____ Heavy manual work (e.g. construction worker, bricklayer, etc.)

<table>
<thead>
<tr>
<th>Health History</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever had a heart attack?</td>
</tr>
<tr>
<td>If yes, at what age?: ____________</td>
</tr>
<tr>
<td>Have you ever had a stroke?</td>
</tr>
<tr>
<td>If yes, at what age?: ____________</td>
</tr>
<tr>
<td>Have you been diagnosed with diabetes?</td>
</tr>
<tr>
<td>If yes, at what age? ____________</td>
</tr>
<tr>
<td>Have you been diagnosed with high blood pressure or hypertension?</td>
</tr>
<tr>
<td>If yes, at what age? ____________</td>
</tr>
<tr>
<td>Have you been diagnosed with cancer?</td>
</tr>
<tr>
<td>If yes, at what age? ____________</td>
</tr>
<tr>
<td>If yes, what type: ______________________</td>
</tr>
</tbody>
</table>
Have any members of your direct family (mother, father, sibling) suffered from:

i) A heart attack?       YES   NO
   If yes, approximate age: ______________________

ii) A stroke?            YES   NO
   If yes, approximate age: ______________________

iii) Diabetes?           YES   NO

iv) Cancer?              YES   NO
   If yes, what type: ______________________

Are you currently taking any prescribed medications for…

High Blood Pressure?    YES   NO
High Cholesterol?       YES   NO
High Blood Sugar?       YES   NO

Please list all prescription medications you are currently taking (use back of page if necessary):

________________________________   _______________________________

________________________________   _______________________________

________________________________   _______________________________

________________________________   _______________________________

________________________________   _______________________________
If you would like to be informed of the final results of this study, please complete your contact information below. This information will not be used for any other purpose.

<table>
<thead>
<tr>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
</tr>
<tr>
<td>Street Address:</td>
</tr>
<tr>
<td>City:</td>
</tr>
<tr>
<td>Home phone:</td>
</tr>
<tr>
<td>e-mail:</td>
</tr>
</tbody>
</table>
B.3 DATA RECORDING SHEET
<table>
<thead>
<tr>
<th>SUBJECT ID#:</th>
<th>VISIT: 1 2</th>
</tr>
</thead>
</table>

**BLOOD PRESSURE**

Systolic: ___________  Diastolic: ___________

**ANTHROPOMETRIC MEASUREMENTS**

Height (cm): ______________  Weight (kg): ______________

Narrowest Waist (cm) ________________ ________________ ________________

Umbilicus (cm) ________________ ________________ ________________

Iliac Crest (cm) ________________ ________________ ________________

Midpoint (cm) ________________ ________________ ________________

Hip (cm) ________________ ________________ ________________

**BLOOD ANALYSIS**

Total Cholesterol _____________  Triglycerides _____________

HDL-C ________________  TC/HDL Ratio ________________

LDL-C ________________  Fasting Glucose ________________

NonHDL-C ________________
B.4 PARTICIPANT SUMMARY SHEET
Name: ______________________________

Blood pressure: __________________
Waist Circumference:______________

Date:___________________________

What do these measures indicate?

**Blood Pressure** measures how hard your heart has to work to circulate blood throughout your body by measuring how hard blood is pushing on blood vessel walls. The top number represents the pressure when the heart contracts, the bottom when the heart relaxes between beats. High blood pressure is a risk factor for other cardiovascular diseases. Factors that can raise blood pressure include stress, dietary salt, obesity and physical inactivity.

**Waist Circumference** measures the degree of excess accumulation of fat in the abdominal region which is associated with increased risk of heart disease, stroke and type II diabetes. Waist circumference can usually be decreased by physical activity and weight loss.

**Total Cholesterol** is a measure of the circulating fat in your bloodstream, and includes the total amount of both “good” and “bad” cholesterol in your blood at a given time.

**High Density (HDL) Cholesterol** is known as the “good” cholesterol. A higher level of HDL lowers your risk for cardiovascular disease. Avoiding cigarette smoking, maintaining a healthy body weight and being physically active will help maximize your level of HDL.

**Low Density (LDL) Cholesterol** is known as the “bad” cholesterol because it contributes to the buildup of fat deposits in your blood vessels over time (atherosclerosis) which can cause decreased blood flow and heart attacks. LDL cholesterol can be reduced with a low fat diet, weight loss, and medication.

**Triglycerides** circulate in your blood like cholesterol, but are stored in body fat and used when the body needs extra energy. Triglycerides can be significantly affected by how recently you’ve eaten, but will decrease naturally if your body is processing the fat efficiently.

