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Waist circumference and risk of cardiovascular disease, type 2 diabetes and mortality among Aboriginal adults in an Australian community.

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Abstract

Introduction

Chronic diseases such as cardiovascular disease (CVD) and diabetes are the greatest contributors to the rapidly increasing public health burden worldwide. About two thirds of mortality reported globally was attributed to chronic diseases, to which these two conditions contribute significantly, and the disadvantaged are mostly affected, dying prematurely. Accelerating rates of deaths from chronic diseases have been reported in developing countries and poorer population groups in developed countries. This situation relates to the Aboriginal people of Australia, who suffer about two and half times greater burden of disease than the general Australian population with chronic diseases accounting for 70% of the health gap, to which CVD and diabetes are chief contributors. It is widely documented and accepted that elevated waist circumference (WC), causes, or aggravates a number of medical conditions, and is also associated with reduced life-expectancy. Aboriginal people have experienced higher and rising rates of diabetes and related outcomes such as CVD and kidney disease. And while WC has been linked to increased risk of CVD and Type 2 diabetes in the Aboriginal population, cut-off points which are often used for defining central obesity for population screening and health promotion are not available for Australian Aboriginal people.

This thesis has four objectives:

1. Assess the relationship WC has with morbidity outcomes (CVD and Type 2 diabetes) and all-cause mortality in a remote Aboriginal Australian community
2. Determine which of WC, body mass index (BMI) and waist-to-hip ratio (WHR) has the strongest association with CVD and Type 2 diabetes; and which of WC and BMI had stronger association with all-cause mortality
3. Provide estimates of gender-specific absolute risks of CVD and Type 2 diabetes for specific WC and age values and
4. Generate gender-specific WC values derived from equivalent BMI points with same absolute risks of CVD and Type 2 diabetes.

Methods

Three datasets collected from Aboriginal people in the Tiwi Islands in the Northern Territory of Australia were utilized:

1. Baseline dataset: collected at a community screening program from 1992 to 1998, including 976 adult participants.
2. Hospitalization dataset: consisting of Northern territory hospital records of participants from 1992 to 2012.
3. Mortality dataset: collected from 1992 to 2010 from death registry records.

Eligible participants for the studies in this thesis were adults (18 years and over), who had WC measures and were free of the outcome of interest at baseline screening. Survival analysis was conducted in all the studies, which included eligible participants being followed up prospectively for up to 20 years from the baseline screening measurement until the occurrence of the end point of interest for each participant as recorded on the hospitalization and/or mortality datasets. Statistical methods used include: Cox proportional hazards regression model to test the associations of WC with the risk of CVD, Type 2 diabetes and all-cause mortality; and Weibull accelerated failure-time model to provide absolute risk estimates of CVD and Type 2 diabetes using WC values.

Results

Objective 1: WC was statistically significantly associated with CVD and Type 2 diabetes in crude and multivariable analyses. Association of WC with all-cause mortality was statistically significant in the crude analysis and in multivariable analysis after adjusting for BMI and other covariates. There was no statistically significant difference between the genders in the association between WC and any study outcome.

Objective 2: Waist circumference compared to BMI or WHR had the strongest association with CVD in females; and with Type 2 diabetes in both males and females. WC had stronger associations than BMI with all-cause mortality.

Objective 3: Absolute risk of CVD and Type 2 diabetes increased as WC and age increased for males and females.

Objective 4: For CVD, coronary artery disease (CAD) and heart failure (HF), WC equivalent to overweight BMI (>=25 kg/m^2) ranged from 91 to 93 cm; and obesity BMI (>=30 kg/m^2) ranged from 99 to 103 cm for males and females. The derived WC for equivalent overweight (BMI of 25 kg/m^2) were 91.5 for males and 90.9 cm for females; and for obesity (BMI of 30 kg/m^2), equivalent WC were 105.7 cm and 102.3 cm for males and females respectively for Type 2 diabetes.

Conclusions

The findings of this thesis show that WC was associated with CVD, Type 2 diabetes and all-cause mortality. The absolute risks of CVD and Type 2 diabetes increased as WC and age increased. Despite their high WC averages, females were not different from males in their risk of disease or death in relation to WC. The absolute risk findings are useful in creating awareness and educating the Aboriginal people in the study community on the risk associated with elevated WC and CVD and Type 2 diabetes. Future studies should examine the risks in other Aboriginal populations to further contribute to guidelines required for the recommendation of WC cut-off points for Aboriginal people in Australia.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

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Publications during candidature

Peer-reviewed papers

1. **Adegbija O.O** and Wang Z. Gender variations in waist circumference levels between Aboriginal and non-Aboriginal Australian populations: A systematic review**.** *Obesity Research and Clinical Practice* (2014); 8(6), e513- e524.
2. **Adegbija O**, Hoy W, Wang Z. Prediction of cardiovascular disease risk using waist circumference among Aboriginals in a remote Australian community. *BMC Public Health Journal* (2015); 15(1):57.
3. **Adegbija O**, Hoy W, Wang Z. Predicting absolute risk of Type 2 diabetes using age and waist circumference values in an Aboriginal Australian community. *PLOS ONE* (2015); 10(4), e0123788.
4. **Adegbija O**, Hoy WE, Dong B, Wang Z. Body mass index and waist circumference as predictors of all-cause mortality in an Aboriginal Australian community. *Obesity Research & Clinical Practice* (2016); Doi: 10.1016/j.orcp.2016.06.003.
5. **Adegbija O**, Hoy WE, Wang Z. Waist circumference values equivalent to body mass index points for predicting absolute cardiovascular disease risks among adults in an Aboriginal community: a prospective cohort study. *BMJ Open* (2015); 5:e009185. doi:10.1136/bmjopen-2015-009185.
6. **Adegbija O**, Hoy WE, Wang Z. Corresponding waist circumference and body mass index values based on 10-year absolute Type 2 diabetes risk in an Australian Aboriginal community. *BMJ Open Diabetes Research and Care* (2015); 3:e000127. doi:10.1136/bmjdrc-2015-000127.

Seminar presentation

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Keywords

waist circumference, body mass index, cardiovascular disease, type 2 diabetes, mortality, absolute risk, aboriginals.

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Table of Contents

List of Figures

List of Tables

List of Abbreviations

AIHW	Australian Institute of Health and Welfare
AR	Absolute risk
BMI	Body mass index
CAD	Coronary artery disease
Cm	Centimetres
CI	Confidence intervals
CRP	C-reactive protein
CVD	Cardiovascular diseases
EuroSCORE	European system for cardiac operative risk evaluation
HF	Heart failure
HR	Hazard ratio
Kg	Kilogram
M	Metre
NT	Northern Territory
PROCAM	Prospective Cardiovascular Muster
ROC	Receivers operating curve
SD	Standard deviation
SCORE	Systematic Coronary Risk Evaluation
T2D	Type 2 diabetes
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio

CHAPTER 1
INTRODUCTION

1.1 CHAPTER OVERVIEW

In this chapter, a general introduction of the burden of chronic illnesses in the Aboriginal Australian population is presented, with emphasis on cardiovascular diseases (CVD) and Type 2 diabetes. Next, there is a brief discussion on the importance of the use of waist circumference (WC) in identifying risk of diseases, and the heterogeneity of WC in the Aboriginal group which vary in different communities. Finally, the aims and objectives of the thesis are discussed, and an overview of the thesis structure as well as the description of the methods used was presented.

Background

The Aboriginal people of Australia, also referred to as Aborigines, are people who identify themselves as Indigenous to the Australian continent. Over time, numerous evidence has emerged of Indigenous Australians (Aboriginal people and Torres Strait Islanders) being at a disadvantage in the Australian population, which extends to issues concerning their health and wellbeing (1, 2). Specifically, Australian Aboriginal people have significantly poorer health and have a lower life expectancy, dying at younger ages than non-Aboriginals. From 2010 to 2012, there was reported 10.6 and 9.5 years decrease in life expectancy of Aboriginal males and females respectively (3). In Australia, chronic diseases are the main cause of morbidity and mortality, accounting for 90% of all deaths in 2011 (4). Also, there is a disproportionate distribution in risk of chronic diseases in Australia with Aboriginal people being affected most, and also at much younger ages (5). Chronic illnesses contribute to two-thirds of the gap in life expectancy between Aboriginal people and non-Aboriginals (6). Obesity-related chronic illnesses such as CVD and Type 2 diabetes are significant contributors to the burden of ill health in Australia. Risk factors that contribute to these two obesity-related conditions are mostly excess body weight (obesity and central/abdominal obesity), behavioural/lifestyle (poor nutrition, physical inactivity, smoking and excessive alcohol consumption), biomedical (excess body weight, high blood pressure and cholesterol, and impaired glucose tolerance), environmental, genetic/ family history of disease and demographic factors (7).

In the Aboriginal population, abdominal obesity measured by waist circumference (WC) has been linked to increased risk of developing CVD and Type 2 diabetes (8-10). Moreover, some studies have reported WC as a better predictor of CVD and Type 2 diabetes in comparison to other

anthropometric measurements such as body mass index (BMI), waist-to-hip ratio (WHR), hip circumference and weight (8, 9). The importance of WC in health assessment in relation to chronic illness prevention for Aboriginal people is well recognized in the current Australian guidelines and policies such as the National guide to preventive health evaluation in Aboriginal and Torres Strait Islander peoples by National Aboriginal Community Controlled Health Organisation (NACCHO). However, there is a lack of WC cut-off points for identifying high risk Aboriginal individuals. The currently recommended WC cut-off points of 94 and 102 cm for men and 80 and 88 cm for women derived from BMI of 25 kg/m^2 and 30 kg/m^2 respectively, mostly used by Australian non-Aboriginals, have been suggested as unsuitable for Aboriginal people due to differences in body habitus profiles (11). Aboriginal females have been reported as having significantly higher WC measures compared to Aboriginal males and non-Aboriginal females (12). Furthermore, significant variations in WC profiles have been documented in different Aboriginal communities which signal a need for caution when generalising body composition in this heterogeneous Australian group (12). More often than not, the method that optimises sensitivity and specificity is employed to generate WC cut-off values in epidemiological studies. However, this method may over-simplify the complexity for defining WC cut-off values, as optimal cut-offs vary substantially across populations, with variations mainly driven by the population WC mean levels (13). Therefore, in relation to the substantial differences in WC mean values in diverse Aboriginal communities (subpopulations), a consensus might not be reached with the application of the currently used optimising method as optimal WC cut-off values will vary across different communities. There have been suggestions for future research to focus more on searching and applying alternative methods (13).

1.2 RESEARCH AIMS AND OBJECTIVES

This thesis focused on one remote homogenous Aboriginal community and aimed to use the absolute risk method to provide epidemiological evidence of the importance of WC in association with CVD and Type 2 diabetes to contribute to the information needed for the development of WC cut-off points for Aboriginal people in Australia. As high WC has been associated with these two conditions in the Aboriginal population (8-10), identifying the level of risk of high WC on these two related chronic disease and mortality outcomes is potentially useful for planning effective health policy in the context of chronic disease associated burden on the health of Aboriginal people in the community. Also, as the current trend of maximising sensitivity and specificity to determine cut-off values may over-simplify the complexity for defining WC cut-off points, the absolute risk method was used in this thesis to generate the level of risk of CVD and Type 2 diabetes at different

WC points. Also provided, were derived WC values with equivalent absolute risk of CVD and Type 2 diabetes to BMI points, providing some evidence required for the establishment of WC cut-off points in the Aboriginal population.

More specifically, the research objectives for the thesis are as follows:

1. Assess the relationship between WC and disease outcomes (CVD and Type 2 diabetes) as well as all-cause mortality in a remote Aboriginal Australian community
2. Determine which of WC, BMI and WHR has the strongest association with each of the CVD and Type 2 diabetes in the Aboriginal community; and which of WC and BMI had stronger association with all-cause mortality
3. Provide estimates of gender-specific absolute risks of CVD and Type 2 diabetes for specific WC values and
4. Provide WC values corresponding to equivalent BMI values with same absolute risks of diseases (CVD and Type 2 diabetes) for both males and females.

1.3 OVERVIEW OF THESIS STRUCTURE AND DESCRIPTION OF METHODS USED

The thesis comprised of ten chapters, and incorporates six individual research studies. A brief contextual introduction prior to each study has been added to integrate them into the thesis document.

Chapter 2 provides a literature review on anthropometric indices (BMI, WC, and WHR) and the epidemiology of CVD, Type 2 diabetes and mortality with further focus on Aboriginal people. Also, there was discussion on some underlying biological mechanisms of WC associated with CVD and Type 2 diabetes. Lastly, this chapter provides a comprehensive description of the absolute risk method used in the study chapters.

Chapter 3 is an extension of the literature review and presented as a systematic review conducted to assess the level of heterogeneity of WC levels in various Aboriginal and non-Aboriginal population studies while examining the differences between males and females WC. Furthermore, this chapter examined if the gender differences found in these two Australian populations could be explained by their height and weight.

Chapter 4 describes the methods, and provides details of the datasets and study sample used in the current research.

Chapters 5 to 7 are research studies that used the prospective cohort study design with a maximum of 20-year follow-up to assess associations of WC with CVD, Type 2 diabetes and deaths among adult participants in the study community. The Cox proportional-hazards regression was used in the analysis. In addition to the results derived in chapters 5 and 6, further calculations using the Weibull accelerated failure-time model were carried out to generate the absolute risks of each of CVD and Type 2 diabetes according to WC and age values to show changes in the risk of disease outcomes with changes in WC and increasing age.

In chapters 8 and 9, all individuals with baseline WC and BMI measurements were followed up for up to 20 years. Using the Weibull accelerated failure-time model, WC points with equivalent absolute risks to various BMI values were generated for CVD and Type 2 diabetes.

Chapter 10 summarises the entire thesis, and discusses the implications of the findings from the research studies. In conclusion, possible directions for future research in Aboriginal populations and the thesis's contribution to Aboriginal health were discussed.

CHAPTER 2
BACKGROUND AND LITERATURE REVIEW

This chapter describes in Section 2.1, the relevant historical background theory and research that provides the justification for this Doctorate. Sections 2.2 and 2.3 cover the epidemiology of chronic diseases such as cardiovascular disease (CVD) and Type 2 diabetes from the descriptive epidemiology to the aetiology through to the management and treatment). Section 2.4 describes the risk factors and burden of mortality in Australia, with emphasis on Aboriginal people. Section 2.5 reviews obesity and central obesity with more focus on waist circumference (WC) and this was followed by discussion on some underlying biological mechanisms of WC associated with CVD and diabetes. Next, the lack of WC cut-off points for Aboriginal Australians was discussed. Finally, section 2.6 describes the absolute risk method used to present the results in this thesis.

2.1 HISTORICAL BACKGROUND

The history of Aboriginal people, the first settlers in Australia, was believed to have spanned from 40,000 to 80,000 years before European settlement. Prior to colonization by Europeans, Aboriginal people lived as nomads, hunter-gatherers and fishermen (14). There was not much reported on the burden of chronic illnesses and infections among them until post-colonization. The colonization of Australia in the 18th and 19th century introduced changes in diet, housing and lifestyle which replaced the primitive traditions of strenuous but healthy living of Aboriginal people (15). The effect of colonization was and is profound as reflected in their lack of wellbeing which took dominance over their previous wellness. According to Colquhoun and Dockery (2012), "the wellbeing of Indigenous people is enhanced when they maintain their 'traditional' culture" (16). The embrace of this different lifestyle, and particularly with the readily available energy-dense food and more sedentary living, which results in more weight gain, have increased the trends and risk of developing long-term chronic illnesses and premature deaths over the last few decades.

Weight gained due to lifestyle and behavioural factors leads to excess fat in the human body, and escalates the risk of disease conditions. As human body fat continues to be extensively researched, there has been much focus on the measurement indices and methods of measurement. Anthropometric measurements have been used to estimate body composition, in order to investigate individual or population's growth, development and nutritional status (17). Body mass index (BMI), which measures overall general body fat, and indices such as WC and waist-to-hip ratio (WHR) that

measure regional body fat (in this case, abdominal fat), are mostly used to measure body adiposity. Obesity (BMI≥30 kg/m^2) and abdominal obesity (WC>=102 and 88 cm mostly used in men and women of European descent) have been considered over time to have deleterious consequences as a result of the high energy food intake and low levels of physical activities (18). There have been evidence indicating that WC coupled with BMI predicts obesity-related health risk better than does BMI alone (19, 20). Professor Jean Vague, in 1947, was the first to identify the effect that regional distribution of body fat had on the risk of metabolic abnormalities as compared to excessive general fat (21). Epidemiological studies in the early 1980s also confirmed the link between elevated WC and increased chronic disease morbidity and mortality rates (22, 23). Aetiological associations between excessive abdominal fat and the development of chronic diseases, such as CVD and Type 2 diabetes, have been well established. More recently, among Aboriginal people in Australia, abdominal obesity measured by WC has been implicated as a risk factor, showing stronger associations than BMI with CVD and Type 2 diabetes (8, 9).

2.2 CARDIOVASCULAR DISEASE (CVD)

CVD, a condition that develops over time, is a collective term for disorders of the heart (cardio) and blood vessels (veins and arteries). Generally, CVDs include coronary heart disease (ischemic heart disease), cerebrovascular disease (stroke), heart failure and other vascular diseases (24). CVD can also result in severe disability, particularly among those who survive a myocardial infarction or stroke, and can also lead to death (25). Coronary artery disease is the most common form of CVD in Australia, manifesting as acute myocardial infarction and angina (26). The common underlying problem of coronary artery disease is atherosclerosis, which causes a fatty substance called plaque to build up in the walls of the arteries, causing thickening and loss of elasticity (26).

2.2.1 Risk factors for CVD

In addition to the non-modifiable risk factors which include age, genetics and family history of CVD, researchers have identified a range of modifiable CVD risk factors such as unhealthy diet, physical inactivity, smoking and excessive alcohol consumption. Those modifiable risk factors increase the risk of biomedical determinants- overweight and obesity which includes central/abdominal obesity, high blood pressure, high blood cholesterol and diabetes which in turn heightens the risk of developing CVD and its complications (27). About 70% of the burden of CVD

is related to these modifiable risk factors (28). Physical inactivity, high-energy packed diets and high prevalence of tobacco use are common among Aboriginal people (29).

Risk factors due to poor beginnings such as intrauterine growth restriction (IUGR) and prematurity, and their causes, which include lack of essential nutrients, toxins, maternal smoking and alcohol consumption and stress, have been identified as contributors to early CVD in adulthood (30). In addition to this, there is also strong evidence of an association between low birth weight and CVD (31). Women with history of preeclampsia and pregnancy complicated by IUGR have been known to have an increased risk of CVD in later life (32, 33). Another factor is high density micronutrient deficient diet, which has been shown to increase the likelihood of obesity and linked to higher risk of CVD (34). Ongoing inflammation or infection throughout the life course also contributes to the risk of developing CVD. The role of C-reactive protein (CRP), a marker for inflammation has been documented in the cardiovascular disease process (35, 36). CVD markers such as hypertension and high cholesterol are silent and build up over a time period. Other symptoms are more noticeable and include signs of a heart attack or stroke, for example: discomfort or pain in the centre of the chest; discomfort or pain in the arms, left shoulder, elbows, jaw or back (27). In addition symptoms may include irregular heartbeat, dizziness, weakness, nausea, vomiting, numbness, fatigue and shortness of breath.

2.2.2 Management and treatment of CVD

There are a number of ways of managing and treating CVD. The most common types of obesity-related CVD include coronary artery disease and heart attack. One important aspect of obesity-related CVD management is lifestyle changes (physical activity, healthy diet, reduction of salt in diet, and smoking cessation and maintenance of a healthy weight). With the management of lifestyle and behavioural determinants, risk factors such as blood pressure and cholesterol are better controlled (37). Implementation of interventions targeting modification of lifestyle and behavioural factors with focus at the population level, more importantly with emphasis on different ethnic groups, can be beneficial in reducing CVD risk. Likewise at the individual level, preventing obesity-related CVD using health-care interventions will produce great results if focus is more on individuals at high CVD risk or those with risk factors above the conventional thresholds, such as hypertension and hypercholesterolemia (27).

Established guidelines on absolute CVD risk showing the likelihood of an individual experiencing a CVD event within the next 5 years are used to provide guidance in the management of CVD in Australia. These guidelines target among others, adult Aboriginals, aged 35 years and above (38). A number of risk factors including WC are incorporated in the guidelines. However, while the

guidelines considered WC thresholds of Asians, there was no focused consideration for WC thresholds for Aboriginal people.