**TC/HDL ratio** is the total cholesterol divided by HDL cholesterol. A lower ratio represents lower risk.

**Fasting glucose** is a measure of the sugar level in the blood. Consistently high levels (hyperglycemia) can be an indication of diabetes. Blood sugar can be reduced by a careful diet, physical activity, maintaining a healthy body weight, and medications when necessary.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Desirable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>&lt;135/85</td>
</tr>
<tr>
<td>Total Cholesterol (TC)</td>
<td>&lt; 5.2 mmol/L</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>&gt; 1.0 mmol/L (men)</td>
</tr>
<tr>
<td></td>
<td>&gt; 1.2 mmol/L (women)</td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>&lt; 3.5 mmol/L</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt; 1.7 mmol/L</td>
</tr>
<tr>
<td>TC/HDL Ratio</td>
<td>&lt; 4.5</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>&lt; 6.1 mmol/L</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>&lt;88 cm (women)</td>
</tr>
<tr>
<td></td>
<td>&lt;102 cm (men)</td>
</tr>
</tbody>
</table>

If one or more of your test results is outside of the desirable range or you are concerned about your results, please contact your family physician who can review them in detail with you.
APPENDIX C:

Equipment
C.1 CHOLESTECH LDX
**Cholestech LDX**

The Cholestech LDX Lipid Profile Analyzer (Cholestech Corporation, Hayward, CA) was used to measure lipids and glucose for the purpose of studies 1 and 2. This portable analyzer system was ideally suited to the purposes of these studies because of its capability to provide rapid results (approximately 5 minutes) from small volume samples obtained from a fingerstick. The LDX can analyze whole blood, serum, or plasma samples and can analyze total cholesterol, HDL-cholesterol, triglycerides and glucose separately or in combination. It has been certified by the Cholesterol Reference Method Laboratory Network (CRMLN), which validates that the system meets the gold standards for accuracy and reproducibility developed by the Centers for Disease Control and Prevention (CDC) for the measurement of total and HDL cholesterol, consistent with the National Cholesterol Education Program (NCEP) analytic goals. Several previous studies have confirmed the reliability of the Cholestech LDX System in comparison with standard laboratory values (1-4) and its use has been documented in numerous peer-reviewed research studies (5-8).
References


CHOLESTEROL REFERENCE METHOD LABORATORY NETWORK

Certificate of Traceability

This certifies that

Cholestech Corporation
Hayward, California

has documented traceability to the National Reference System for Cholesterol by performing a direct comparison with the cholesterol reference method using fresh human specimens which cover the National Cholesterol Education Program medical decision points. This analytical system is representative of the manufacturer’s product and has demonstrated the ability to meet the NCEP’s performance criteria for accuracy and precision. The comparison shows that the performance of this analytical system is as follows:

<table>
<thead>
<tr>
<th>Among-run</th>
<th>Average</th>
<th>%Total Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>%CV</td>
<td>%Bias</td>
<td></td>
</tr>
<tr>
<td>2.0%</td>
<td>0.1%</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

The comparison was performed with

Northwest Lipid Metabolism and Diabetes Research Laboratories
Seattle, Washington

The system evaluated was:

Instrument:
Cholestech LDX® System

Calibrator:
Streck Serum Calibrators
Lot #: 6278
Set Points: 116, 206, 296, 376, 451 mg/dL

Matrix:
Whole Blood

Cholesterol reagent:
Cholestech Lipid Profile
Lot #: C086782

Date of evaluation: May 29, 2007

Date of expiration: May 29, 2009

CRMLN Laboratory Director

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Cholestech LDX Operation

Introduction

Cholestech LDX is a clinical laboratory system designed for rapid and accurate quantitation of lipid and lipoprotein levels. The system consists of an instrument, a software application, and a suite of reagents and materials. This manual provides instructions on how to operate the Cholestech LDX system.

System Components

The Cholestech LDX system includes a instrument, a software application, and a suite of reagents and materials. The instrument is a compact, modular device that can be configured to meet the needs of a variety of clinical laboratories.

Quick Reference Guide

Cholestech LDX Operation Manual

Setup

1. Connecting the Cholestech LDX to the Power Source
2. Configurability Menu
3. Startup Check
4. Imaging Test
5. Quality Control
6. Result Review
7. Submission of Results
8. FAQ

Test Procedure

1. Operator Overview
2. Perform Fingerprinting
3. Collect the Sample
4. Dispense the Sample
5. Insert the Cassette
6. Begin the Test
7. View the Results
8. Print the Results

FAQ

1. Frequently asked questions about the use of the Cholestech LDX
2. How do I get the Certificate of Waiver?
3. How often should the instrument be validated?
4. How often should the instrument be calibrated?
5. How often should the instrument be cleaned?
6. How often should the instrument be maintained?
7. How often should the instrument be serviced?
8. How often should the instrument be upgraded?

How often should the instrument be validated?

The Cholestech LDX system is designed to be self-contained and requires no external validation procedures. However, it should be validated at least once per year or as required by local regulations. The validation process should be performed by a qualified technician.

How often should the instrument be calibrated?

The Cholestech LDX system is designed to be self-contained and requires no external calibration procedures. However, it should be calibrated at least once per year or as required by local regulations. The calibration process should be performed by a qualified technician.

How often should the instrument be cleaned?

The Cholestech LDX system is designed to be self-contained and requires no external cleaning procedures. However, it should be cleaned at least once per week or as required by local regulations. The cleaning process should be performed by a qualified technician.