2.2.3 Burden of cardiovascular disease in Australia

Cardiovascular disease is the major cause of death and disability globally, with an estimated 17.5 million deaths from CVD in 2012, which represents about 31% of all deaths worldwide (39). In Australia, CVD is the leading cause of death; it accounted for nearly 44,000 deaths in 2013 (40), and remains a significant burden on the country's health system, contributing immensely to rising health care costs (40, 41). An estimated 3.7 million Australian adults had one or more CVD according to a 2011/12 report (42). While the prevalence of the disease is similar for men and women, the older age group (>64 years) are at higher risk than those <54 years (42). In 2012, three in ten mortality outcomes were due to CVD (43). The level and impact of the burden of CVD is substantially higher among Aboriginal people than in non-Aboriginals in Australia. CVD is the leading cause of premature and overall deaths for Aboriginal people, as it is for non-Aboriginals in Australia (44, 45). In 2012-2013, 1 in 8 (13%) Aboriginals reported having a form of CVD (46). Of these, 4% were attributed to heart disease, stroke and vascular diseases (46, 47). Aboriginal people are among those with the highest hospitalizations resulting from CVD in Australia (40). Heart-related conditions are 1.2 times more common among Aboriginals than non-Aboriginals (48). Furthermore, the heart attack rates in adults are about 2.6 times as high in Aboriginal people compared to non-Aboriginals (49). There are excess CVD deaths in every age group and across all jurisdictions where reliable data are available (50). The rate of death from CVD is particularly high among young and middle aged Aboriginal adults (28, 44) compared to non-Aboriginals; and in 2009-2010, death rates in five Australian regions for all coronary artery disease were 7 to 13 times higher among Aboriginal people in the 25-39 and 40-54 years age groups than the rates for non-Aboriginals (51). From the gender perspective, more Aboriginal women than men reported having CVD (14% to 11%) in 2012-2013 (48).

2.3 TYPE 2 DIABETES

Type 2 diabetes mellitus is now the most common form of diabetes. About 85-90% of those with diabetes have Type 2 diabetes (52, 53). This condition is a progressive condition, and occurs when the body becomes resistant to the insulin produced by the pancreas and/or the amount produced is insufficient to meet the body's needs (54). Obesity and sedentary lifestyle trigger the development

of insulin resistance (55). The cause of this condition is complex and probably results from a combination of genetic and environmental factors (53). This condition can be life-threatening and can result to other complications such as chronic CVD, renal disease, blindness, limb amputation, retinopathy and death (52, 56, 57). Symptoms of Type 2 diabetes include increased thirst, dry mouth, nausea, increased urination, fatigue, increased hunger, slow healing of sores and wounds, frequent itchy skin infections, blurred vision, dizziness, leg cramps, headaches, mood swings and weight gain. Furthermore, Type 2 diabetes affects psychological wellbeing contributing to depression (58).

2.3.1 Risk factors and diagnosis of Type 2 diabetes

Increased risk of Type 2 diabetes is associated with overweight/ obesity/ abdominal obesity, advancing age (over 45 years, or over 35 years and of Aboriginal background), high blood pressure, physical inactivity, family history of diabetes, low HDL cholesterol or high triglycerides, low birth weight, gestational diabetes and poor living standards.

Type 2 diabetes can be diagnosed in the following ways:

1. *Oral glucose-tolerant test (OGTT)*: also referred to as glucose tolerant test (GTT) is used to determine whether the body has difficulty metabolising sugar or carbohydrate intake. The patient fasts for at least 8 hours, but not more than 16 hours, the night before the test. Afterward, the patient's fasting blood sugar is tested (59). The patient is then asked to take a glucose drink and their blood glucose level is measured at intervals after taking the sugary drink (59).
2. *Fasting blood sugar*: The test is easy to perform. After an overnight fast, blood is drawn early in the morning and test is carried out to examine whether blood sugar is within the normal range (70-99 milligrams per decilitre- mg/dl, or <5.5 mmol/L). A fasting blood glucose test result between 5.5-6.9 mmol/L should be investigated further with OGTT or by measuring the blood sugar level (60).
3. *Random blood sugar*: A level of ≥11.1 mmol/L in the blood sample indicates diabetes and should be further investigated with a fasting blood glucose test.
4. *Haemoglobin A1C test (HbA1c)*: HbA1c value of 48 mmol/mol (6.5%) or greater is recommended as the blood level for diagnosing diabetes (61).

2.3.2 Burden of Type 2 diabetes in Australia

Until recently, Type 2 diabetes was mostly common among the older age group, and the prevalence of the disease was higher in developed countries than in developing countries, and thus was considered to be a disease of the affluent. However, the dynamics of the disease is changing, affecting people in every country worldwide with increasing proportions in low- and middle-income populations and among the younger age group (62), indicating it as a worldwide epidemic. The World Health Organisation (WHO) reported 9% diabetes prevalence among adults (+18 years) (63) of whom 90% were Type 2 diabetes (64).

In Australia, describing Type 2 diabetes as a 'huge' and growing problem is not simply a play on words. As expected, the incidence and prevalence of diabetes are substantial, different between Indigenous and non-Indigenous peoples. In 2012-2013, 11% of Indigenous adults had diabetes, and a further 4.7% at risk of developing diabetes (65). Indigenous adults were 3.3 times (age-standardised rates) as likely to have diabetes as non-Indigenous adults (65). The incidence of Type 2 diabetes increases with far greater burden among Aboriginal children and adolescents, compared to their non-Aboriginal counterparts (66-68). According to a 2004-2005 report, the prevalence of this condition increases with age, with the increase occurring at younger ages among Aboriginal people (69). The reported prevalence in Aboriginals aged 35-44 years is about five times that of non-Aboriginals. Diabetes is a notable contributor to mortality among Aboriginal people, being the underlying cause of about 8% of overall deaths (70). This condition inflicts significant financial and human cost on the Australian government and community. The higher incidence of Type 2 diabetes among Aboriginal people is strongly related to a modern lifestyle that comprises of high-energy and fatty food and sedentary lifestyle, which has increased the rates of obesity. It was reported in 2012-2013 that Indigenous adults who were obese were 7 times as likely as those of normal weight and underweight to have diabetes (17% compared to 2.4%) (65).

2.4 MORTALITY

2.4.1 Risk factors for mortality

The adverse consequences of obesity and central obesity on multiple health aspects presume that these conditions increase premature mortality. Overweight and obesity alongside high blood pressure, tobacco use, high blood glucose, and physical inactivity are listed as the top five leading global risks for mortality in the world (71). These factors are responsible for increasing the risk of chronic diseases such as CVD, Type 2 diabetes, cancers and other causes (22, 71-73). In Australia,

these factors as well as poor nutrition and lower utilisation of health services, have been identified as contributors to the excess Indigenous mortality (74).

2.4.2 Burden of mortality in Australia

There is substantial inequality in mortality rates in the Australian population despite the relatively high standards of health care in the country. Although mortality rates of Aboriginal Australians are understated as a result of incomplete identification of Aboriginal status in death records (75), and of the delays in registration in deaths which is common among this group (76), the overall mortality rate of Aboriginal people in 2009-2011 was almost as twice as that of non-Aboriginal people, and five times as high among adults aged 34 to 44 years (77). The mortality gap between Aboriginals and non-Aboriginals was about 10.6 and 9.4 years for males and females respectively (77). Generally, Aboriginal people have a much younger population structure and mortality rates are higher at younger ages, with a greater percentage of deaths occurring before a significantly advanced age (3). Between 2008 and 2012, about 65% of Aboriginal deaths occurred before the age of 65 years (3). In 2012, CVD was the leading cause of death among Aboriginal people, with a crude rate of 102 deaths per 100,000 population, and responsible for 25.2% of deaths (78). During a 5-year period (from 2008 to 2012), a total of 11,612 deaths were registered for Indigenous people from five Australian jurisdictions (New South Wales, Queensland, Western Australia, South Australia and the Northern territory), representing 2.3% of all deaths in these regions (65). Based on this report, the most common cause of death among Indigenous Australian people was CVD (about 25% of total deaths), with Indigenous people dying from CVD at 1.5 times the rate of non-Indigenous people (65). Endocrine, metabolic and nutritional disorders (including diabetes) are also common causes of death among Indigenous people (9.1% of deaths). Other common causes of death include cancers, respiratory and digestive diseases. The overall diabetes death rate in Aboriginal people was 7 times higher than that in non-Aboriginal people in the year 2012-2013 (79). There was a significant decline (16%) in the age-standardised mortality rate for Indigenous Australians between the 1998 and 2012 period, with a significant narrowing (by 17%) in mortality gap between Indigenous and non-Indigenous people (65). During this period, for Indigenous people, the age-standardised mortality rates reduced for CVD (40%) (65).

2.5 OBESITY AND CENTRAL OBESITY

2.5.1 Obesity

Aetiology of obesity

Obesity is defined as an excess amount of body fat accumulation in adipose tissue that results in an energy imbalance over a sustained period. This may have adverse effect on health, leading to a reduced life expectancy (80). When body fat due to long term energy intake (mostly from food) exceeds energy expenditure (physical activity), the result is the accumulation of adipose tissue which contributes to the epidemiology of obesity (81, 82). The human body, on average, stores around 50,000 to 60,000 kilocalories of energy in adipocytes (83). Obesity predisposes to many chronic conditions, which themselves are associated with mortality. It involves a complex, multifactorial process influenced by genetics, environmental, lifestyle (high-energy diets and physical inactivity), socio-cultural factors, or as a result of medications which promote weight gain (82, 84). Among Aboriginal people in Australia, factors such as geographical, historical, social, economic and infrastructure contribute to obesity among them (85, 86). The amount of body fat varies between populations and depends on the regional distribution of the amount of excess fat stored in the body which could pose as a risk for chronic illnesses. An increased overall body fat mass, in particular excess fat stored in the abdominal area, contributes significantly to an increased fat content in the liver and deposition of fat in areas such as heart, blood vessels and kidneys, leading to impaired function of these organs (87).

Obesity measurement

In general, the assessment and classification of overweight and obesity are dependent on practical definitions mostly based on BMI. BMI relates weight to height, and calculated as weight (kg) divided by height (m^2). BMI is the most commonly used parameter for defining underweight, overweight and obesity (88). Although, this measure does not separate fat mass from muscle mass, it is highly correlated with both adipose tissue and muscle mass (89). Based on the strength of association between BMI and chronic diseases, the World Health Organisation (WHO) has adopted standardised cut-off points that defines underweight as having a BMI of less than 18.5, normal weight from 18.5 to 24.9, overweight as 25 to 29.9 and obese as BMI of 30 or greater (90) (Table 2.1). Obesity also ranges in degree of severity, with class I (BMI 30-34.9), II (BMI 35-39.9) and III (BMI≥40) (90). In Australia, guidelines for healthy weight correspond with the WHO BMI cut-offs (91).

Table 2.1 The International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI(kg/m²)	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00-16.99	16.00-16.99
Mild thinness	17.00-18.49	17.00-18.49
Normal range	**18.50-24.99**	**18.50-22.99**
		23.00-24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00-29.99	25.00-27.49
		27.50-29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00-34.99	30.00-32.49
		32.50-34.99
Obese class II	35.00-39.99	35.00-37.49
		37.50-39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004 (90).

In the Asian population, different cut-off values have been recommended- 23.0 and 27.5 kg/m^2 for overweight and obesity respectively (92). There have been earlier suggestions that the appropriate BMI range for Australian Aboriginal people is between 17 and 22 kg/m^2, with increased risk of metabolic conditions above 22 kg/m^2 (93, 94). However, this is yet to be confirmed for in the Aboriginal population.

Uniqueness and limitations of the use of BMI

The major advantage of BMI is that it is relatively cheap and easy to measure; and a convenient, non-intrusive measurement of obesity for large epidemiological studies. It is a universally accepted measure that allows for comparison across populations. Moreover, the same BMI cut-off can be applied to all ages and both genders. However, a number of limitations should be considered when employing BMI as an indicator of body fat. BMI cannot differentiate between fat mass and lean body mass (7). And while height and weight are simple measures with some level of accuracy, muscular individuals with low proportion of body fat may be misclassified as overweight or obese (95). The use of BMI can also be misleading especially during the aging process and menopausal transition when muscle mass can be converted to body fat mass which does not necessarily

implicate a change in BMI (96). BMI vary between individuals and populations (7) and the use of a universal BMI classification is unlikely to account for ethnic differences in body fat distribution (97). Differences in fat distribution between Aboriginal and non-Aboriginal Australians have been well reported, suggesting that the currently used BMI thresholds might be inappropriate for Aboriginal people, who tend to have lower BMI mean estimates compared to non-Aboriginals, particularly among men (12, 98). There is a possibility of incorrectly estimating health risks attributable to overweight and obesity depending on the BMI threshold employed.

Burden of obesity in Australia

In Australia, the prevalence of overweight and obesity is on a dramatic increase among adults and children, Aboriginal and non-Aboriginal peoples, and people from every socio-economic background (85). This condition ranks as the second largest contributor to burden of disease in Australia with about 63% of Australian adults being overweight or obese, and over 25% of the total are classified as obese (99). Based on data from the Australian national surveys for the period between 1995 and 2012 (100), the prevalence of overweight and obesity increased from 56.3% to 62.8% in adults aged 18 years and over. The likelihood of being overweight or obese was higher among adults that reside in regional and remote areas (69.5%) compared with those in the major cities (60.2%) (100).

The problems of overweight and obesity vary across the Australian population with higher prevalence among Aboriginal people (80), rural dwellers (101) and the low socio-economic background (85). According to a 2012-2013 Health survey report, Indigenous adults were 1.5 times as likely to be obese as non-Indigenous Australians (rate ratio of 1.4 for males and 1.7 for females) (102). The same report also stated that about 30% of Indigenous children aged 2-14 years and 66% of Indigenous adults 15 years and over were overweight or obese. Figure 2.1 shows the percentage of people 15 years and older according to BMI category and Indigenous status (103).

There have been reports of lower BMI among Aboriginal men compared to their non-Aboriginal counterparts (12, 98). In a study comparing body fat distribution among Australian Aboriginal and non-Aboriginal peoples, BMI was reported to be significantly lower for Aboriginals compared to non-Aboriginal men ($P=0.01$) (98). Also, another study assessed body habitus in three remote Aboriginal communities in Australia and compared with those of the general Australian population and reported that Aboriginal males were less often overweight and/or obese by BMI than non-Aboriginal males ($P<0.001$) (12). The latter study found the proportion of Aboriginal males with BMI$\geq$25kg/m^2 was smaller when compared to non-Aboriginal males (37% vs. 68%, $P<0.001$).

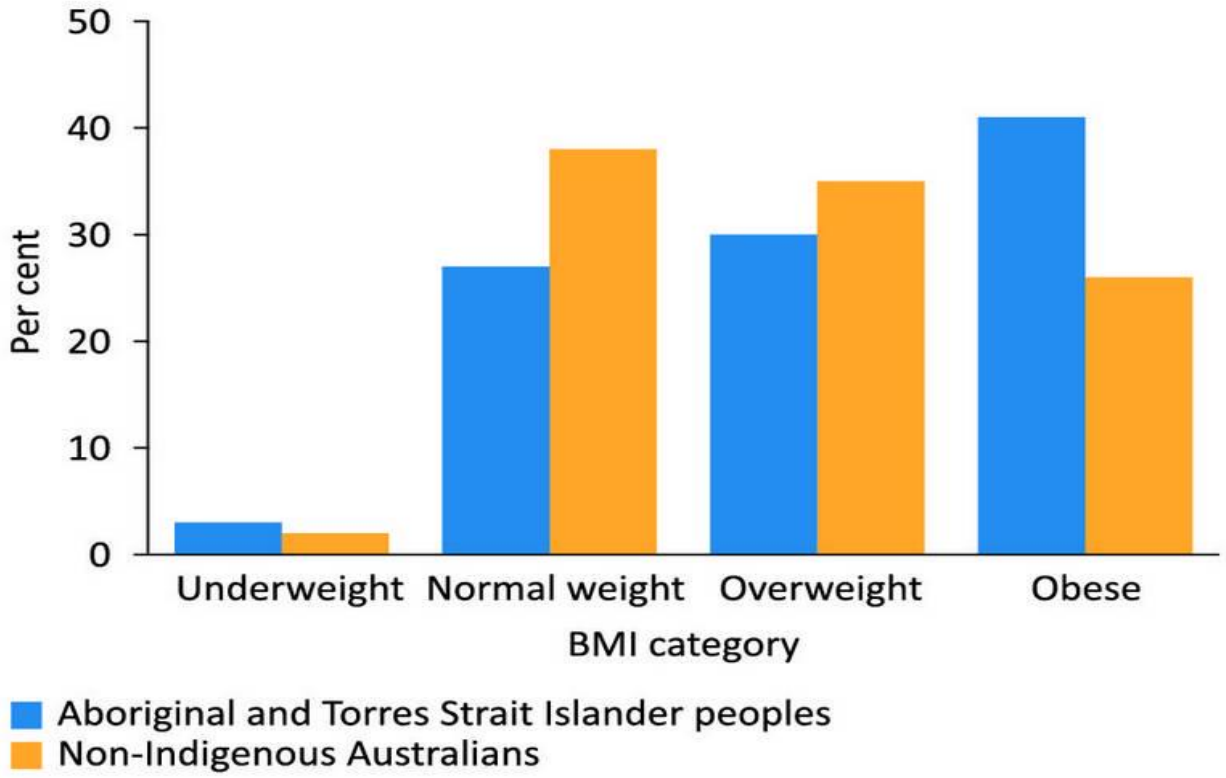

Figure 2.1 Proportion of persons 15 years and over (age-standardised) by BMI category and Indigenous status, 2012-2013

SOURCE: ABS and AIHW analysis of 2012-13 AATSIHS

BMI has been found to be consistently associated with an increased risk of CVD, Type 2 diabetes and mortality. This condition contributes 16% of the health gap between Aboriginals and non-Aboriginals in Australia (28). Obesity-related health conditions such as CVD and Type 2 diabetes impose substantial economic burden not only on individuals and families, but also on the community and government. In 2008/2009, the estimated direct and indirect costs of obesity and obesity-related conditions in Australia was about $37.7 billion (104). An estimated 7,200 Australians die every year as a result of obesity and related illnesses (104).

2.5.2 Central Obesity

There is growing evidence suggesting abdominal obesity as detrimental to health and wellbeing (105). The two most common measures of central obesity are WC and WHR. These two indices have been reported to have strong associations with incident CVD events (106, 107), metabolic risk factors (108) and mortality (109). Although this thesis focused on WC as a measure of central

obesity, WHR alongside WC was used to assess associations with study outcomes in relevant result chapters.

2.5.2.1 WC

What is WC and how is it measured

WC refers to the numerical measurement of the body girth at the level of the abdomen. As there is currently no consensus as to how and where to measure WC, protocols for measurement existing in research literature on clinical studies are based on identifying anatomical landmarks which also requires the individual in a standing position, bare midriff, with feet touching, arms hanging, without holding one's breath (110). Measurement is usually done with a measuring tape made of material that is not easily stretched, placed perpendicular to the long axis of the body and horizontal to the floor and applied with tension without compressing the abdominal wall (110). The different anatomical landmarks for determining the exact location for measuring WC in clinical studies include:

1. midpoint between the lowest rib and the iliac crest
2. at the umbilicus
3. the narrowest (minimum) or widest (maximum) WC
4. just below the lowest rib
5. just above the iliac crest (111).

WC has standard thresholds to identify individuals at high risk of chronic diseases. The defined cut-offs for WC, that is, the point at which an individual has a greater risk for chronic disease, differ by gender and ethnicity. The WHO recommended WC gender-specific thresholds are presented in **Table 2.2** (112).

Table 2.2 Waist circumference categories

WC Classification	**Males**	**Females**
Normal-weight	<94 cm	<80cm
Overweight	94-102 cm	80-88 cm
Obese	>102 cm	>88 cm

These thresholds have been recognised and used mostly in European populations or in ethnic regions where there is absence of specific recommendations. The International Diabetes Federation

(IDF) recommends lower WC thresholds and ethnic-specific cut-off values for Asian adults (112). These thresholds are (men/women): ≥90/≥80 cm for South Asians; ≥90/≥80 cm for Chinese; and ≥85/≥90 cm for Japanese (11).

Uniqueness and limitations of the use of WC

WC assessment provides a measure of fat distribution that cannot be obtained by measuring BMI. Although WC is a crude measurement, it is cheap, easy to measure, interpret and better correlated with total body fat measured by BMI (113) and visceral fat mass, and is a surrogate marker for abdominal fat mass (110). WC is a practical tool to evaluate abdominal fat before and during weight loss (114). The measurement of WC is simple, more reliable and feasible when compared to WHR, (115). Despite the high correlation between WC and BMI, they measure different body fat characteristics. While BMI assesses overall adiposity and is unable to separate lean from fat mass, WC measures abdominal fat and contributes information about overall body fat independent of BMI (116). In addition, WC provides an independent prediction of risk over and above that of BMI (114). Studies have found that abdominal fat increases the risk of metabolic syndrome (117, 118). More specifically, the International Diabetes Federation has reported that WC increases the risk of the metabolic syndrome (119). WC can serve as a screening tool to identify individuals in need of further assessment for obesity-related chronic illnesses, targeting health actions in communities (120). High WC could be an indicator of the level of internal fat deposits which coats the heart, kidneys, liver and pancreas, and increase the risk of chronic diseases (121). Excessive abdominal fat could be an indicator of a greater risk of health problems in adults such as hypertension (122), diabetes (123, 124), dyslipidemia (122, 125), CVD (126, 127), metabolic syndrome (128, 129) breast cancer in women (130), colon cancer (131, 132) and mental illnesses (133). Risk of Type 2 diabetes with WC for any level of adiposity is amplified by the excessive abdominal fat mass (134).

While WC is important and useful in epidemiological and clinical settings to assess the risk of obesity-related conditions, there are some limitations to this index. In some situations, WC might be an inaccurate central adiposity measure for pregnant women or for people who suffer from medical conditions which cause distention of the stomach (7). Next, WC measurement procedure has not been standardized and could result an under- or overestimation of WC measured, depending on the method used for the measurement. This could lead to a potential measurement bias. Moreover, WC may be difficult to measure and less accurate in obese individuals, particularly when measured at the umbilical level (135). Although there is good reproducibility of WC at all sites (136), arguments have been raised by experts on the variability of WC measurements which could differ in measurements when taken by the same healthcare provider or between healthcare professionals (137, 138).

2.5.2.2 WHR

What is WHR and how is it measured

WHR is determined by dividing waist measurement by hip measurement. Hip circumference is measured at a level parallel to the floor, around the widest portion of the buttock using a stretch-resistance tape that is wrapped snugly around the subject but not pulled so tight that it is constricting (138).

The WHO suggested WHR greater than 0.9 for men and greater than 0.85 for women as indicators of increased health risk (59), and these standards are mostly used in populations of European origin. However, different studies have suggested cut-offs suitable in specific populations (139-141).

Uniqueness and limitations of the use of WHR

WHR is correlated with body fat; it is inexpensive and has been shown to be associated with the development of CVD, Type 2 diabetes and death in adults (7). This measure can be used to indicate the prevalence of abdominal obesity, to evaluate health promotion and disease prevention and to monitor progress towards national public health policy (142). However, there are some limitations to using WHR. The first is that it is prone to measurement error as it requires two measurements (waist and hip measurements). Second, hip circumference measurement may be more difficult than measuring WC alone. Third, WHR is less dependent on body size and height, and might not be a suitable measure to assess fatness and weight loss as theoretically it could remain unchanged during weight loss (143). It has been suggested that WHR is insensitive to weight gain (144).

There has been evidence of the importance of WHR in identifying Aboriginal people at risk of chronic illnesses. Wang *et al*., showed that WHR compared to BMI, WC, hip circumference and waist-to-height ratio, was a strong predictor of diabetes (Odds ratio= 2.44(95%CI: 1.94-3.06) and estimated coronary heart disease risk in Aboriginal people from Central Australia (145).

2.5.2.3 Waist circumference of Aboriginal people in Australia

Variations in WC levels of Aboriginal and non- Aboriginal Australians has been reported in public health researches in Australia (12, 146-148). Chapter 3 of this thesis reviews the gender differences in WC of Aboriginal and non-Aboriginal peoples (149).

Aboriginal people have a lower sitting-height to stature ratio, relatively short trunks, long legs, central fat deposition (150-153) and higher percentage of body fat (12, 98, 154). Despite the significance of WC in detecting obesity-related health risks, until recently it has been seldom used in both clinical and population health settings in Aboriginal Australia. Lately, WC is being

acknowledged and used alongside other anthropometric alternatives such as BMI, WHR, and weight in the assessment of chronic diseases in the Aboriginal population (8, 9, 155, 156). The central fat deposition evidenced by the elevated WC relative to the body weight, particularly among females, has been a topic of considerable interest (9, 10, 12, 157). This has significant implications, considering that central or abdominal obesity mostly measured by WC has been known to bear strong linkage with the risk of cardiovascular disease (9) and diabetes (158). However, the higher WC in Aboriginal people is beyond the simple generalization that inappropriate eating is the main cause. There have been some speculations on the causes and potential biologic mechanisms of high WC which includes adaptation to hot climate particularly in the tropical environment (159). Some potential mechanisms for high level WC observed in other populations include older age (160-162), behavioural/lifestyle factors (162, 163), genetic factors (163, 164), medical conditions which cause distention of the stomach (7), inflammation as a result of highly sensitive c-reactive protein (CRP) concentration (165, 166), and parity or menopausal status (161, 167). Although the biological mechanisms that explain the increased health risk predicted by WC in the Aboriginal population are not well-known, it is often proposed that the added risk is explained by the complex and multi-determinant phenomenon associated with elevated abdominal obesity (168). It has been reported that specific hormones, cytokines, and free fatty acids secreted by adipose tissue contribute significantly to the mechanism (169). As WC correlates highly with central fat mass (170) and associated with cardio metabolic risks (118), WC cut-off points are mostly required to identify individuals at high risk of diseases. In 2012-2013, three in five Indigenous male adults (≥18 years old) and four in five Indigenous females had WC that associated with increased chronic disease risk. However, the WC cut-off points (112) used to identify these Indigenous individuals were based on individuals of European origin and might be unsuitable for Indigenous people in Australia. Increasing research had indicated WC as an important risk factor for disease and mortality (171-173). Obesity-related problems such as diabetes and CVD are still on the increase in Australia (174) with rising incidence in spite of intervention efforts and considerable health care costs (175). As Aboriginal people in Australia have the tendency to store abdominal fat rather than a more peripheral distribution of body fat (9, 12), it is not surprising that their risk of developing CVD and Type 2 diabetes is high compared to their non-Aboriginal counterparts. Clustering of a number of the risk factors mentioned earlier (smoking, excessive alcohol consumption, physical inactivity and poor diet) confers a higher risk of chronic diseases and premature deaths in the Aboriginal population (176, 177).

The observational studies reporting on association of WC with CVD and Type 2 diabetes have varied considerably in relation to their study design, participant characteristics and their method of

data collection. A cross-sectional study of 117 Aboriginal adults in a large urbanised community in Queensland reported strong associations between WC, CVD and diabetes in women (178). Also, McDermott et al, in their follow-up study of 225 indigenous adults in North Queensland, reported WC increased the risk of Type 2 diabetes with rate ratio of 2.0 (95%CI: 1.1-3.6) (10). Wang and Hoy reported significant associations between WC and CVD and Type 2 diabetes in Aboriginal people in a remote Northern Territory community using cross-sectional study design (8, 9). They, and other studies, also provided evidence that WC was a better predictor than BMI and WHR for CVD and Type 2 diabetes in their researched Aboriginal communities (9, 145, 146, 178). According to Wang and Hoy, the relative risks of CVD after adjusting for diabetes, cholesterol, systolic blood pressure and smoking status, were 1.31 (95%CI: 1.11-1.54), 1.29 (95%CI: 1.09-1.53), 1.28 (95%CI: 1.08-1.52) and 1.10 (95%CI: 0.93-1.30) per standard deviation increase in WC, BMI, hip circumference and waist-to-hip ratio respectively (8). They also found that WC had the highest odds ratio for type 2 diabetes (2.16 (95%CI: 1.75-2.66) associated with 1 standard deviation increase in WC as compared to BMI, weight, WHR and hip circumference (9).

2.5.2.4 Underlying biological mechanisms of waist circumference associated with CVD and diabetes

Although it is unknown the extent to which the elevated waist measure observed in Aboriginal people is modifiable, several potential biological mechanisms may be responsible for the increase in the risk of chronic diseases and premature death associated with high WC.

High waist circumference: a genetic chronic disease risk factor in Aboriginals

As mentioned earlier, compared to non-Aboriginals, Aboriginal people in Australia generally have higher WC levels in relation to their body weight (12). Also, studies have observed higher WC estimates in Aboriginal women compared to the men in Aboriginal communities (9, 10, 12, 157). The reasons for the significantly higher WC among Aboriginal women remains elusive, although hormonal factors could be a possible mechanism. In general, in the transition from pre- to post-menopausal, there are changes in body composition of women, with fat redistribution in locations towards the upper body, which can occur in the absence of changes in the total body fat mass (179, 180). This suggests that abdominal fat mass accumulation is accelerated by menopause in women. There might be independent casual links between genes that predispose to preferential deposition of fat in abdominal depots and obesity-related conditions (84). Therefore, the interaction between genes and environment/ lifestyle would be beneficial for future research on the genetics of high WC

among Aboriginal people, as the propensity of fat accumulation is influenced by the genetic characteristics of individuals or populations (181).

High waist circumference: Lifestyle (diet, physical inactivity, smoking and alcohol consumption)

There have been suggestions that the obesity rates of Aboriginal people escalate with 'Westernization' compared to other population groups (11). Since colonization, Aboriginal Australians have experienced rapid lifestyle changes, with increase in the consumption of processed foods and dramatic reduction in physical activities, shifting from the traditional hunter-gatherer lifestyle. These in turn have been accompanied by an epidemic of increased body fat and chronic diseases such as CVD, Type 2 diabetes and their sequeale leading to pre-mature deaths (182). There are limited reports on how lifestyle choices affect the association between WC and obesity-related diseases among Aboriginal people. The knowledge, attitude and practise of diet pattern and physical activity have been assessed in few qualitative and quantitative studies (183), but the role of diet and level of physical activity on changes in WC have not been explicit. Routine physical activity has been shown to improve body composition by reducing weight and abdominal adiposity and enhance the general well-being (184, 185). In a social survey on Aboriginal people in 2004-2005, low levels physical activity were reported among them, which was 1.5 times higher than in non-Aboriginals (186). Environment impacts on individual and population's likelihood of obesity (and central obesity) through high energy-dense food intake or a reduction in energy expended with sedentary living (84). Furthermore, smoking and alcohol consumption increase the risk of obesity (84) and visceral fat accumulation, thereby accelerating the development of obesity-related disorders (187). There is the potential of maintaining a healthy WC and reducing the risk of CVD and Type 2 diabetes if behavioural factors in terms of healthy nutritious diet, physical activity and reduced smoking and alcohol consumption are channelled appropriately. Moreover, adequate nutrition and balanced diet are required for healthy living and survival. However, caution should be exercised when proposing on the healthy lifestyle that comes with weight loss in the Aboriginal population, as the practice of energy-dense but nutrient-deficient diet is common among them due to limited availability and affordability of healthy nutritious food (188).

High waist circumference: older age

Substantial redistribution of fat tissues depot has often been linked with the ageing process, and the positive association of age with an increase in visceral adipose tissue (VAT), independent of sex have been documented (189). WC increases with age, so does the risk of other chronic diseases. Epidemiological studies have reported on the association between ageing and increase in WC, with

women showing a greater increase in WC than men of the same age and ethnicity, which increases throughout their lifespan (190-192), independent of body weight (189, 193). The increase in WC as age increases has been mostly attributed to a disproportionate increase in visceral adiposity (161, 193).

High waist circumference: a marker of the inflammatory process

C-reactive protein (CRP) is made and released by the liver, mainly in response to the cytokine interleukin-6 (IL-6) (194). It is a marker for inflammation as it increases in the presence of inflammation in the body. A few studies have identified high-level CRP among Aboriginal people in Australia (195, 196). These studies also reported that CRP levels were higher in females than males. Wang and Hoy showed geometric means of CRP were 4.1 (95% CI: 3.7-4.6) and 7.3 (95% CI: 6.6-8.1) for males and females respectively (195). And the overall levels were the highest reported in any population to date. Data from the Diabetes and Related conditions in Urban Indigenous people in the Darwin Region (DRUID) study showed higher CRP levels among women compared with men (196). In the DRIUD study, after including WC in the multivariate analysis, the odds of high CRP (>3.0 mg/L) relative to another national population-based study data were no longer statistically significant. This could indicate a possible correlation between CRP and WC. In a study conducted in another remote Aboriginal population, over 50% of participants had high risk CRP (over 3.0 mg/L), with higher levels found in women than men (157). Wang and Hoy commenting on higher CRP levels in this particular Tiwi study community (195), remarked on common skin infections and other infections among Aboriginal children (197, 198).

Elevated CRP has been suggested to be associated with WC (165, 199), diabetes and coronary artery disease (200, 201), with clearly recognized links in their pathophysiological mechanism (202). Additionally, WC as well as high CRP levels, are strong markers of CVD risk (203). Prospective epidemiological studies have reported on the predictive ability of CRP in the development of CVD (35, 36).

High waist circumference: a contributor to inflammatory process

Elevated WC is one in the group of metabolic risk factors that increases the risk of heart diseases and diabetes. Other factors include high triglycerides, impaired fasting glucose, low high-density lipoprotein and elevated blood pressure (204). Interestingly, large WC contributes to the increased risk of hypertension (205) although they are both factors of metabolic abnormalities. Elevated WC is the most prevalent manifestation of metabolic abnormalities and has a considerable influence on inflammatory process (206). Increased adipose tissue has been thought to promote resistance to insulin, resulting in increased levels of fatty acids that are toxic to the liver, thereby causing a drop

in insulin clearance, increased glucose production and dyslipidemia (87, 108). The mechanism for developing insulin resistance stems from macrophage infiltration in the abdominal tissue and the unbalanced production of adipocyte protein factors and the hormone, adipokines (55). Also, visceral fat depots within the abdominal cavity have been implicated in the role of high metabolic and inflammatory cavity (207). The inflammation status linked with the increased secretion of adipokines from excess adipose tissue (208), and the change in fatty acid metabolism are involved in insulin resistance pathogenesis (209). Insulin resistance, which is associated with central fat mass, and a key etiological factor for Type 2 diabetes, increases the risk for CVD which is a major cause of death for those with Type 2 diabetes.

High waist circumference: a correlate for other comorbidities

CVD and Type 2 diabetes may be caused by, or be a complication of, one or more other diseases. Risk factors such as central obesity do not necessarily work in isolation, and can involve the synergy and combination of other determinants. Elevated WC is associated with comorbidities such as obesity, hypertension, gallstone disease (210, 211) and sleep disordered breathing (212) which may be competing risks with the development of CVD (213).

Risk of gallstone disease is higher among individuals with diabetes. Although there are controversies regarding risk factors such as BMI, sex and age for gallstone disease in diabetics (214), one potential reason is their level of overweight and elevated WC. These factors in turn are important and independent determinants for gallstone disease (211, 214, 215). Type 2 diabetes, usually linked to insulin resistance, is also associated with increased colon cancer risk (216).

High waist circumference: social determinants and cultural status

Finally, understanding biological factors cannot fully explain the association central obesity has with CVD and Type 2 diabetes without considering socio-economic, psychological and cultural influences. In Australia, the gap between Aboriginal people and non-Aboriginals is not limited to health alone but embraces the aspect of socioeconomic status which includes income, educational attainment, home ownership, and employment. In all these areas, Aboriginal people are disadvantaged (217, 218). However, socioeconomic and health disparities between these two Australians groups are complex and exist simultaneously. The relationship between socioeconomic determinants and WC although understudied, could be influenced by non-modifiable factors like sex, age and ethnicity, as well as modifiable factors such as physical activity and knowledge. This relationship may be complicated by the fact that low socioeconomic status individuals, particularly

remote and rural dwellers, often have less access to health care services and limited knowledge of weight management.

An important factor to consider in terms of culture is the perception and awareness of elevated WC in relation to chronic diseases. This includes the knowledge, attitude and practices of a population towards issues pertaining to health. This factor is vital in implementing interventions and policies. Aboriginal people have a holistic approach to health which encompasses land, body, community, relationships, environment and law (186). Programs to raise awareness on obesity-related chronic illnesses in Aboriginal settings will benefit greatly and involve sustainable participation if targeted to incorporate all aspects of what is considered vital to health and wellbeing by this Australian group.

2.5.2.5 Lack of WC thresholds for Aboriginal People

Guidelines such as the 'National guide to a preventive health assessment in Aboriginal and Torres Strait Islanders peoples' and the 'Clinical Practice Guidelines for the Management of Overweight and Obesity in Adults' recognize the importance of WC in health assessment. The Central Australian Rural Practitioners Association (CARPA) Standard Treatment Manual also recommends the inclusion of WC measurements in all yearly Adult Health Checks (219). While high WC is well recognized for increasing the risk of CVD and Type 2 diabetes in Aboriginal people, there is a lack of WC cut-off points for identifying Aboriginal individuals at high risk of chronic diseases. WC cut-off points are thresholds used to identify individuals at increased risk of chronic diseases, and is one of the strategies for weight management in health promotion and intervention. WC cut-off points have been estimated in a number of cultures and ethnic communities worldwide (115, 139, 220-222). The differences in disease risk levels with WC in different populations make it inadvisable to identify universally applicable risk thresholds (11, 223). Currently, the only available WC cut-off points for weight management for Australians are those proposed by the National Institutes of Health and the World Health Organization (115, 223). Those cut-off points were based on studies in populations of European origin (11), therefore more suitable for non-Aboriginals than Aboriginal Australians. Those thresholds are above 80 cm for women and 94 cm for men as an indication of increased risk of developing chronic diseases; while WC over 88cm for women and 102 cm for men as a sign of a greater disease risk. The Australian Government launched the Measure-Up Campaign in 2008, to increase awareness of the high waist size and healthy choices to prevent lifestyle-related chronic diseases. Among other initiatives, the campaign highlighted the link between high level WC and risk of heart disease and Type 2 diabetes, advising on the need to measure WC monthly to stay within low disease risk levels.

A number of population studies have developed prediction models for risk of cardiovascular disease (CVD). However, the studies have been based on non-representative samples and WC was neither an exposure nor covariate variable for prediction. These studies include the Systematic Coronary Risk Evaluation (SCORE) project (224), the Framingham coronary heart disease prediction scores (225), European system for cardiac operative risk evaluation (EuroSCORE) (226) and Prospective Cardiovascular Muster (PROCAM) (227). The present guidelines for CVD risk in Australia included Aboriginal people from the age of 35 years and non-Aboriginals. However, WC, which has been reported as a good predictor of CVD and Type 2 diabetes among Aboriginal people was not included (8, 9, 178).

The Receiver operating curve (ROC) and Youden Index have been mostly used to give 'optimal' WC cut-points in several populations worldwide (13, 228). Wang *et al*. conducted a literature review of 75 relevant articles defining WC cut-off points in different populations worldwide using the ROC approach (13). They found the derived WC cut-off points from ROC do not take into account variations in WC levels. Rather, this method optimises the sum of two statistical measurements of sensitivity and specificity to obtain the 'optimal' WC cut-off value for a given outcome. Therefore, the suitability in the Aboriginal population is questionable due to the variations in WC in different communities. This approach has its limitations in the differences in cut-off points based on differences in population characteristics such as average body size or disease prevalence (138). As noted by Wang et al (13, 229), this method will not give a consensus on WC cut-off values for Aboriginal people in Australia due to the variations in WC mean values in different communities (12) which also changes over time in the same community.

In light of the gaps in the literature thus highlighted, the goal of this research work was to address some of these concerns in Aboriginal people by examining CVD, Type 2 diabetes and mortality outcomes in relation to WC of both adult males and females. Identifying the effect of WC on related chronic disease outcomes is useful for planning effective health policy in the context of chronic disease burden in Aboriginal people.

2.6 THE ABSOLUTE RISK METHOD

Absolute risk is the likelihood that a disease-free individual in a population under study will develop a disease over a specified time interval, given current age and individual risk factors, and in the presence of competing risks (230). This method determines an individual's overall disease risk level over a defined time period. Mostly expressed in percentage, this method is a meaningful way of measuring a person's actual disease risk, and is suited to predicting risk for individuals.

Important properties of the absolute risk method include (230):

1. Estimates using the absolute risk can be done in reference to a specified time interval which is dependent on time span and could be short, long or lifetime span. Absolute risk increases with increasing time span which varies with the severity of the disease being investigated.
2. In some cases, this method can be influenced by competing risks or competing causes of disease which could be different from the disease under study.

The absolute risk method is useful in a number of ways. First, it is convenient for counselling, as the method provides an individual's probability of disease occurrence. Second, the method can be used to design trials and define eligibility criteria in intervention studies. Third, this method is not only useful in clinical settings in defining individual patient management, but it is important in decisions regarding public health (231).

In a cohort study, parametric and non-parametric estimation of absolute risk can be worked out under several models. This thesis used the Weibull model to present the absolute risk estimates presented in the results of the studies carried out. Details of how this statistical method was used in the thesis are explained in 'Research Methods'- Chapter 4, under the 'Statistical analysis' section (4.8).

The absolute risk approach used in this research work takes into account both additive and synergistic effect of clusters of risk factors of specific diseases (232) to give evidence of risk associated with CVD and Type 2 diabetes according to WC and age for Aboriginals in the study community. It is an informative measurement of the probability of developing CVD and/or Type 2 diabetes at a particular WC and specific age (233). The absolute risk method also gives information on health effects of potential risk factors which indicates easy interpretation by both health professionals and patients (233).

2.7 CONCLUDING REMARKS

Current Australian guidelines acknowledge the importance of WC measurement in the prevention of chronic diseases. However, none of those guidelines have been able to recommend WC cut-off points specifically for Aboriginal people. This thesis used data from an Aboriginal community to present results of relationship between WC and two disease outcomes (CVD and Type 2 diabetes), and took a further step to calculate WC values that corresponded with equivalent BMI points for CVD and Type 2 diabetes using the absolute risk method.

The next chapter is a systematic review and meta-analysis of studies on Aboriginals and non-Aboriginals conducted to assess the differences in WC of males and females, in order to provide a background to the work presented in subsequent chapters.

CHAPTER 3

SYSTEMATIC REVIEW AND META-ANALYSIS ON WAIST CIRCUMFERENCE OF ABORIGINAL AND NON-ABORIGINAL PEOPLES

3.1 INTRODUCTION AND AIM

As described in Chapter 2, generally, Aboriginal people in Australia have the tendency to store abdominal fat (central obesity) relative to their weight and are at greater risk of obesity-related chronic diseases than non-Aboriginals. However, there are not many studies that have assessed the differences in waist circumference of Aboriginal people and non-Aboriginals in Australia. The aims of this chapter are:

1. To conduct a systematic review of all available published literature till June 2013 reporting WC estimate (mean or median) among Aboriginal and non-Aboriginal Australians.
2. To conduct a meta-analysis of available estimates to assess the differences between Aboriginal men and women, and also in comparison to their non-Aboriginal counterparts.
3. To examine whether height and weight could explain the high WC found in Aboriginal females.

In this chapter, Section 3.2 details my contributions to the review. The results of the review have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O.O and Wang Z. Gender variations in waist circumference levels between Aboriginal and non-Aboriginal Australian populations: A systematic review. *Obesity Research and Clinical Practice* 2014; 8(6): p. e513- e524.

3.2 CONTRIBUTION TO THE STUDY

The concept, design of methodology for the systematic review and meta-analysis of the study were formulated by me with the assistance of Dr Zhiqiang Wang. I conducted the systematic review and was responsible for the collection and management of data, which Dr Wang and I abstracted from each of the studies. Data analysis was conducted by me and the interpretation of the results was discussed with Dr Wang. I was responsible for writing the manuscript, taking into account contributions from Dr Wang.

ABSTRACT

Objectives

To compare gender-specific waist circumference (WC) levels of Aboriginal Australians with non-Aboriginal Australians.

Methods

A systematic search on Medline, PubMed, EMBASE and Google Scholar databases was conducted to identify papers that reported gender-specific waist circumference (WC) estimates of participants from the age of 15 years and above among Aboriginal and non-Aboriginal Australians. Means and their 95% confidence intervals of gender differences in WC, height and weight were recorded or calculated where they were not provided. Gender-specific WC, height and weight mean estimates were pooled and the I^2 statistic was used to test heterogeneity among Aboriginal and non-Aboriginal Australians.

Results

Of 17 selected cross-sectional studies, 9 focused on Aboriginal and 8 on non- Aboriginal Australians. Seven studies reported significantly higher WC estimates among Indigenous females than males. On the other hand, non-Indigenous males had significantly higher WC levels than females. Males had greater height and weight estimates than females in both groups.

Conclusion

Although Indigenous women were shorter and had lower weight estimates, they had greater WC levels than Indigenous men. This is the first systematic review to assess the gender-specific differences between Aboriginal and non- Aboriginal Australians. The findings of this review warrant more efforts to understand and reduce the high prevalence of central obesity and related chronic diseases among Aboriginal women.

INTRODUCTION

A number of studies have emerged in the last decade that provide evidence of waist circumference (WC), a proxy for central obesity, as a better tool for predicting a number of sequelae related to this condition in some Aboriginal communities in Australia (9, 145, 146, 178). Prior to this time, body mass index (BMI) and waist-to hip ratio (WHR) were the main reported anthropometric indices for the Aboriginal Australian group (234, 235). Evidence of variations in the body habitus, including waist circumference (WC) levels of Aboriginal and non- Aboriginal Australians (12, 146-148) has been the subject of numerous work in the field of Australian public health. Recent reports have shown that adult Aboriginal females have the propensity for greater central adiposity when compared to the males in this populace and therefore have higher WC levels (9, 10, 12, 157), the reverse appears to be apparent for non- Aboriginal Australians (98, 236). This has significant implications particularly for Aboriginal females, considering that central or abdominal obesity mostly measured by WC has been known to bear strong linkage with the risk of chronic diseases such as cardiovascular and diabetes (9, 158).

Nationally, there have been reports of a higher risk of chronic diseases among Aboriginal Australians in comparison with non- Aboriginal Australians, so much so that there is an unacceptable gap in the life expectancy between these two populations as a result of chronic diseases (5). The Australian Institute of Health and Welfare (AIHW) reported a mortality gap of 80% between the Indigenous and non-Indigenous groups among individuals aged 35-74 years between 2005 and 2007 due to chronic diseases (5). Since the indigenes have the tendency to store abdominal fat rather than a more peripheral distribution of body fat (9, 12), it is not surprising that the risk of developing chronic diseases is high among them compared to their non-Aboriginal counterparts.

In this review, we analysed the data from 9 studies in Aboriginal Australians and 8 in non-Aboriginals (focusing on Australians of European descent) with the aim of assessing gender differences in WC levels and to explore the heterogeneity of the variations in gender among studies in different Australian regions. The first hypothesis we tested was that adult Aboriginal females have higher WC levels in comparison to the males and that generally Aboriginals have different WC levels when compared to the non-Aboriginals in Australia. Also, we investigated whether height and weight explained the higher WC levels of adult Aboriginal females. Understanding if higher WC in Aboriginal women than in the men are a common phenomenon is an important step to alert policy makers and health professionals of the need for a more concentrated effort on Aboriginals particularly for women to promote weight management with the aim of preventing and controlling chronic disease risks.

METHODS

Search strategy

This systematic review and meta-analysis was conducted according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (237). Keyword searches were completed on Medline, PubMed, EMBASE and Google scholar for reports published from inception to June 2013. Search terms were: - 'Waist circumference OR Waist girth OR WC Central obesity OR Body mass index OR BMI OR Abdominal adiposity' and 'Aboriginal OR indigenous' AND 'Australia OR Australians' AND 'adults'. The reference lists of all eligible articles and reviews were thoroughly scanned to identify additional studies for inclusion.

Note: BMI was included in the search terms to identify studies that reported WC levels that correspond to well established BMI estimates, recommended by the World Health Organisation (WHO) for overweight and obesity.

Study selection

A comprehensive literature search of electronic databases was conducted to identify publications reporting WC mean values in Aboriginal and non-Aboriginal regions. For the non-Aboriginal Australian group, we focused on Australians of European origin (or at least 90-93% of the participants in the study were of European descent). The selected studies targeted the adult population, however, a number of studies that included participants from the age of 15 years along with the adult population were also included in the analysis.

Studies were excluded if they focused on children and/or adolescents or pregnant women or men alone; presented overall WC estimates without stratifying by gender; focused on chronic diseases without reporting population WC means or median; the dataset from a particular Indigenous community had already been selected as meeting the inclusion criteria; and if papers were not published in English.

Data Extraction and quality assessment

Articles were reviewed independently by the two authors and data items extracted as per Tables 3.2 and 3.3. All titles were screened for relevance using exclusion criteria, duplicates were removed and abstracts reviewed within inclusion and exclusion criteria. Next, a thorough review of the full-text of remaining articles was done. The reference lists of all eligible articles and reviews were thoroughly scanned to identify papers additional studies for inclusion. Quality was assessed by abstracting information on the study population, measurement of WC, ascertainment of means and

95% confidence intervals (Table 3.1). Gender-specific WC, height and weight- means, standard deviation, or gender comparative estimates with their 95% confidence intervals were extracted or calculated from relevant studies and coded according to the combinations of the following divisions: (1) demographic factors: age range, gender, group (Aboriginal and non-Aboriginal Australians) (2) WC, height and weight according to gender.

Table 3.1Quality Assessment of Studies Included in Systematic Review

Author	Population Source		WC Ascertainment		
	Population-based cohort	Clinical-based cohort	Measured by Investigators	Self-reported	Not Stated
Aboriginal studies					
Bambrick, H.J (178)	X		X		
Burke et al (238)	X		X		
Hodge et al (196)	X		X		
Kondalsamy-Chennakesavan et al (12)	X		X		
Li & McDermott (146)	X		X		
Maple-Brown et al (239)	X		X		
Piers et al (98)	X		X		
Shemesh et al (157)	X		X		
Wang & Hoy (9)	X		X		
Non-Aboriginal studies					
Craig (240)	X		X		
Janus et al (241)	X		X		
Maclnnis et al (242)	X		X		
Piers et al (98)	X		X		
Snijder et al (243)	X		X		
Welborn (244)	X		X		
Molarius (245)	X		X		
Molarius (245)	X		X		
OAC (246)	X				X
OAC (246)	X				X
OAC (246)	X				X

Data synthesis and statistical analysis

WC mean estimates were stratified by gender as it has been shown that significant differences in WC levels exist between Aboriginal and non-Aboriginal males and females. Where possible, sample population WC mean estimates comparing males and females, as well as the 95% confidence intervals (CI) in males and females were directly obtained from original reports, otherwise 95% CI were calculated from extracted WC means and standard deviation estimates. We extracted data for participants without disease from studies that compared diseased and non-diseased people. Meta-analysis was conducted to assess heterogeneity among studies in the gender differences in WC, height and weight within Aboriginal and non-Aboriginal groups using the I^2 statistic by Higgins et al (247). STATA 12.0 was used for all analysis (248).

Ethical issues

Ethical clearance was not required for this review as we extracted data from already existing studies.

RESULTS

The search strategy yielded a total of 996 papers of which 894 were excluded (28 were duplicates). A total of 102 studies were retained because of eligible titles but after a thorough check of the abstract and results sections, fourteen of the studies were retained. There was an additional three articles identified and included by secondary searches of reference lists of included publications as well as Google scholar. Of the 88 studies that were excluded, fourteen presented BMI values but did not present a specific WC values; in nineteen studies, the prevalence and trends of the chronic disease outcomes were presented without evidence of WC levels; five were studies on women or pregnant women; three were studies on only men; fourteen gave overall WC values without separating the gender; nine had datasets from other included studies; nineteen were studies of children only; and five did not contain data (commentaries, narrative reviews etc.). Consequently, a total of 17 cross-sectional studies were retained for the final analysis. Figure 3.1 below illustrates the selection process of included articles.

A Systematic Flow Diagram of Study Selection Process

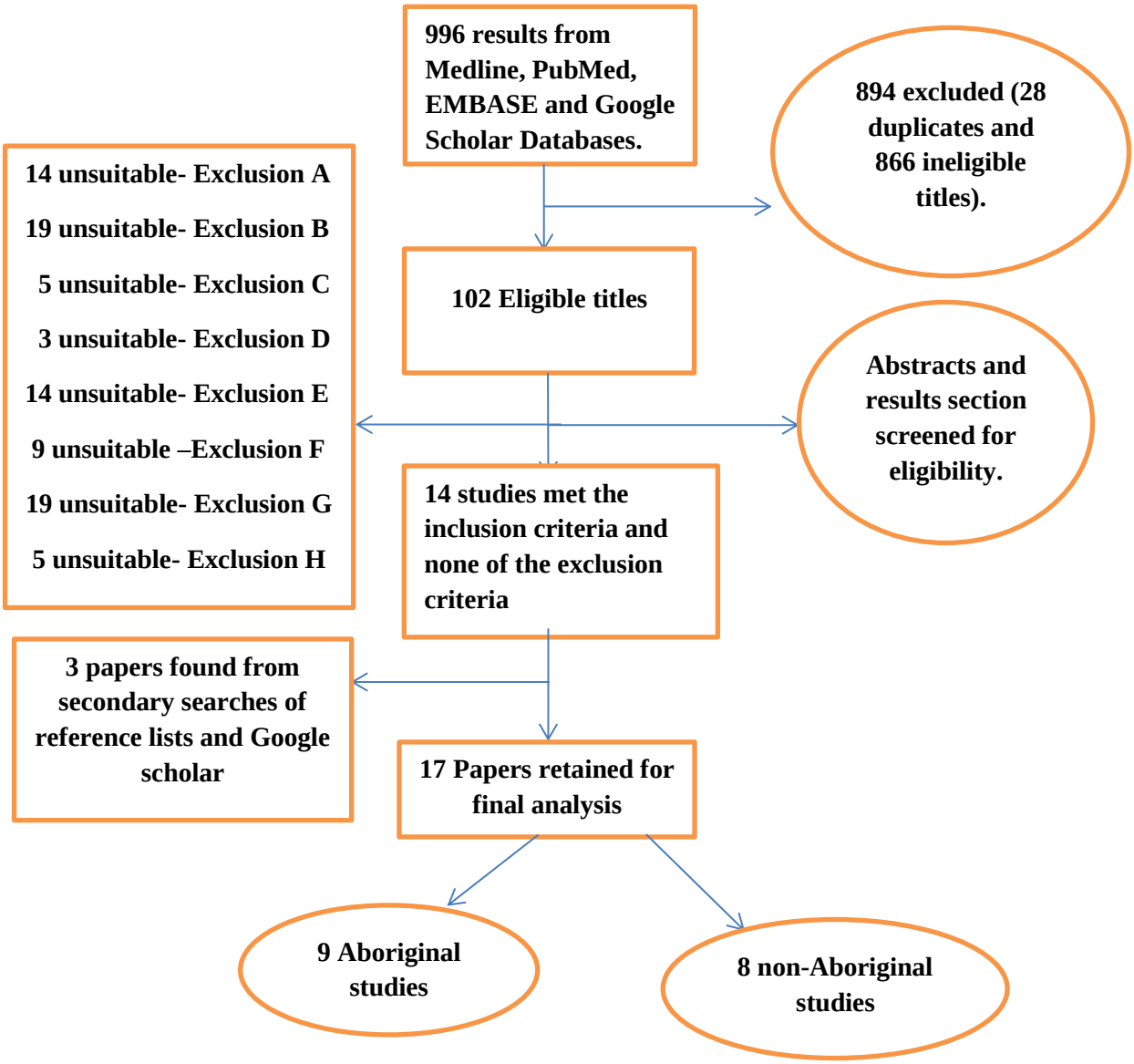

Figure 3.1 Study selection flow chart

Note: Exclusion criteria A- focused on chronic diseases without reporting population WC means or median. Exclusion criteria B- focused on the prevalence of chronic diseases and their relationship with WC but without WC population estimates. Exclusion criteria C- focused on women or included pregnant women in their analysis. Exclusion criteria D- were studies conducted to include men only. Exclusion criteria E- gave overall WC estimates without separating the gender. Exclusion criteria F- used the dataset from studies already included in the review. Exclusion criteria G- were studies focused on children. Exclusion criteria H- contained no data (commentaries and narrative reviews).

Characteristics of the study

Overall 17 cross-sectional studies were included in the final analysis with 9 focusing on the Australian Aboriginal population (9, 12, 98, 146, 157, 178, 196, 238, 239) and 8 on the non-Aboriginal Australians (98, 240-243, 245, 246). The participants included in these studies were aged between 15 and 88 years. The sample size ranged from 54 to 1641 in Aboriginal participants and from 393 to 41253 in non-Aboriginal participants. Aboriginal communities included were from different regions of Australia: one of the studies was conducted in Western Australia (Kimberley, Perth Aboriginal community) (238), one in south eastern Queensland (North Stradbroke Island and Redland bay and Torres Strait Island) (178), one in Central and Northern Australia (98), one in Northern Queensland (146) and five focused on the Northern Territory (NT) (9, 12, 157, 196, 239). Data relating to non-Aboriginal Australians were from several population based surveys including the AusDiab (Australian Diabetes, Obesity and Lifestyle Study) (243), MONICA (MONitoring trends and determinants of CAdiovascular Disease) study (245), Melbourne Collaborative Cohort study (MCCS) (242), Obesity in Asia Collaborative study (246), the third Risk Factor Prevalence Study of the National Heart Foundation of Australia (244), staff of Central Sydney Area Health Service (240), staff and students of Deakin University in Melbourne (98), and two cross sectional studies in the Great Green Triangle region of South-Eastern Australia (241).

Tables 3.2 and 3.3 present the summary mean values of WC, height and weight for both male and female Aboriginal and non-Aboriginal Australians.

Table 3.2 Descriptive summary of demographic characteristics and WC estimates of selected Aboriginal and non-Aboriginal studies

Author	Study year	Area of Residence	Age range (years)	Sample (n)	Mean WC (95%CI)- cm	
					Males	Females
Aboriginal studies						
Bambrick, H.J (178)	2000	South-East Queensland	18-66	117	99.9 (95.9-104.1)	109.0 (104.8-113.2)
Burke et al (238)	1988-1989	Western Australia	15-88	487	88.5 (86.9-90.1)	94.4 (92.4-96.4)
Hodge et al (196)	2003-2005	Northern Territory	>=15	512	99.9 (97.8-102.0)	97.5 (95.7-99.3)
Kondalsamy-Chennakesavan et al (12)	2000-2003	Northern Territory	25-74	814	92.2 (90.9-93.5)	96.7 (95.4-98.1)
Li & McDermott (146)	1999-2001	Northern Queensland	15-74	1641	89.7 (88.7-90.8)	92.2 (91.1-93.3)
Maple-Brown et al (239)	2001-2002	Northern Queensland	47	54	91.1 (84.5-97.8)	94.1 (90.2-98.0)
Piers et al (98)	1995-1997	Central & NE Australia	18-35	250	79.7 (78.1-81.3)	77.7 (75.7-79.7)
Shemesh et al (157)	2001-2003	Northern Territory	>=15	379	82.4 (80.3-84.4)	86.6 (84.6-88.5)
Wang & Hoy (9)	1992-1995	Northern Territory	18-74	915	86 (84.8-87.2)	91 (89.6-92.4)
Non-Aboriginal studies						
Craig (240)	2001	Sydney	26-47	393	92.7 (90.9-94.5)	80.7 (78.9-82.5)
Janus et al (241)	2004-2005	Victoria & South Australia	25-74	806	101.2 (99.8-102.5)	92.2 (90.8-93.7)
Maclnnis et al (242)	1990-1994	Melbourne (MCCS)	40-69	5879	91.7 (91.3-92.1)	78.0 (77.7-78.3)
Piers et al (98)	-	Melbourne	18-35	147	80.7 (78.4-83.0)	68.5 (67.5-69.5)
Snijder et al (243)	1999-2000	AusDiab	>=25	8400	96.3 (95.9-96.7)	83.4 (83.0-83.8)
Welborn (244)	1989	Metro Centres in Australia	20-69	9206	90.0 (89.7-90.3)	77.0 (76.7-77.3)
Molarius (245)	1987-1992	Newcastle-MONICA Project	25-64	1349	95.0 (94.2-95.8)	83.0 (82.0-84.1)
Molarius (245)	1987-1992	Perth- MONICA Project	25-64	1272	92.0 (91.3-92.7)	78.0 (77.2-78.8)
OAC (246)	2002	OAC	26-66	9276	90.4 (90.1-90.7)	76.5 (76.2-76.8)
OAC (246)	2002	OAC	26-66	11104	97.5 (97.2-97.8)	85.4 (85.1-85.7)
OAC (246)	2002	OAC	26-66	41253	93.5 (93.4-93.6)	80.0 (79.9-80.1)

Note: All estimates of waist circumference (WC) are in centimetres (cm). Study year- Year the study was conducted.

QLD: - Queensland, WA: - Western Australia, ACT: - Australia Capital Territory, AUS: - Australia, NE: - North-Eastern, LCI: - Lower Confidence Interval, UCI: - Upper Confidence Interval, AusDiab: - Australian Diabetes, Obesity and Lifestyle Study, MONICA:- MONitoring trends and determinants of CAdiovascular Disease survey, MCCS- Melbourne Collaborative Cohort Study, OAC:- Obesity in Asia Collaboration

Table 3.3 Descriptive summary of the height and weight estimates of selected Aboriginal and non-Aboriginal studies

Author	Year	Area of Residence	Mean Height (cm)		Mean Weight (kg)	
			Males	Females	Males	Females
Aboriginal studies						
Bambrick, H.J (178)	2005	South-East Queensland	-	-	-	-
Burke et al (238)	2007	Western Australia	-	-	70.3	65.5
Hodge et al (196)	2010	Northern Territory	-	-	-	-
Kondalsamy-Chennakesavan et al (12)	2008	Northern Territory	174.7	163.7	74.5	71.2
Li & McDermott (146)	2010	Northern Queensland	171.5	160.1	72.7	67.8
Maple-Brown et al (239)	2005	Northern Queensland	174.8	161.3	71.2	65.7
Piers et al (98)	2003	Central & NE Australia	172.1	160.2	66.8	57.3
Shemesh et al (157)	2007	Northern Territory	-	-	-	-
Wang & Hoy (9)	2004	Northern Territory	-	-	67.8	63.0
Non-Aboriginal studies						
Craig (240)	2001	Sydney	177.0	163.8	83.0	69.2
Janus et al (241)	2007	Victoria & South Australia	175.6	162.4	87.1	75.8
Maclnnis et al (242)	2013	Melbourne (MCCS)	173.5	160.8	80.2	67.2
Piers et al (98)	2003	Melbourne	178.8	165.8	76.3	60.2
Snijder et al (243)	2004	AusDiab	176.3	162.8	83.7	69.3
Welborn(244)	2003	Metro Centres in Australia	175.0	162.0	79.0	65.0
Molarius(245)	1999	Newcastle- MONICA Project	-	-	-	-
Molarius(245)	1999	Perth- MONICA Project	-	-	-	-
Obesity in Asia Collaboration (246)	2008	Obesity in Asia Collaboration	-	-	-	-
Obesity in Asia Collaboration (246)	2008	Obesity in Asia Collaboration	-	-	-	-
Obesity in Asia Collaboration (246)	2008	Obesity in Asia Collaboration	-	-	-	-

Centimetres (cm). Kilogram (kg).

Meta-analysis

Waist circumference: - The mean gender differences of the WC levels of Aboriginals and non-Aboriginals are illustrated in Figure 3.2. Seven of the nine studies in Aboriginal Australians showed that women had higher WC levels than men while two showed that men had higher WC than women. On average, WC was 3.1 cm (95% CI: 2.3-3.9, P<0.001) higher in women than in men. On

the other hand, in non-Aboriginal Australians, all studies consistently showed that men had higher WC than their women counterparts with an average difference of 13.2 cm (95% CI: 13.1-13.4, P<0.001). Heterogeneity tests were significant with I^2 = 82.6% within Aboriginal studies (P<0.001) and I^2= 90% (P<0.001) within non-Aboriginal studies. The pooled average WC levels were 89.1 cm (range: 79.7 to 100.0 cm) for Aboriginal men, 92.9 cm (range: 77.7 to 109.0) for Aboriginal women, 93.5 cm (range: 80.7 to 101.2 cm) for non-Aboriginal Australian men and 80.3 cm (range: 77.0 to 92.2 cm) for non-Aboriginal women.

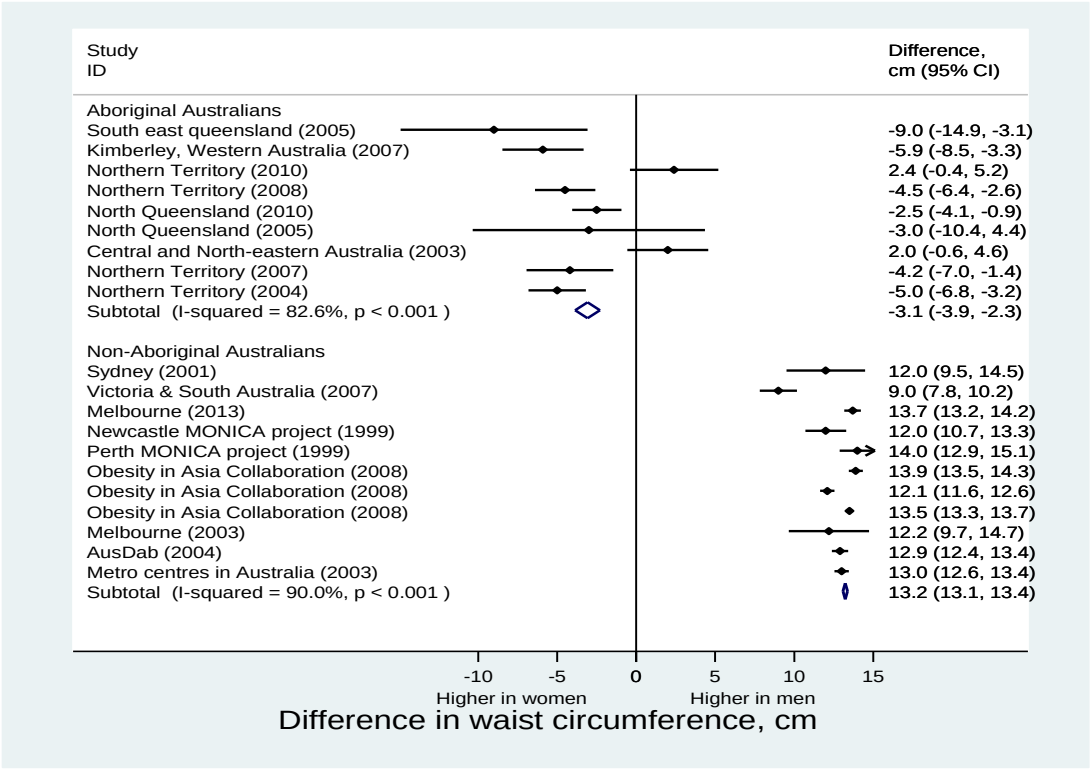

Figure 3.2 Meta-analysis and pooled waist circumference estimates (cm) of Males and Females in Aboriginal and non-Aboriginal communities

Height: - Four Aboriginal studies and six non-Aboriginal studies gave height estimates for males and females. Generally, height estimates in both groups showed males were taller than the females by at least 11 cm (Figure 3.3). On average, pooled height estimates for Aboriginal males and females were 173.2 cm and 161.3 cm respectively and men were 11.4 cm (95% CI: 10.8-12.0) taller than women. The gender differences in height was homogenous (I^2= 22.7%, P=0.27). Pooled height mean estimates for non-Aboriginals was 176 cm for males and 162.9 cm for females indicating

males had 13.1 cm (95% CI: 12.9-13.3) height advantage over the females. However, the difference in height was not significant (I^2= 58.6%, P=0.03).

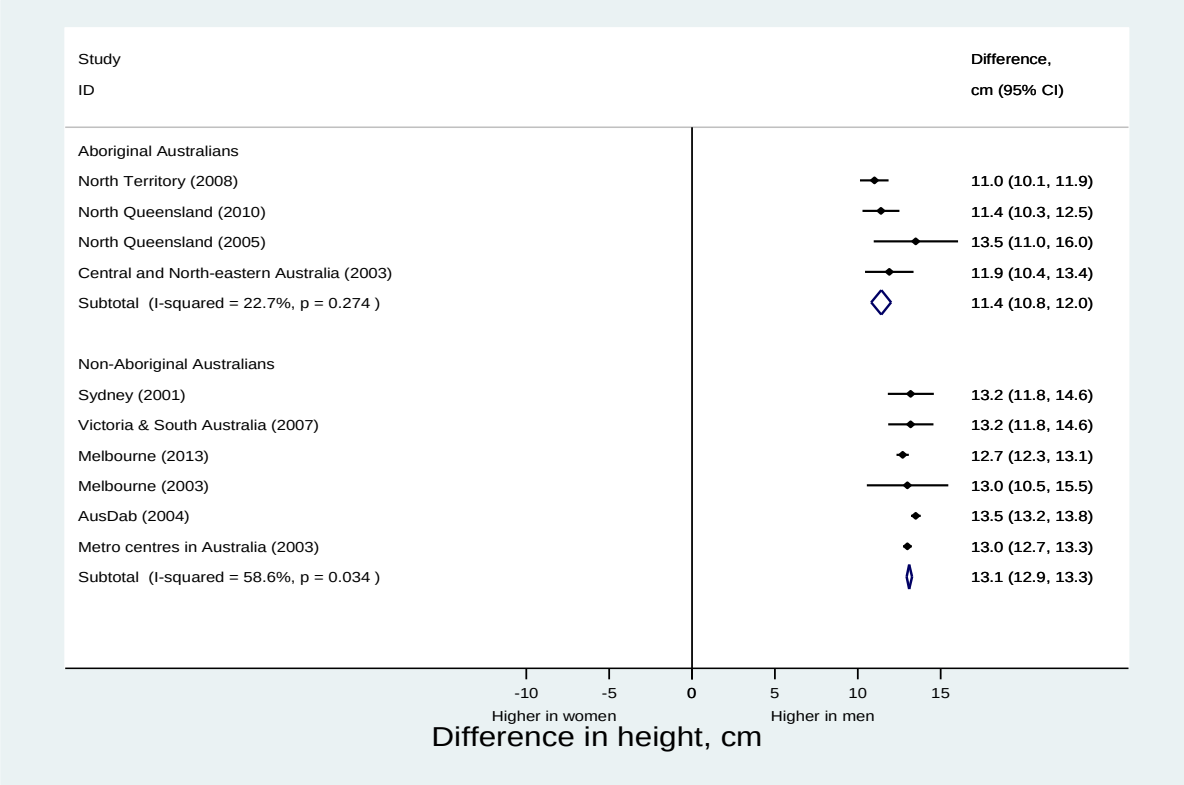

Figure 3.3 Meta-analysis and pooled height estimates (cm) of Males and Females in Aboriginal and non-Aboriginal communities

Weight: - Twelve studies reported weight estimates from Aboriginal (n=6) and non-Aboriginal (n=6) communities. Similar to what was observed for height, males generally had higher weight estimates than females (Figure 3.4). For the Aboriginal group, pooled weight estimates showed females had lower mean weight values than males with 65.1 kg versus 70.1 kg and men were 5 kg (95% CI: 4.4-5.7) heavier than women. For the non-Aboriginal populations, on average, males had 81.6 kg weight and weighed 13.6 kg (95% CI: 13.3-13.9) more than the females whose average weight was 67.8 kg. Non-Aboriginal males were 11kg heavier than their Aboriginal male counterparts; however, the difference among the females was relatively small (2.7 kg), with non-Aboriginal females having the higher value. Gender differences in weight were heterogeneous among studies within Aboriginal and non-Aboriginal groups.

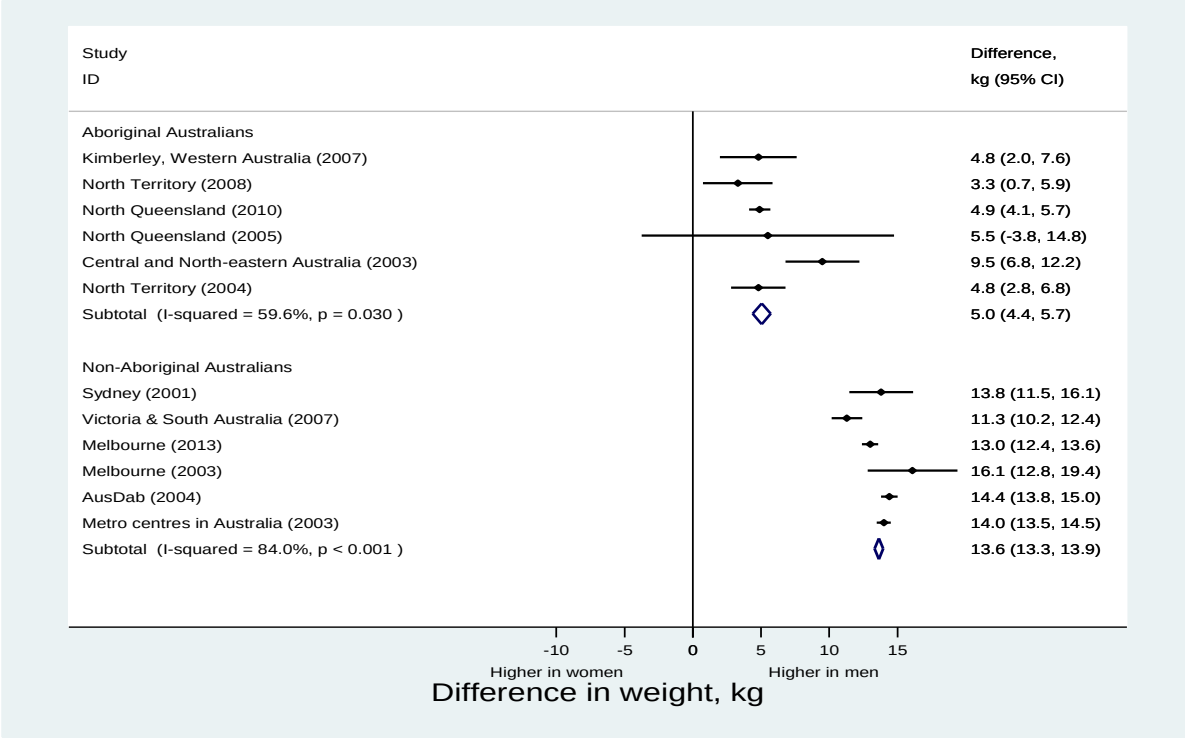

Figure 3.4 Meta-analysis and pooled weight estimates (kg) of Males and Females in Aboriginal and non-Aboriginal communities

DISCUSSION

This review study has shown differences in WC levels between Aboriginal and non-Aboriginal Australians. It appears to be a common phenomenon that Aboriginal women have significantly higher WC levels than Aboriginal men, although there was significant heterogeneity among different studies. In the non-Aboriginal Australian population, WC in men was over 10 cm higher than in women.

In seven of nine Aboriginal studies, women had higher WC levels than men by a range of 2.5 to 9.0 cm. However, this remarkable observation was not explained by the size of their body frame as Aboriginal women were on average 11 cm shorter than Aboriginal men, similar to that of the 13cm in the non-Aboriginal Australian population. Furthermore, Aboriginal males had greater weight than the females in the studies that presented weight values. Differences in weight estimates for males and females ranged from 3.3 kg (12) to 9.5 kg (98). The higher WC in Aboriginal women with lower height and weight levels indicated that they had higher abdominal fat than Aboriginal men.

The phenomenon of higher waist circumference in women has also been reported in some other populations in Tonga (249) and Oman (139). They showed females had higher WC estimates or cut-off points than males but the differences between the genders within studies did not appear to vary significantly.

Although regional differences (urban and rural) were not the focus of this review, it is worthy of note that the significant heterogeneity within Aboriginal and non-Aboriginal groups could be due to differences among study populations. WC estimates were lower for Aboriginals residing in the rural regions in comparison to those in the urban areas. On the other hand, non-Aboriginals in the rural areas showed higher WC levels than those in the urban settings. We cannot elucidate on the reasons for these remarkable differences; however, possible explanations are the effects of urbanization due to the western lifestyle which could be positive or negative.

A number of studies conducted earlier in Australia on Aboriginals and non-Aboriginals reported WHR and BMI rather than WC (234, 235, 250). BMI measures relationship between weight and height and does not adequately reflect fatness (or adiposity) (251); and WHR is less dependent on body size and height, therefore may be inappropriate to assess fatness and weight loss as theoretically it could remain unchanged during weight loss (143). These two indices may misclassify highly muscled individuals with high muscle mass in the body and around the hip region (244) in the category of overweight. On the other hand, WC relates to both body weight and fat distribution identifying it as the best indicator for changes in intra-abdominal fat during weight loss (115). Furthermore, measurement of WC is simple when compared to WHR, and more reliable and feasible compared to WHR (115, 127). Therefore, our focus on WC which several studies have shown to be a better index for predicting some chronic diseases in Aboriginal communities is unlikely to lead to a bias in both Aboriginal and non-Aboriginal populations.

We utilized measurements of weight and height across studies instead of the commonly used BMI, to assess how these two relate to WC in both populations, particularly among Aboriginals. While none of these two measures solely explain frame size on its own, we are keen to know if measurement of each could explain reasons for the size of WC in these populations.

Our findings have several potential implications. First, Aboriginal women may be more sensitive to lifestyle transition which may be due to sedentary lifestyle. However, the paucity of information about the daily routine of Aboriginal women is conflated with the limited amount of intervention research among this Australian group, resulting in little evidence about whether lifestyle or genetics is responsible for the higher WC levels among women. Also, with the high levels WC reported as predictor of the risk of chronic diseases among Aboriginals (9, 178) and Aboriginal women at higher risks of diabetes and coronary heart disease than men (252-254), further analysis is needed to assess to what degree the increased risk of chronic diseases in Aboriginal women is contributable

to the higher WC levels. Second, our finding of the higher WC levels in Aboriginal women and further understanding why such a phenomenon exists in this population are important for planning effective intervention efforts.

Strengths and Limitations

To our knowledge, this is the first systematic review comparing WC, height and weight levels of Aboriginal and non-Aboriginal Australians. Also, no study was identified outside Australia that compared WC differences between Indigenous and non-Indigenous groups.

There are limitations to our review. First, there is a possibility that not all the relevant studies have been included in this review, however, the search strategy was broad, identified studies and reference lists of selected studies were thoroughly checked by the authors. Second, few studies have been conducted on waist circumference levels of Indigenous Australian people making it impossible to compare estimates of diverse Indigenous Australian communities in other parts of the country. There is not adequate information from other regions to establish enough evidence of the differences in levels of WC in the different Australian regions; therefore, the Aboriginal population for this review was restricted to studies mostly from Australian Northern Territory, Queensland and one from Western Australia that met the inclusion criteria. The studies may over-represent Aboriginal people in remote communities. Although our results may not be representative of the whole Australian Aboriginal group, they provide novel ethnic-based information comparing WC, height and weight of males and females Australian Aboriginals and non-Aboriginals. Third, WC measurement across studies was a potential measurement bias as methods of measuring varied across studies and also depended on the accuracy of individuals carrying out the measurements. Fourth, age was imbalanced across studies as most studies did not stratify into age groups but gave the age range of participants. There is a possibility of age biasing the measured outcome as older age is commonly associated with greater WC and poorer health outcomes. Therefore the younger participants in studies were likely to have lower WC values than those in older age group. However, none of the study acknowledged controlling for age as a confounder, and as we do not have access to original data, age was not adjusted for in this study.

We did not control for group factor (Indigenous and non-Indigenous) as we separated and focused on Aboriginals and separated Aboriginals from TSI for studies that worked on indigenous group (146). Although, Hodge et al (2010) utilized data from the DRUID study (255), where 85.85% of participants were Aboriginals and 4.95% were TSI, this is unlikely to affect the our results since the proportion of Aboriginals was high and a sample was drawn from the entire DRUID study which

will further reduce the number of TSI participants. Likewise for the non-Aboriginal group, we targeted only Australians of European descent.

We were unable to compare incidence and prevalence of central obesity which have been on the increase over time between the two groups. This is due to the few numbers of studies selected for this review as well as the large amount of variability about the time point of studies' conduction. A working cut-off standard for WC is non-existent for Aboriginals as the present standard by Lean et al (115) classified more Aboriginal overweight than by BMI criteria (147). This could potentially affect the comparison of the increasing prevalence of central obesity that is apparent for this Australian group and the non-Indigenous population. In their study of Indigenous Australian group, Li & McDermott stated a contrast exists in the optimal WC cut-offs found in North Queensland and the existing cut-offs (146). Nonetheless, four of the Aboriginal studies selected used the existing standards while others provided no WC cut-off definition. Lastly, while we did not include studies that focused on pregnant women, we are not able to ascertain if our analysis comprise of those pregnant as none of the study stated whether pregnant women were included in the analysis.

CONCLUSION

This review found considerable variation in WC of males and females and Aboriginal and non-Aboriginal Australians. Aboriginal females had higher WC levels than the males and these differences were independent of both height and weight as the males consistently had higher weight and height estimates. The findings of this review are vital for informing public health policies and programs more focused and targeted to Aboriginal women in the control of central obesity which is a risk factor for developing chronic diseases.

CHAPTER 4
RESEARCH METHODS

4.1 INTRODUCTION

This chapter describes briefly the study population and an overview and description of datasets used for the original research in the thesis. This is followed by the study design used in sample selection for the subsequent chapters. Next, study variables which include the exposure, outcome and confounding variable are described. Finally, discussions on the process of data management, ethical approval and statistical analysis are provided.

4.2 STUDY POPULATION

Tiwi Islands are remote Aboriginal populations located in Australia's Northern Territory (NT), 80 km to the north of Darwin. The NT is a federal Australian territory in the centre and central northern regions. The Tiwi Islands comprise Melville Island, Bathurst and nine smaller uninhabited Islands. There are approximately 2,228 people on the Islands, based on the 2001 Census. The map of the Island and surrounding communities is presented in Figure 4.1.

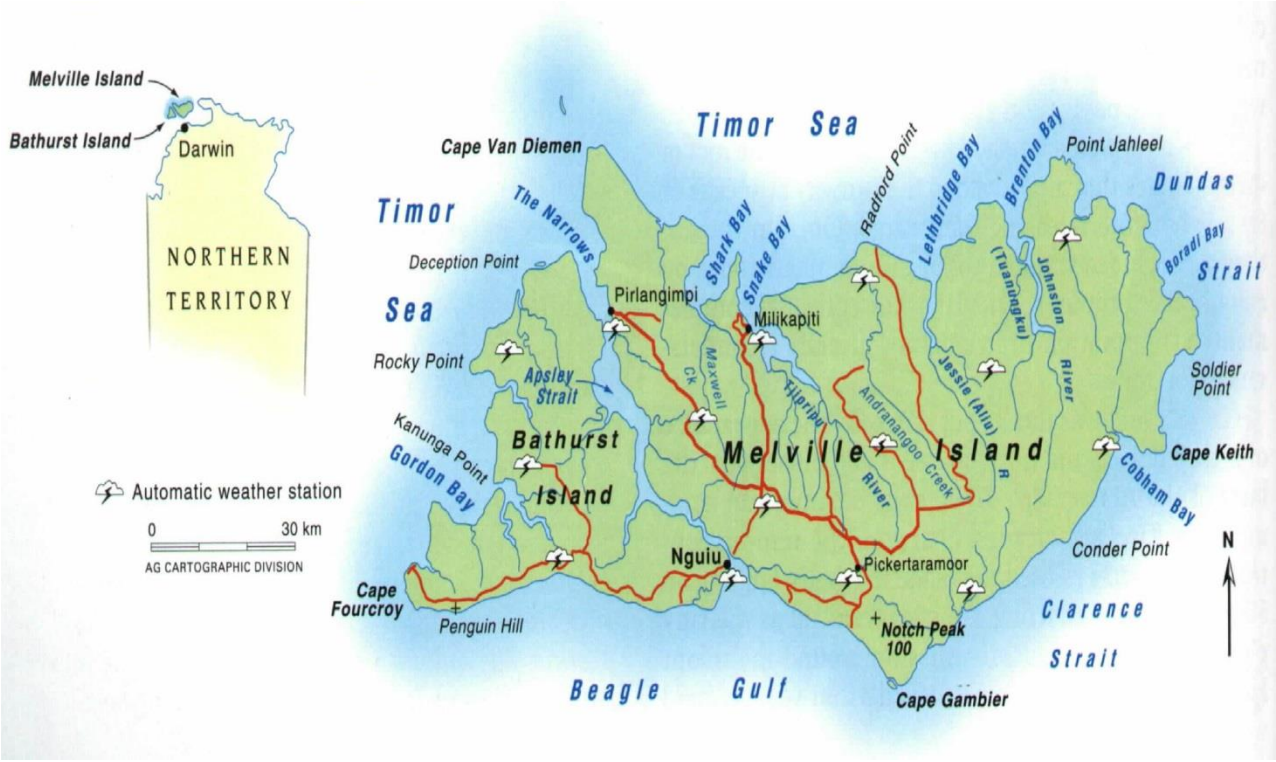

Figure 4.1 A map of the study population and surrounding communities

4.2.1 Baseline dataset

The baseline data was collected by Prof Wendy Hoy and her team, which involved population-based baseline records of 1490 participants in Tiwi Islands from 1992 to 1998. Over 80% of the population are of Tiwi origin. Health screening examinations were offered to every Aboriginal individual aged between 5 and 76 years, who resided in the communities on the Islands. People in hospital, in old age care, on dialysis, resident elsewhere, or out of community at the screening period did not participate in the health screening. Over 80% of eligible adult community members were participants at the baseline screening examination (256). Data were collected at baseline examination through interview questionnaires. Some of the baseline data included age (years), waist circumference (WC- cm), weight (kilograms), height (centimetres), sex (male or female), smoking status (smoker or non-smoker), alcohol consumption status (drinker or non-drinker), and diabetes status (yes or no). Body size measurements were single measurements made by one field worker and two Aboriginal health workers. More detailed descriptions of the baseline data collection have been presented in earlier studies (9, 147, 257, 258). Individuals were included in the thesis analysis if they fitted the following inclusion criteria:

1. Participated in the baseline health screening program
2. Were ≥18 years old at baseline screening
3. Had WC data recorded at baseline examination

Of 1490 participants at the baseline screening survey, 976 were adults aged between 18 and 76 years, which represented over 70% of the (1,328) total age-eligible population, based on the 2001 Census. As adults were the focus of this thesis, data of the 976 adults were utilized. Out of 976 adults, a total of 935 individuals (474 males and 461 females) had WC measures at baseline and were eligible to participate and included in this research project work. Figure 4.2 is a flowchart of the process of participants' selection for analysis.

The mean ages of the eligible participants were 33.9 years (ranging from 18 to 73) for males and 36.9 years (ranging from 18 to 76) for females. Their WC ranged from 63 to 138 cm in males and 60 to 135 cm in females. WC means were 87.6 cm (SD=13.0) for adult males and 91.0 cm (SD=14.5) for females. Body mass index (BMI) mean was 23.6 kg/m^2 for males and 24.7 kg/m^2 for females.

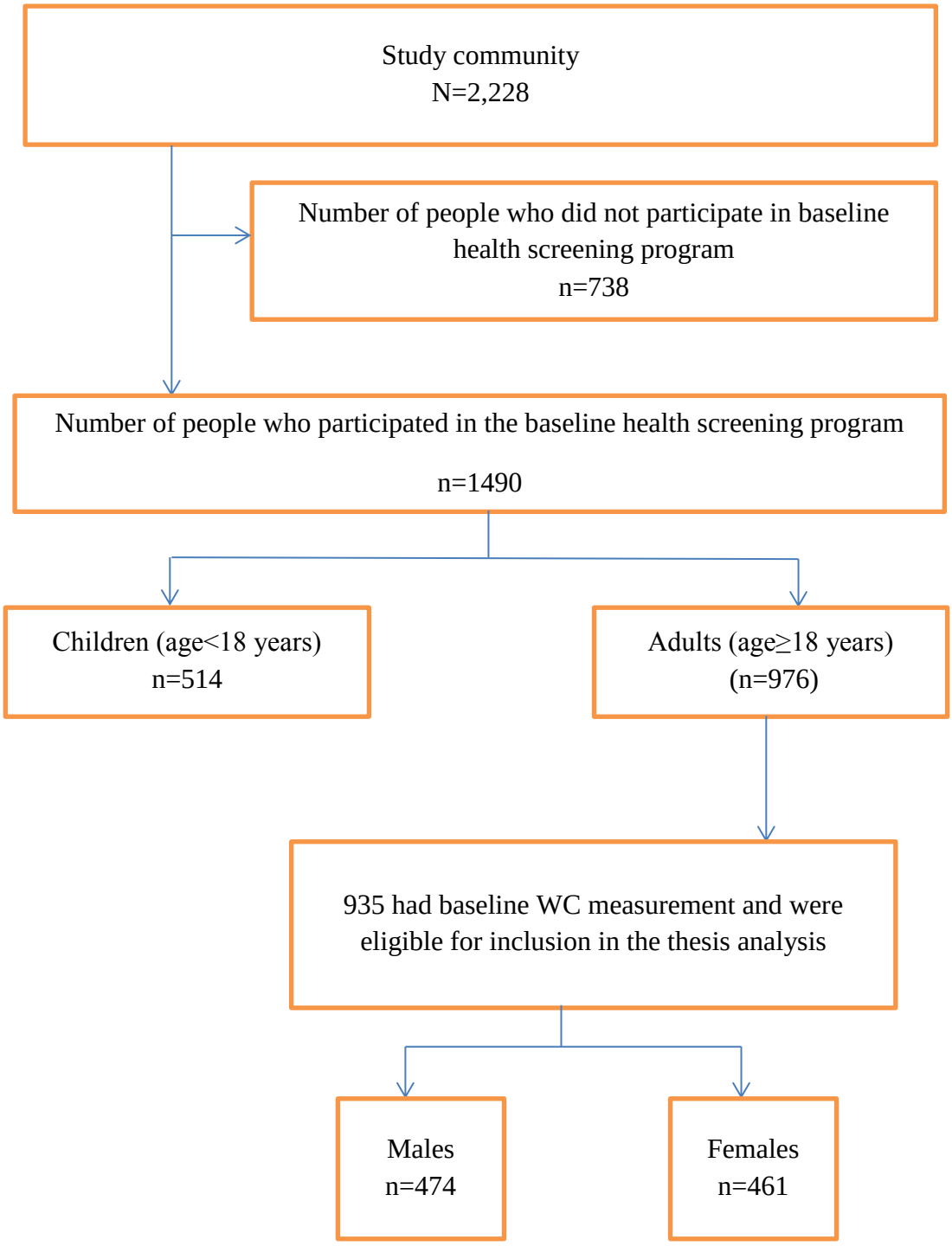

Figure 4.2 Study selection process

4.2.2 Follow-up datasets

4.2.2.1 Hospitalisation dataset

The hospitalisation dataset used for this study was obtained from the Northern Territory Department of Health. It included the records of hospitalisation and emergency admissions of individuals who had been hospitalised within the public health system in the Northern Territory. Each condition diagnosed during the hospitalisation was recorded according to the International Classification of Disease: *English Revision International Classification of Diseases (*ICD-9 code) *code* and *International Statistical Classification of Diseases, 10th Revision* (ICD-10- AM code). Hospitalisation data were collected for 20 years (from 1992 to December 2012). To identify morbidity outcomes, patients' hospitalization records were filtered using ICD-9 and ICD-10 codes. A morbidity event was defined as the first identified ICD code representing the disease of interest after baseline examination. Each participant was identified through hospital admissions by Hospital Registration Number (HRN).

4.2.2.2 Mortality dataset

Mortality data from January 1992 to December 2010 among study participants were collected by the Centre of Chronic Disease Research team led by Prof Hoy. Death records were obtained through community networks, records at the local clinics and hospital and the death registry records. There were 218 adult deaths during the follow up period. Death causes were divided into:

1. Injury deaths (including acute intoxications, accidents, drowning, suicide, homicide, etc.)
2. Natural deaths included fatality from old age, cardiovascular (heart attack, cardiac arrest, acute myocardial infarction, congestive heart failure, pulmonary oedema, aortic valve disease, atherosclerosis, coronary artery disease), diabetes, renal (death with terminal renal failure without dialysis, maintenance dialysis commenced, acute renal failure), pulmonary (pneumonia, bronchitis, bronchiectasis, respiratory failure, chronic obstructive pulmonary disease, primary pulmonary hypertension, acute respiratory disease), cancers (throat, breast, larynx, nasal, lung), others (liver failure, rheumatic heart disease, cirrhosis, colloid cyst, congenital abnormalities, sepsis, epilepsy).

The methods of the mortality data have been described in detail elsewhere (257). Death outcomes were identified to assess their relationship with WC and BMI to provide mortality estimates in Chapter 7.

4.3 STUDY DESIGN

Prospective cohort study design

This research project was a prospective cohort study where all adults (≥18 years old), with WC measurements and free of the outcome of interest at baseline examination were followed up for a maximum of 20 years for disease or mortality outcomes. This study design allows evaluation of the temporal sequence between exposure and outcome; and permits direct calculation of incidence rates in both the exposed and unexposed groups.

4.4 SAMPLE SELECTION

4.4.1 Disease outcomes

All participants were followed-up from baseline screening examination until December 2012 in the hospitalisation dataset. For events of CVD and Type 2 diabetes, the first ever incident cases for participants were included in the analysis. For individuals who had been diagnosed as having an endpoint event during the follow-up period, their follow-up duration was calculated as the period from the time of the baseline screening visit when WC was measured to the time of the outcome diagnosis. Those who had survived and had not reached the endpoint were considered "censored" on 31 December 2012. Participants who had been free from the endpoint event and died from other causes before the end of the follow-up were censored at the time of death.

4.4.2 Mortality outcomes

4.4.2.1 All-cause mortality: The mortality records were ascertained from mortality records at the local clinics and hospital records. Participants were followed up from baseline examination (1992-1998) to December 2010 as recorded on the mortality dataset. Those who died during the follow-up time were considered to have had the event, while those who had not reached the endpoint were considered 'censored' at December 2010.

4.5 STUDY VARIABLES

4.5.1 Exposure Variables

4.5.1.1 Waist circumference (WC)

WC was measured on a horizontal plane using a tape measure while the participants were wearing light clothing. WC was measured midway between the lower border of the ribs and the iliac crest (9). As there are no WC cut-points to classify normal, overweight and obese for Aboriginal people, baseline WC as a continuous variable was grouped (into quartiles or tertiles) separately for males and females in the analyses.

4.5.1.2 Body mass index (BMI)

BMI was calculated as weight divided by height squared (kg/m^2). For the purpose of the analysis for mortality, we categorised participants by baseline BMI into sex-specific tertiles. BMI tertiles for males were as follows: tertile 1= 14.20-20.98 kg/m^2, tertile 2= 20.99-25.10 kg/m^2 and tertile 3= 25.11-41.80 kg/m^2. BMI tertiles for females were as follows: tertile 1= 13.58-21.14 kg/m^2, tertile 2= 22.22-27.12 kg/m^2 and tertile 3= 27.14-43.74 kg/m^2.

4.5.2 Outcome variables (Disease outcomes)

Morbidity outcomes for this study were CVD and Type 2 diabetes, as ascertained from hospitalization records. The diseases were determined according to the 9th (ICD-9) or 10th (ICD-10) revisions of the *International Classification of Diseases* (ICD-9 and ICD-10) codes (259, 260) as illustrated in Table 4.1.

Table 4.1 ICD 9 and 10-AM codes

Disease	ICD 9 code	ICD 10 code
CVD	390-458	I00-I99
Type 2 diabetes	250	E11

4.5.3 Covariates

A number of confounding factors were considered in the analyses, including age (years), cigarette smoking status (smokers and non-smokers) and alcohol consumption status (drinkers and non-drinkers), as measured at the baseline examination. These confounding factors were controlled for during the analysis stage through multiple regression analysis.

4.6 DATA MANAGEMENT

After baseline screening, all participants were de-identified and each participant was assigned a unique Study Identification Number (SIN). Each individual's SIN number was also assigned to their hospitalization record(s) and mortality record (for those that had died). The SINs were used to merge the baseline data to the hospital and mortality data to identify morbidity and mortality outcomes.

All data were coded and entered into Stata. Participants were grouped according to gender-specific WC categories or BMI groups. Datasets were stored in computers that require passwords to access them to ensure confidentiality.

4.7 ETHICAL APPROVAL

The protocol of the baseline screening program was approved by the Ethics Committee of the Menzies School of Health Research and Territory Health Service, and the Aboriginal community. This project was approved by the Behavioural and Social Science Ethical Review Committee of the University of Queensland (#2011001232). All participants gave informed consent to participate.

4.8 STATISTICAL ANALYSIS

Means (standard deviations) were calculated for continuous variables such as age, BMI, WC and waist-to-hip ratio (WHR). Categorical variables including smoking (smokers and non-smokers) and alcohol consumption (drinkers and non-drinkers) were expressed in numbers (percentages).

To assess the association of WC and each of the outcomes (CVD, Type 2 diabetes and mortality), hazard ratios (HRs) and their 95% confidence intervals were estimated using the Cox proportional-

hazards model adjusting for potential confounding factors (age, smoking and alcohol consumption status). The formula used for fitting the Cox regression model was:

$$h(t|x_j) = h_0(t)\, exp(x_j\ \beta_x)$$

where $h_0(t)$ is the baseline hazard, X_j represents WC or BMI or WHR variables and β_x is the regression coefficients to be estimated from the data (261).

The modelling that takes place in the model is inherent to the linear predictor below (261):

$$x\beta_x = \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k, \text{ for k covariates}$$

Baseline WC, BMI and WHR values were converted into gender specific z-scores (or SD score) thereby eliminating the differences in units to ensure that the magnitude of the HR results for both measures were directly comparable (262), and also to assess which had the strongest association with disease outcomes (263).

First, the means (μ) and SDs (σ) of each WC, BMI and WHR were calculated separately for males and females. Next, the mean and SD of the measure (WC or BMI or WHR) and gender (male or female) to be examined was substituted into the formula (264) below:

Z-score (or SD-score) = (measured value-average value of the reference population)/standard deviation value of reference population

$$\text{Z-score} = (x-\mu)/\sigma$$

An interaction term was included in the model to examine the difference between males and females in the association between WC and diseases as well as mortality (265).

The Weibull accelerated failure-time model was fitted to assess the gender-specific absolute risk of each disease outcome according to different WC and age values (261).

Absolute risk of each outcome was presented graphically. The probability of having an endpoint according to WC values up to a specific time point was calculated as:

$$Absolute\ risk\ = 1 - \exp\left[-\left\{exp\left(-\beta_0 - X_j\,\beta_j\right)\,t_j\right\}^p\right]$$

Where β_0 and β_j are coefficients from the Weibull model, p is an ancillary shape parameter from the data, t is time, and X_j represents WC variables including linear and nonlinear components and other covariates (261). All analyses were carried out on Stata (248). Statistical significance was set at $P<0.05$ and the stability of the estimates were shown by 95% confidence interval (CI).

CHAPTER 5

WAIST CIRCUMFERENCE AND CARDIOVASCULAR DISEASE RISK AMONG ABORIGINAL PEOPLE IN A REMOTE AUSTRALIAN COMMUNITY

5.1 INTRODUCTION AND AIM

Aboriginal people in Australia have a high risk of developing cardiovascular disease (CVD). CVD contributes significantly to the reduced life expectancy of Aboriginal people. Waist circumference (WC) is an important risk factor that has been associated with the risk of CVD in Aboriginal communities. Creating tools to alert individuals of the risk of CVD and associated risk factors such as WC among others, in Aboriginal communities has the potential to make a significant difference in CVD-related health outcomes. Presently, the risk chart for identifying people at high risk of CVD in Australia targets only middle-aged Aboriginals aged 35 to 44 years, without considering body habitus such as WC. There is a need to bridge the gap on the risk of elevated WC and CVD among Aboriginal people in Australia.

Therefore, the aims of this chapter are:

1. To assess the association between WC and CVD among individuals who participated in the baseline community screening program from 1992 to 1998 in Tiwi Islands.
2. To examine which of WC, body mass index (BMI) and waist-to-hip ratio (WHR) has the strongest association with CVD in the study population.
3. To provide a simple tool which shows levels the absolute risk of CVD with changes in WC and age.

In this chapter, Section 5.2 provides a summary of my contributions to the study. Results from the study have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O, Hoy W and Wang Z: Prediction of cardiovascular disease risk using waist circumference among Aboriginals in a remote Australian community. *BMC Public Health 2015;* 15(1): p. 57.

5.2 CONTRIBUTION TO THE STUDY

I, with the assistance of Dr Wang formulated the concept of the study. I was responsible for the data management, data analysis and interpretation of the results, with close supervision by Dr Wang. I was also responsible for writing the manuscript, taking into account the comments and suggestions of Dr Wang and Dr Hoy.

ABSTRACT

Background

Elevated waist circumference (WC) is an important risk factor for cardiovascular disease (CVD). Aboriginals in Australia are at higher risk of CVD compared to non-Aboriginals. We examined the association between waist circumference and CVD, and developed a model for projecting absolute risk of cardiovascular disease using WC and age in one high risk Australian Aboriginal community.

Methods

We followed up 920 (470 men, 450 women) participants (more than 80% of the eligible population) aged 18 to 76 years, without CVD at baseline, for up to 20 years. Hazard ratios were estimated using Cox proportional hazards models adjusting for potential confounding factors. Absolute risk was estimated using the Weibull regression model.

Results

Of 920 study participants, 156 males and 177 females developed CVD in the follow-up period. Incidence rates for males and females in the 4th WC quartile (Q4) were 38.3 (95% CI: 29.6-49.7) and 47.2 (95% CI: 37.1-60.3) per 1,000 person-time respectively. Crude hazard ratios of CVD for Q4 WC group using Q1 (quartile 1) as the referent quartile were 2.9 (95% CI: 1.8-4.6) for males and 3.5 (95% CI: 2.2-5.5) for females. Association remained after controlling for age, smoking status and alcohol drinking status (HR = 1.8 for males and HR = 3.1 for females). At 45 years of age with baseline waist circumference of 100 cm, a male had an absolute CVD risk of 32.5%, while a female had a 30.6% risk of the disease.

Conclusions

Risk of CVD among participants increased with increasing WC, and the relationship was accentuated with increasing age. The prediction model provides a tool for understanding the combined effects of WC with age on CVD events in the Australian Aboriginal community. It is simple and easily understood and will assist in identifying individuals at risk of CVD in relation to WC values.

INTRODUCTION

Cardiovascular disease (CVD) is the second largest contributor to the total disease burden in Australia, accounting for about 16% of the total disease burden and recorded as the underlying cause of 46,100 and 45,600 deaths in 2009 and 2011 respectively (266-268). Inequality exists in the number of those affected by CVD with greater impact on the Aboriginals than non-Aboriginals in Australian (267, 269, 270). Among the Australian Aboriginal population, CVD is the leading cause of disease burden and deaths and lists as one of four chronic conditions that accounts for 70% of the indigenous Australian health gap (266). Australian hospitalization records for CVD were reported at about 1.7 times among Aboriginals in comparison to other Australians (270). As CVD is a substantially significant contributor to illnesses, disability and premature death particularly among the Aboriginal group (270, 271), there is a need to alert them of health risks associated with greater CVD risk among them.

In the management of CVD, guidelines have been provided to predict CVD in the presence of a number of the modifiable and non-modifiable risk factors. However, most of the available guidelines are based on non-specific populations resulting in unsuitability of the tool for some groups of individuals. Some modifiable risk factors identified with CVD include overweight and obesity, tobacco smoking, diabetes, unhealthy diet, high blood pressure, high blood cholesterol and physical inactivity. Incidence of CVD also increases with non-modifiable risk factors such as age and ethnicity. Australia's cardiovascular risk chart related an individual's diabetes status, sex, smoking history and age with systolic blood pressure and cholesterol levels to present the risk of CVD (272). However, the CVD risk chart focused on the non-Aboriginal Australian population while also targeting middle aged Aboriginals (35 to 44 years of age) only, without considering differences in body habitus of Australians. Aboriginal Australians vary in their body habitus which includes waist circumference (WC) compared to non- Aboriginal Australians (12, 146-148). This Australian group also has the tendency of abdominal fat storage, particularly in women, having relatively large WC measurements (12, 273). The phenomenon of higher waist circumference in Aboriginal females compared to males, have been reviewed in a meta-analysis conducted to compare WC estimates in Aboriginal and non-Aboriginal Australian populations (149). Some studies in Australia that examined the relationship between WC and risk of CVD included other anthropometric indices such as body mass index (BMI) and waist-to-hip ratio (WHR) to present the best predictor of the disease and the findings have been controversial. While WHR compared to WC and BMI was found to be the most useful obesity measure in identifying individuals with CVD risk among non-Aboriginal Australians (158), WC better predicted CVD compared to BMI and

WHR among Aboriginals (8, 274). Due to the differences in WC profiles and the higher level of CVD risk of Aboriginals compared to non-Aboriginals in Australia, this study evaluated the relationship between WC and risk of developing CVD during the 20 years of follow-up study period. Also, we developed a simplified cardiovascular prediction model by estimation of absolute risk of CVD using different waist circumference (WC) values, over a 10 year period in Aboriginal subjects between the ages of 20 to 65 years in a remote Australian community. This prediction tool can be used to educate and alert Aboriginals of the risk of developing CVD according to WC and age. Furthermore, this tool will be helpful for the planning and conducting obesity-related health education programs for the prevention and management of CVD in Aboriginal communities in Australia.

METHODS

Study design

This was a prospective cohort study in a remote Aboriginal community in Australia designed to follow up adult individuals with WC measurement at baseline for up to 20 years to identify newly-diagnosed CVD events.

Study population

The original cohort included 1490 participants from a remote Aboriginal community in Australia's Northern Territory (NT), whose baseline data were collected from 1992. Those participants were followed for up to 20 years until 31st of May 2012.

Eligible participants recruited from the study group fulfilled the following criteria: 1) aged between 18 and 76 years, 2) had WC measurement at baseline and 3) free from known CVD at baseline. A total of 920 (470 men and 450 women) participants met the study criteria. CVD events were defined according to the *English Revision International Classification of Diseases (*ICD-9 code) *codes 390 to 458* and *International Statistical Classification of Diseases, 10th Revision (*ICD-10 code*) codes I00 to I99*. CVD outcomes were classified as hypertensive heart and renal diseases, coronary artery disease, pulmonary circulation, cardiac arrest, heart failure, myocardial infarction, stroke, cerebrovascular disease, diseases of arteries and veins, which were identified by patient hospitalization records using ICD-9 codes 402-404, 410-417, 427.5, 428, 430-459 and ICD-10 codes I11-I13, I20-I28, I50, I60-I89. We eliminated those with hypo- and hypertension (high blood pressure) and hemorrhoids as these occurrences may be physiologic (as with hypotension) rather than a disease, or with no obvious underlying medical cause (primary hypertension). Each study

participant had been assigned a unique Study Identification Number (SIN) to merge the baseline, follow-up morbidity data sets and the mortality data (death records helped identify those who had died as a result of CVD but had not been recorded in the hospital records, to add to our list of those who developed the disease). Our end point was incidence of CVD among study participants. Therefore, participants were followed up to identify cases of newly diagnosed CVD. Written informed consents were obtained from all participants at baseline measurements. The original baseline data collection was approved by the relevant Aboriginal community and the Menzies School of Health Research Ethics Committees and the hospitalization data collection for the current project was approved by the University of Queensland.

Baseline measurements

Existing baseline dataset was used for the analysis of this study and has been described elsewhere (9, 258). In summary, characteristics of participants were collected through interview questionnaires and they included demographic and clinical variables such as age, gender, WC, height, weight, WHR, smoking status and alcohol consumption. WC was measured using flexible tapes on a horizontal plane, midway between the lower border of the ribs and the iliac crest. Height and weight were measured with subjects wearing light clothing and no shoes and BMI was calculated as weight in kilograms divided by height in meters squared. Due to the disparity in WC of Australian Aboriginals and non-Aboriginals, the currently recommended WC cut-off points which were developed for individuals of European origin might not be applicable to this population (275). Therefore, for the current study, waist circumference was grouped into gender-specific quartiles. Quartiles for males (Q1 = 63–78 cm, Q2 = 79–85 cm, Q3 = 86–95 cm, Q4 = 96–138 cm). Quartiles for females (Q1 = 60–79 cm, Q2 = 80–90 cm, Q3 = 91–101 cm, Q4 = 101.5-135 cm). Q1 was the reference group for comparison.

Statistical analysis

Continuous variables were expressed as mean and standard deviation. We expressed categorical variables as frequencies and percentages. Using the Cox proportional hazards model, we assessed the association between WC and CVD outcomes adjusting for potential confounding factors (age, smoking status and alcohol consumption status). Age was a continuous variable, while smoking (smokers and non-smokers) and alcohol consumption (drinkers and non-drinkers) were categorical variables. Separate hazard functions were calculated for males and females. Survival was calculated using the Kaplan Meier proportional survival probability estimates. To predict 10-year risk of CVD using WC and age as covariates, we treated both age and WC as continuous variables. We used the

Weibull regression to estimate the absolute risk of developing CVD. The absolute risk formula used was

$$Absolute\ risk\ = 1 - \exp\left[-\{exp(-\beta_0 - X_j\,\beta_j)\,t_j\}^p\right]$$

where β_0 represented the baseline coefficient, β_j was the regression coefficient for covariates (WC and age), X_j represented the value of the covariates (WC and age), t = time and p = the shape parameter that indicates the hazard level (261). To compare the associations of WC, BMI and WHR with CVD between males and females, we converted original WC, BMI and WHR values into gender specific z-scores for both genders while also controlling for age, smoking and alcohol consumption status. An interaction term was included in the model to examine the gender effect in the association between WC and CVD (265). Data were analysed using Stata 12 (248). A P-value of <0.05 was considered to be statistically significant.

RESULTS

Baseline characteristics of study participants

The baseline characteristics for 920 study participants who met the study criteria for cardiovascular (CVD) are presented in Table 5.1. The mean (SD) ages at baseline screening for men and women were 33.5 (11.5) years and 36.2 (12.9) years respectively. WC mean (SD) for men was 87.3 (13.0) cm and 90.6 (14.5) cm for women. BMI mean was slightly lower in males than in females (23.5 kg/m^2 versus 24.5 kg/m^2). The mean (SD) WHR for males and females were 1.0 (0.1) and 0.9 (0.1) respectively. Men had higher mean body weight estimate compared to women (69.3 kg versus 63.4 kg). 373 (80%) males and 296 (67%) of females were smokers. 394 (85%) males and 153 (35%) females were alcohol consumers from the total population.

Table 5.1 Baseline descriptive statistics and clinical data of male and female participants

	Males	Females
Demographics	n=470	n=450
Age, years- mean (SD)	33.5 (11.5)	36.2 (12.9)
Waist circumference (cm)- mean (SD)	87.3 (13.0)	90.6 (14.5)
BMI (kg/m^2)- mean (SD)	23.5 (4.6)	24.5 (5.9)
Waist-to-hip ratio- mean (SD)	1.0 (0.1)	0.9 (0.1)
Weight (kg)- mean (SD)	69.3 (14.8)	63.4 (15.9)
Height (cm)- mean (SD)	171.6 (6.3)	161.0 (5.8)
Lifestyle factors- n (%)		
Current smoker	373 (80.0)	296 (67.0)
Current alcohol drinker	394 (84.6)	153 (34.7)

SD: Standard Deviation.

During the 20 year follow-up period, 333 (36.2%) people- 156 men and 177 women were diagnosed as having CVD. A total of 87.3% of the cohort were observed for at least five years, and 1.6% was observed for one year or less. 24.3% of the CVD events have occurred within the first 5 years of follow- up in 35 men and 46 women, and the percentage increased to 50.5% within 10 years of follow-up with a further increase to 82.0% at 15 years follow-up. Participants that developed CVD at the end of the follow up period had mean age estimate of 38.5 years, mean WC estimate of 94.0 cm and mean BMI estimate of 25.4 kg/m^2. 26.5% of those who developed CVD were non-smokers while 41.2% were non-alcohol consumers.

Incidence rates of CVD

The incidence rate of developing hospital diagnosed CVD was 23.8/1,000 person-years for males while the incidence rate for females was 28.5/1,000 person-years. Because of the differences in WC of males and females, waist circumference was categorized into gender-specific quartiles. Table 5.2 shows numbers of CVD cases and incidence rates by WC quartiles. Rates ranged from 13.8 (95% CI: 9.5-20.0) in Q1 WC quartile to 38.3 (95% CI: 29.6-49.7) per 1,000 person-years in Q4 for males and 14.3 (95% CI: 9.7-21.2) in Q1 to 47.2 (95% CI: 37.1-60.3) per 1,000 person-years in Q4 for females. As shown in Figure 5.1, CVD incidence rate among participants increased considerably with increasing WC and females had higher rates than males in the 4th WC quartile.

Table 5.2 WC quartiles and rate per 1,000 (95% confidence interval) of participants during the 20-year follow-up

	Males			Females		
Waist quartiles(cm)	**CVD cases**	**Person-years**	**Rate (95% CI)**	**CVD cases**	**Person-years**	**Rate (95% CI)**
Q1	28	2029.0	13.8 (9.5-20.0)	25	1748.3	14.3 (9.7-21.2)
Q2	27	1687.5	16.0 (10.9-23.3)	37	1567.8	23.6 (17.1-32.6)
Q3	44	1349.7	32.6 (24.3-43.9)	50	1529.1	32.7 (24.8-43.1)
Q4	57	1488.3	38.3 (29.6-49.7)	65	1377.1	47.2 (37.1-60.3)

Quartiles for males (Q1 = 63–78 cm, Q2 = 79–85 cm, Q3 = 86–95 cm, Q4 = 96–138 cm).
Quartiles for females (Q1 = 60–79 cm, Q2 = 80–90 cm, Q3 = 91–101 cm, Q4 = 101.5-135 cm).

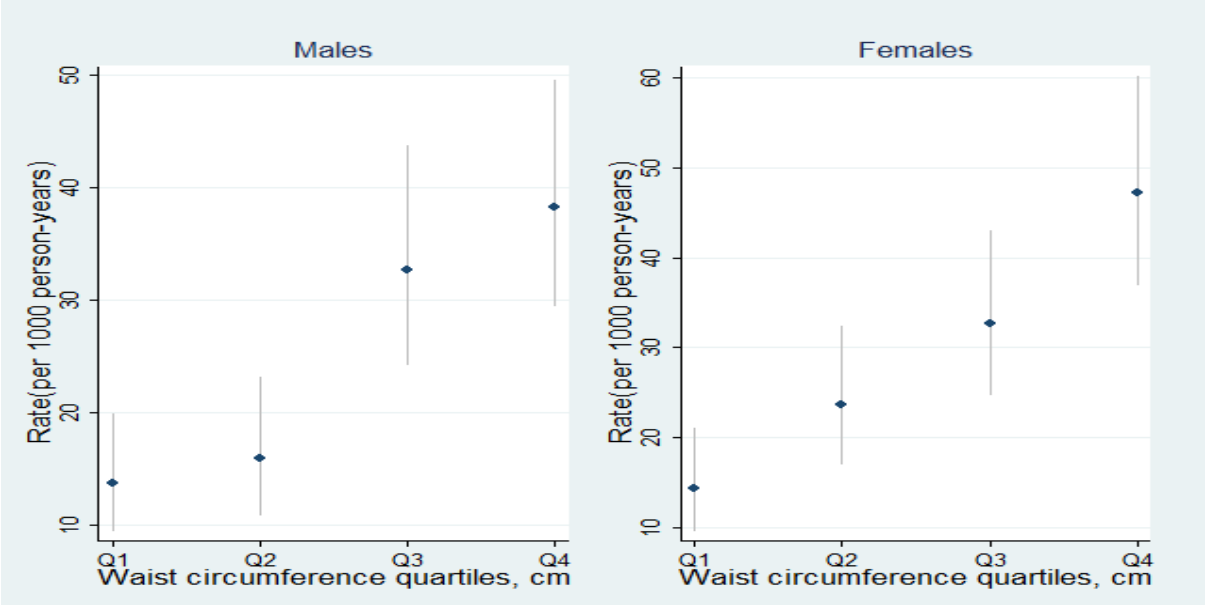

Figure 5.1 Rate per 1,000 person-years of males and females by WC quartiles measured in cm

Association between WC and CVD

Table 5.3 shows the hazard ratios of CVD for different WC quartiles. The crude association between WC and CVD were statistically significant for both genders. In comparison to the referent WC quartile (Q1), crude HR for males in Q4 was 2.9 (95% CI: 1.8-4.6), while HR for females in Q4 was 3.5 (95% CI: 2.2-5.5). After adjusting for age, smoking status and alcohol status, association between WC and CVD remained strong for both males and females. When WC and age were included in the same multivariable model (results not shown in Tables), the HRs for Q2, Q3, Q4 in comparison to Q1 were 0.9, 1.6 and 1,6 respectively for men and 1.5, 1.9 and 2.9 accordingly

for women. The model that included WC and smoking gave HRs for Q2 = 1.2, Q3 = 2.5 and Q4 = 3.0 for males and Q2 = 1.8, Q3 = 2.5 and Q4 = 3.6 for females. Multivariable model including WC and alcohol consumption were same as WC and smoking for both males and females. To assess the gender effect using WC quartiles, HR = 1.1 (95% CI: 0.9-1.4) showing women had slightly higher risk of CVD than men. However, there were no significant differences between males and females, P-value = 0.4.

Table 5.3 Crude and adjusted association between WC and CVD

	Crude		Adjusted	
Males	**HR (95%CI)**	**P-value**	**HR (95%CI)**	**P-value**
WC Quartiles				
Q1	1	<0.0001	1	<0.0001
Q2	1.2 (0.7-2.0)		0.9 (0.5-1.5)	
Q3	2.5 (1.5-4.0)		1.6 (1.0-2.7)	
Q4	2.9 (1.8-4.6)		1.8 (1.1-2.9)	
Females				
WC Quartiles				
Q1	1	<0.0001	1	<0.0001
Q2	1.7 (1.0-2.8)		1.7 (1.0-2.8)	
Q3	2.4 (1.5-3.8)		2.1 (1.3-3.5)	
Q4	3.5 (2.2-5.5)		3.1 (1.9-5.0)	

Adjusted for age, smoking status and alcohol consumption status.
HR: Hazard ratio; CI: confidence intervals.
Quartiles for males (Q1 = 63–78 cm, Q2 = 79–85 cm, Q3 = 86–95 cm, Q4 = 96–138 cm).
Quartiles for females (Q1 = 60–79 cm, Q2 = 80–90 cm, Q3 = 91–101 cm, Q4 = 101.5-135 cm).

Assessing WC, BMI and WHR and the risk of CVD

WC had the strongest association with CVD compared to BMI and WHR particularly among women as shown in Table 5.4. We converted original WC, BMI and WHR values into standard deviation scores (z-score) to make their associations with CVD comparable. For males, 1 standard deviation (SD) increase in WC, BMI and WHR increased CVD risk by 1.6 (95% CI: 1.4-1.8), 1.3 (95% CI: 1.2-1.6) and 1.6 (95% CI: 1.4-1.8) respectively. For females, 1 SD increase in WC, BMI and WHR increased CVD risk by 1.5 (95% CI: 1.3-1.8), 1.3 (95% CI: 1.2-1.6) and 1.3 (95% CI: 1.1-1.5) respectively. When WC, BMI and WHR were independently included in models containing

other risk factors of CVD (age, cigarette smoking and alcohol consumption status) to assess association with CVD, statistical significance was observed in the results of both genders. While the independent inclusion of each of smoking and alcohol consumption made minimal difference to the association of WC, BMI, WHR and CVD, the adjustment for age alone resulted in HRs of 1.3(95%CI: 1.1-1.6) and 1.4(95%CI: 1.2-1.7) for males and females respectively in the association between WC and CVD, 1.2(95%CI: 1.0-1.4) and 1.3(95%CI: 1.1-1.5) for males and females respectively in the association between BMI and CVD, and 1.4(95%CI: 1.2-1.7) and 1.2(95%CI: 1.1-1.4) for males and females respectively in the association between WHR and CVD.

Table 5.4 Hazard ratios of z-scores of crude and adjusted estimates of WC, BMI and WHR

Variable	Crude		Adjusted	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Waist Circumference (cm)				
Males	1.6 (1.4-1.8)	<0.0001	1.4 (1.2-1.7)	<0.0001
Females	1.5 (1.3-1.8)	<0.0001	1.4 (1.2-1.7)	<0.0001
Body mass index (Kg/m^2)				
Males	1.3 (1.2-1.6)	<0.0001	1.2 (1.0-1.5)	0.01
Females	1.3 (1.2-1.6)	<0.0001	1.3(1.1-1.5)	<0.0001
Waist-to-hip ratio				
Males	1.6 (1.4-1.8)	<0.0001	1.4 (1.2-1.7)	<0.0001
Females	1.3 (1.1-1.5)	<0.0001	1.2 (1.1-1.4)	<0.0001

Adjusted for age, smoking status and alcohol status.
HR (Hazard ratio); 95% CI (95% confidence interval).

Absolute risk of CVD by WC and age

$$Absolute\ risk\ (Males) = 1 - \exp\left[-\{exp(-5.9099 - (-0.0157 * WC - 0.0305 * Age)) * t_j\}^{1.4143}\right]$$

$$Absolute\ risk\ (Females) = 1 - \exp\left[-\{exp(-5.6569 - (-0.0174 * WC - 0.0198 * Age)) * t_j\}^{1.3965}\right]$$

Based on the coefficients of the final Weibull models above, we estimated 10-year absolute risks according to age and WC values. The predicted risk estimates (shown as percentages) for 10-year CVD were calculated and presented in Figures 5.2 and 5.3. The risk of CVD was driven by both age and WC values and it increased with higher WC values and increasing age.

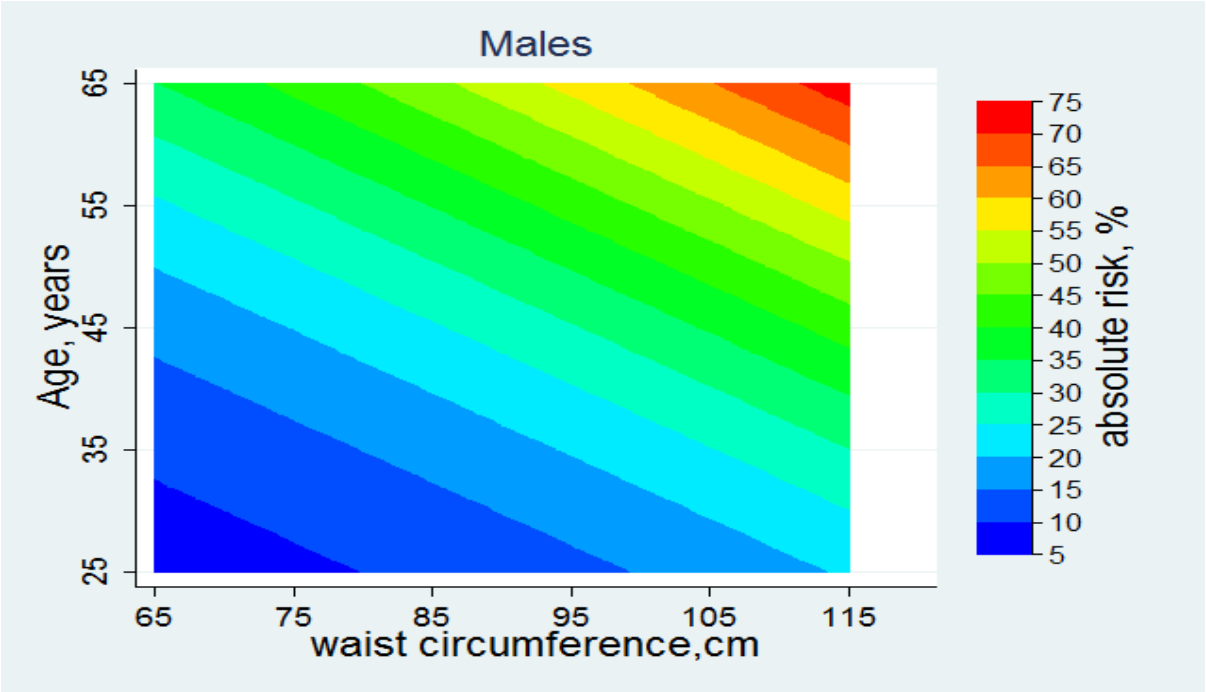

Figure 5.2 Absolute 10-year risk (%) of cardiovascular disease for males, using waist circumference (cm) and age (years)

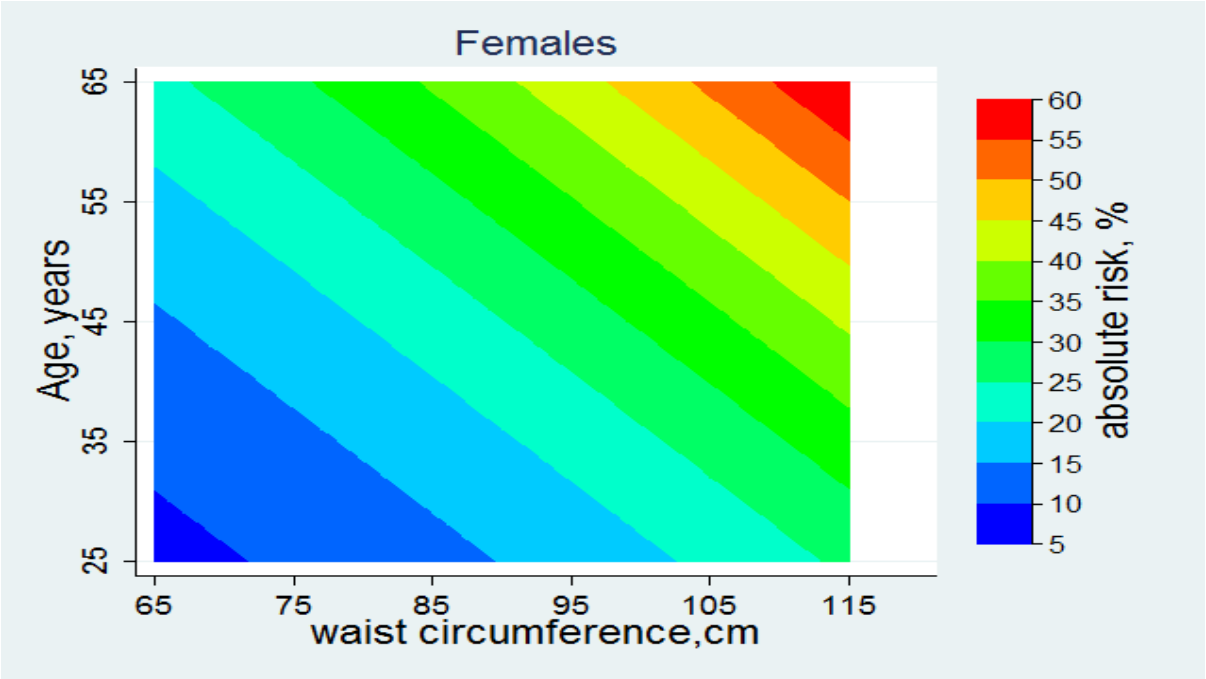

Figure 5.3 Absolute 10-year risk (%) of cardiovascular disease for females, using waist circumference (cm) and age (years)

The use of Figures 5.2 and 5.3 to make CVD predictions is best illustrated by example. Specifically, individual men less than 32 years of age with WC<80 cm had a 10 year absolute CVD risk of 5-10%; those between 42 and 49 years with WC range of 100–112 cm had a 10 year absolute risk of 15-20%; and those above 50 years and WC above 90 cm had 10 year absolute risk of above 50%.

For women, participants less than 30 years with WC less than 70 cm had a 10 year absolute CVD risk of 5-10%; individuals between 48 and 57 years with WC between 90 and 100 cm had an absolute risk of 15-20%; and above 57 years and WC above 105 cm had 10 year absolute risk above 50%.

Gender effect for the same absolute WC risk was not significant HR = 1.0 (95% CI: 0.8-1.3, P=0.9), indicating males and females were not different in their risk of CVD given a WC value.

We next examined the absolute risk of CVD using age and the currently recommended WC-cut-off values for obesity (102 cm for males and 88 cm for females) [19]. As shown in Figure 5.4, at the age of 30 years, absolute risk of CVD was less than 20% for obese individuals. Obese males and females aged 50 years had an absolute CVD risk of about 40% and 26% respectively. Absolute CVD risk was higher in males than females with these WC cut-off values.

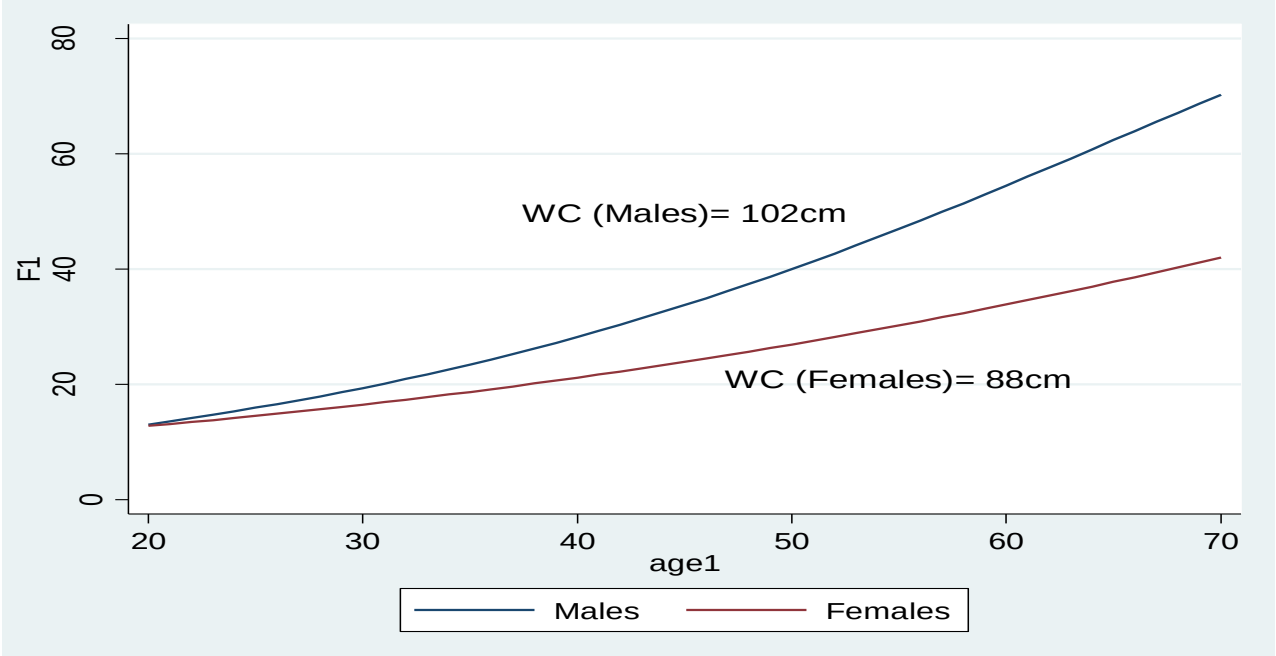

Figure 5.4 Absolute risk (%) of CVD for males and females with currently established WC cut-off values for obesity

DISCUSSION

In the present study, we followed up Aboriginal Australians participating in a community screening program for a maximum of 20 years for first episode of cardiovascular disease. Females in this study had higher WC estimates in comparison to the males. On the other hand, men were taller, had higher weight estimates, and were twice more likely alcohol drinkers and 1.2 times likely smokers when compared to the women. There were no distinctive gender differences in CVD risk for a particular WC value. WC measured at baseline predicted the risk of CVD as the risk increased with increasing WC, with the highest risk in the 4th WC quartile for both genders. The hazard ratio of WC was attenuated with the adjustment of age in the same multivariable model. However, adjusting for smoking and alcohol made little or no difference on the association between WC and the risk of CVD in the model. WC compared to BMI and WHR was a better predictor of CVD particularly in women. Finally, the absolute risks of CVD increased with increasing WC values and age in this population. This simple tool will help alert individuals in the study community of the future risk of CVD according to WC and age. It can also serve as an adjunct for planning and conducting public health education programs for CVD and augment preventive strategies for Aboriginal communities.

The scarcity of reports on absolute risk of CVD and risk factors such as WC and age in indigenous populations of Australia and other countries makes it difficult to compare our findings on absolute risks of CVD morbidity and WC. Nonetheless, our results are in general consistent with the findings from other ethnic populations on the risk associated with high WC and development of CVD (276-278). Hans et al. used the currently recommended WC-cut off points to assess differences in the risk of CVD among overweight and obese individuals, and reported individuals with WC in the obese group had higher CVD risk compared to those in the overweight category (278). Likewise, two studies in the United States used the Physicians' Health Study for men (276) and the Nurses' health Study cohort for women (277) to assess abdominal adiposity and coronary heart disease (CHD) and found that the highest WC quintile had higher risk of developing CHD than those in the lowest quintile. In our study, risk of developing CVD increased as WC increased with the highest risk in the 4th WC quartile. Although, females in the highest WC quartile had higher risk than their male counterparts (from results of hazard ratios in Table 5.3), the gender effect was not statistically significant. This effect could potentially be due to small sample size or some other possible reasons which we cannot explain.

The uniqueness of the present study is reflected in the absolute risk graphs presented to provide a general overview of the combined effects of WC and age on CVD in the Aboriginal community. The currently used Australian CVD risk chart targeted the Australian population while combining

the effects of some risk factors without considering WC which is strongly associated with risk of CVD among Aboriginals (8). Importantly, our study targeted a specific Aboriginal community where WC was strongly associated with risk of CVD (8). Also, we included age in the absolute risk prediction due to the association of increasing age with CVD risk (279). The effect combination of WC and age to predict absolute risk of CVD in this community would assist in efficiently identifying unrecognized CVD in this community. Furthermore, this study shows how absolute risk of CVD changes with WC values as age increases. We adjusted for smoking in our analysis as it has been found to be a CVD risk factor that affects body weight (280, 281). Our findings showed men tend to develop CVD at a younger age than women while the reverse was apparent for females who were more likely to develop CVD with greater WC than increasing age. This is understandable as WC of Australian Aboriginal women have been shown to have higher estimates than that of men.

The currently recommended WC cut-off values for obesity, 102 cm for men and 88 cm for women (115) contradict our findings. Applying these cut-off values to Aboriginal men and women, the absolute risks were much higher for males than females Figure 5.4). Risk of developing CVD increased to 70% and 41% among obese males and females respectively. As shown by our analyses in the incidence rates and hazard ratio estimates, females showed higher risk particularly in the highest WC quartile indicating higher risk of developing the disease among females than males with high WC, albeit, males and females were no different in their CVD risk with same absolute WC values. The currently used WC cut-offs either gives an underestimation of risk in women or an elevated risk in men in this population. Therefore, these WC cut-offs might not be applicable to this Aboriginal community. Adjusting the WC cut-off values to suit Aboriginal men and women will be beneficial to make their risks of CVD comparable.

There may be questions around the accuracy of prediction attained with using only WC and age rather than a combination of factors as seen in previous studies (224, 282). The purpose of this study was to examine the relationship between WC and CVD in relation to age. Moreover, our models based on the current data suggest that WC could be a better predictor than BMI and WHR in females for developing hospital diagnosed CVD in this population (8). On the other hand, for males, our findings concur with a previous Canadian study in concluding that WC was a better predictor of CVD than BMI but not WHR (283). Our results on WC as the best measure compared to WHR and/or BMI in identifying individuals with CVD risk are in agreement with earlier studies (170, 283). Dalton et al., in a previous Australian national study presented a contrasting result to ours when they demonstrated WHR was a more useful obesity measure than WC and BMI to identify individuals with CVD (158). However, they focused on non-Aboriginals and used a cross-sectional

study design which might not present the causal association between the measures and CVD. While we are not comparing WC, BMI and WHR in CVD risk prediction models in presenting a more accurate estimate, emphasis is being placed on the significant role that increasing WC plays in the development of CVD. Importantly, this is the first study assessing the role of WC to the CVD risk prediction in relation to age.

Strengths and limitations

To the best of our knowledge, this is the first CVD prediction model that will include waist circumference in an indigenous Australian population. Our study is population-based comprising of individuals from a homogenous population with over 80% of the eligible community members involved in the baseline screening survey. The prospective design and high rate of follow-up (up to 20 years) minimized the potential for recall bias and loss to follow-up enabling the capture of a good number of CVD morbidity events in the community. Reverse causality bias is unlikely in our study since we excluded those with existing CVD at baseline and included only the first episode of CVD after baseline measurement.

This study may be limited by WC measurements which were from routine examinations and were subject to measurement errors. Second, our end-point was limited as we excluded hyper- and hypotensive as well as haemorrhoids cases. However, we did a cross check to ensure that those with first episodes of the excluded events were free of CVD till end of the follow-up period; otherwise those who developed the disease were included in the analysis. Third, potential confounding effects of other variables (diet, physical activities and family history of CVD) were not adjusted for in the reported strong association between WC and CVD risk in this study as we do not have data on these important risk factors. Therefore, we could only analyse on data available to us (age, WC, smoking, gender, alcohol consumption) in our analysis. Fourth, there may be questions around the use of baseline WC measurement in the prediction of future CVD events without considering the changes in WC over the follow-up time. This is unlikely to affect our findings as the purpose is to relate WC measured at baseline with when CVD develops in the follow-up time. Moreover, WC estimates are not static but change with time depending on the age and lifestyle of individuals. Lastly, findings of this study may not be generalizable to other Aboriginal populations as results were based on just one Aboriginal community. As heterogeneity of body habitus profiles which includes WC vary in different Aboriginal communities, further research will be required to collect data from other Aboriginal communities and analysis carried out to assess whether results are comparable to the present study.

CONCLUSION

Our results suggest that WC may be a valuable factor in the CVD risk prediction models particularly in Australian indigenous communities whose people have higher propensity for abdominal fat than Australians in general. Although the gender effect was quite small for the same absolute WC values in favor of females, the differences were not significant between males and females. Our findings suggest that currently used WC cut-off values in Australia will capture different absolute risks of CVD in Aboriginal men and women and may need to be re-evaluated; a lower cut-off for males and higher cut-off for females than the currently recommended WC cut-offs may be more appropriate for better reflection of risk of CVD. The findings of this study can be used by health professionals to communicate knowledge of the risk of high WC estimates to individuals in the community. This tool could serve to raise awareness of CVD among the people due to the significant burden of illnesses and premature deaths in the Indigenous population.

CHAPTER 6

WAIST CIRCUMFERENCE AND TYPE 2 DIABETES RISK AMONG ABORIGINAL PEOPLE IN A REMOTE AUSTRALIAN COMMUNITY

6.1 INTRODUCTION AND AIM

The importance of waist circumference (WC) among other risk factors in the development of Type 2 diabetes has been documented in the Aboriginal Australian population. Alerting Aboriginal people of the risk of elevated WC in association with this health outcome is crucial and could assist in reducing the risk of other complications of chronic diseases. A number of prediction models have been proposed to alert individuals and communities of the risk of diabetes. However, the majority of the existing studies have been conducted in populations with different body habitus profiles and it is unclear whether these tools apply to the Aboriginal population of Australia.

In this chapter, we aimed to develop a model to predict future Type 2 diabetes according to WC and age in an Aboriginal Australian community. This simple tool can be used by individuals and health care workers to alert individuals of the risk of Type 2 diabetes associated with waist circumference and age. Furthermore, it will improve preventive treatment strategies for Aboriginal people in Australia.

The objectives of this chapter are:

1. To assess the association between WC and Type 2 diabetes.
2. To examine which of WC, body mass index (BMI) and waist-to-hip ratio (WHR) has the strongest association with Type 2 diabetes in the study population.
3. To provide a simple tool which shows changes in absolute risk of Type 2 diabetes with changes in WC.

In this chapter, Section 6.2 details a summary of my contributions to the study. Results from the study have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O, Hoy W and Z Wang. Predicting absolute risk of Type 2 diabetes using age and waist circumference values in an Aboriginal Australian community. *PLoS One 2015;* 10(4); p.1-10.

6.2 CONTRIBUTION TO THE STUDY

With the guidance of Dr Wang, I developed the analysis plan to examine the association between WC and Type 2 diabetes. I was also responsible for the data management and I conducted the data analysis and the results interpretation in consultation with Dr Wang and Dr Hoy. I was responsible for writing the manuscript, taking into account the comments and suggestions of Dr Wang and Dr Hoy.

ABSTRACT

Objectives

To predict in an Australian Aboriginal community, the 10-year absolute risk of Type 2 diabetes associated with waist circumference (WC) and age on baseline examination.

Method

A sample of 803 diabetes-free adults (82.3% of the age-eligible population) from baseline data of participants collected from 1992 to 1998 were followed-up for up to 20 years till 2012. The Cox-proportional hazard model was used to estimate the effects of WC and other risk factors, including age, smoking and alcohol consumption status, of males and females on prediction of Type 2 diabetes, identified through subsequent hospitalisation data during the follow-up period. The Weibull regression model was used to calculate the absolute risk estimates of Type 2 diabetes with WC and age as predictors.

Results

Of 803 participants, 110 were recorded as having developed Type 2 diabetes, in subsequent hospitalizations over a follow-up of 12633.4 person-years. WC was strongly associated with subsequent diagnosis of Type 2 diabetes with $P<0.0001$ for both genders and remained statistically significant after adjusting for confounding factors. Hazard ratios of type 2 diabetes associated with 1 standard deviation increase in WC were 1.7 (95% CI 1.3 to 2.2) for males and 2.1 (95% CI 1.7 to 2.6) for females. At 45 years of age with baseline WC of 100 cm, a male had an absolute diabetic risk of 10.9%, while a female had a 14.3% risk of the disease.

Conclusions

The constructed model predicts the 10-year absolute diabetes risk in an Aboriginal Australian community. It is simple and easily understood and will help identify individuals at risk of diabetes in relation to WC values. Our findings on the relationship between WC and diabetes on gender will be useful for clinical consultation, public health education and establishing WC cut-off points for Aboriginal Australians.

INTRODUCTION

Diabetes is one of the fastest growing chronic conditions in Australia, with an estimated 280 people developing the disease daily (284). Indigenous Australians (Aboriginals and Torres Strait Islanders) (147, 285) are at higher risk of developing the disease, and at earlier ages (286-288) than the non-indigenous group. A large proportion of Aboriginals develop Type 2 diabetes (T2D) in their lifetime, with a lifetime risk in one community of one in two among men and two in three among women (254). Despite the preventive strategies aimed at controlling the development of Type 2 diabetes through healthy diet and lifestyle or medication (289), there has been little, if any reduction in the high prevalence, high burden of mortality and complications imposed by this disease among Aboriginals (284).

Several studies have shown relationship between excess abdominal fat and increased risk of T2D (284, 290, 291). In Australia, Aboriginals have the propensity for excessive abdominal fat which reflected in their higher waist circumference (WC) compared to non-Aboriginals (12, 273). Although, studies conducted in some Aboriginal communities have shown WC was a better predictor of T2D compared to body mass index (BMI) and waist-to-hip ratio (WHR) (9, 178), but WC cut-off points for Aboriginals to alert them of the risk of T2D and other chronic diseases have not been established. Prediction models for the risk of diabetes have been developed in a number of populations with the aim of predicting diabetes occurrences, while providing intervention (292-294). Indeed, the Australian Type 2 diabetes risk assessment tool (AUSDRISK) included WC and ethnicity (Aboriginal or non-Aboriginal) as risk factors for estimating the risk of developing diabetes, suggesting the differences in the effects of WC on diabetes between Aboriginals and other Australians (295-297). However, due to low numbers of indigenous Australians in the AUSDRISK study, Aboriginals were grouped with southern Europeans and Asians to generate a high-risk group, which does not give a true representation of the level of diabetic risk among Aboriginals in Australia. In this study, we reported the first 10-year absolute risk estimates of diabetes using WC and age in a remote Australian Aboriginal community. As there are no specific WC cut-off thresholds for Aboriginals in Australia, we categorised WC into gender-specific quartiles for analysis and developed a model using WC and age values. To quantify the impact of WC on the risk of developing diabetes, we developed a simplified tool that can be used by health professional and the general public to understand how diabetes risk varies with WC values. This tool can also be used to educate and alert individuals of the risk of developing diabetes according to WC and age. Furthermore, this tool will also be helpful for the planning and conducting obesity-related health education programs for the prevention and management of T2D in Aboriginal communities in Australia.

METHODS

Study population

The baseline characteristics of the study population have been described in detail elsewhere (9, 258). From January 1992 to December 1998, a total of 935 adults (>=18 years, over 80% recruitment) were included in a community-wide screening program in a remote Aboriginal community in Australia's Northern Territory. Written informed consents were obtained from all participants at baseline measurements. The baseline database (containing screening of anthropometric measurements) was merged with hospitalisation records to identify type 2 diabetes outcomes according to patients' hospital registration numbers (HRN). Of the 935 individuals, 803 were free of T2D at baseline examination, and were followed up on hospital records for up to 20 years from 1st February 1992 to 31st May 2012. Follow-up stopped for an individual once he/she developed T2D or died. Prior to using the data, each participant was de-identified and given a unique study ID number (SIN). This original baseline database was approved by the Aboriginal community and Ethics Committee of the Menzies School of Health Research and Territory Health Services. The project was approved by the Behavioural and Social Science Ethical Review Committee of the University of Queensland (#2011001232).

Outcome definition

Participants were followed-up through hospitalization records. Each participant was identified by HRN and the patients' health record ID codes. Our outcome was newly diagnosed (incident) T2D as recorded in hospitalization data records. We identified individuals with T2D using the International Classification of Diseases (9th revision; ICD-9) code 250 and (10th revision, ICD-10) code E11 as recorded in the hospitalization dataset. Follow-up period for participants with incident T2D was the time from the baseline survey date to the diagnosis date. For individuals who did not develop T2D, the follow-up period was the interval between the baseline screening and the follow-up time.

Exposure - Waist circumference

WC was measured in centimetres (cm) at baseline screening and grouped into gender-specific quartiles for analysis. Quartiles for males: (Q1= 63-78 cm, Q2= 79-85 cm, Q3= 86-95 cm, Q4= 96-138 cm). Quartiles for females: (Q1= 60-79 cm, Q2= 80-90 cm, Q3= 91-101 cm, Q4= 101.5-135 cm). Q1 was the reference group for comparison. For the T2D absolute risk prediction, we included

WC and age in our model as they have been identified as risk factors for diabetes in Aboriginals (9, 10, 178) and other populations outside Australia (116, 298).

Statistical Methods

Continuous variables were expressed as the mean +/- SD as appropriate. Categorical data were expressed as frequencies and percentages. To assess the association of baseline WC measures on the newly diagnosed T2D, the Cox proportional hazards models were used to estimate hazard ratios (HRs), adjusting for three confounding factors - age, smoking status and alcohol consumption status. Age (years) was included in the analysis as a continuous variable, smoking and alcohol status as categorical variables. The hazard ratios were computed for quartiles Q2, Q3 and Q4 as compared with the lowest quartile (Q1) in different Cox's proportional hazards regression models. To compare the associations of WC with T2D between males and females, we converted original WC, BMI and WHR values into gender specific z scores for both genders while also controlling for age, smoking and alcohol consumption status. The Weibull regression model was used to predict an individual's 10-year T2D risk in adult males and females using the formula:

$$Absolute\ risk\ = 1 - \exp\left[-\left\{exp\left(-\beta_0 - X_j\,\beta_j\right)\,t_j\right\}^p\right]$$

where β_0 represented the baseline WC coefficient, β_j was the coefficient for covariates (WC and age), X_j represented the covariates, t= time and p= the shape parameter. We constructed the regression coefficient based model by assigning β values as estimated regression coefficients (261). WC and age were fitted as continuous variables for the estimating the absolute risks of T2D.

For all analyses, two-tailed P values of <0.05 were considered significant. All statistical analyses