How often should the instrument be maintained?

The Cholestech LDX system is designed to be self-contained and requires no external maintenance procedures. However, it should be maintained at least once per month or as required by local regulations. The maintenance process should be performed by a qualified technician.
C.2 BpTRU
The blood pressure measurements for studies 1 and 2 were taken using a BpTRU model BPM-100 (VSM MedTech Ltd., Vancouver, BC, Canada). The BpTRU-100 has been independently validated (1, 2) and has passed the standards of the British Hypertension Society and the Association of Advancement of Medical Technology (2-4). This automated non-invasive blood pressure monitor performs up to six measurements; the interval of the readings can be varied from 1 to 5 minutes depending on user preference. The device is designed to have the first measurement taken with the observer present to ensure the correct positioning of the cuff and proper functioning of the recorder. The first reading is then discarded and subsequent readings are taken while the patient is resting quietly alone. For the purposes of studies 1 and 2, six measurements were taken, with a one minute interval between each cuff inflation. The mean of the final five measurements was used in all analyses.

Because the BpTRU can be used without an operator present, it can significantly reduce the white coat effect and observer bias frequently seen with the use of manual measurements. Its measurements have been shown to correlate significantly better than manual measurements with 24-hour ambulatory blood pressure, which is the gold standard for predicting risk of future cardiovascular events (5). Furthermore, its measurements offer strong agreement with a trained hypertension nurse specialist when used for clinical decision-making (6).
References


APPENDIX D:

Data Sources
D.1 CANADA FITNESS SURVEY
1981 CANADA FITNESS SURVEY (CFS)

Background

The 1981 Canada Fitness Survey (CFS) was a household survey conducted by Statistics Canada for Fitness and Amateur Sport, Health and Welfare Canada. The CFS was the first nationally representative study of the physical recreation habits, physical fitness, and health status of the Canadian population.

Sample

A total of 23,400 people between the ages of 7 and 97 y participated in the survey. Approximately 3% of the total population was excluded, including Aboriginal people living on reserves, students living in school dormitories, armed forces personnel living on bases, and residents of the Territories and remote areas.

Study Design

A stratified, multi-stage, cluster sample was selected from geographically compact areas. Within each province, major city, urban and rural strata were formed. A random selection of smaller segments within the strata was followed by a systematic sample of households from each segment. Members of each household were interviewed and asked to complete a questionnaire, and to participate in a series of fitness tests known as the Canadian Standardized Test of Fitness (1).
Follow-Up

*Campbell’s Survey of Well-Being (1988)*

In 1988, a place- and participant based subsample of 20% of the CFS participants from 61 of the original 80 geographical areas was selected to participate in the Campbell’s Survey of Well-Being. During household visits, approximately 4,000 respondents filled out a questionnaire and completed the Canadian Standardized Test of Fitness. The majority of the 4,000 respondents in the 1988 survey participated in both the 1981 and the 1988 studies, making the 1988 Campbell Survey on Well-Being (CSWB) the first national longitudinal survey of physical activity in Canada.

*Mortality*

CFS participants have been followed for mortality by linkage with the Canadian Mortality Database (CMDB) through the end of 1994. The CMDB contains all recorded deaths in Canada since 1950, and is regularly updated using death registrations supplied by every province and territory. Record linkage between the CFS database and the CMDB was performed using computerized probabilistic techniques, and the potential for death linkages to be missed using this method is quite small (2, 3).
References


D.2 PHYSICAL ACTIVITY LONGITUDINAL STUDY
PHYSICAL ACTIVITY LONGITUDINAL STUDY (PALS)

Background

The Physical Activity Longitudinal Study (PALS) is a 20-year follow-up of the 1981 Canada Fitness Survey (CFS), designed to investigate physical activity involvement among Canadians, as well as the relevant social and environmental supports for physical activity participation.

Study Design

Subjects

Individuals who participated in either the 1981 CFS or the 1988 Campbell’s Survey of Well-Being (CSWB) and their offspring were eligible to participate in the PALS. Tracing the cohort was a multi-step process. The first step confirmed names and addresses of a family member or contact person provided in 1988 using Internet resources. Interviewers telephoned potential participants to gather additional information to locate other family members. If necessary, more extensive search methods were used. Of the approximately 4900 eligible participants, 10% were lost to follow-up and 19.8% refused to participate. Individuals who could not be traced are currently being linked with Statistics Canada’s Vital Statistics data to confirm possible mortality outcomes.
Measures

All individual-level data were collected by self-administered questionnaire between September 2002 and April 2004, using comparable methods to the CFS and CSWB. Topics included: physical activity; other lifestyle behaviours (smoking, alcohol use, fruit and vegetable consumption); height and weight; health status and chronic disease; depression; health care utilization; perceived neighbourhood trust and social capital; and demographics.

PALS was approved by the Faculty of Medicine’s Ethics Review Board of the University of Montreal. Informed written consent was obtained from all participants.

Related publication: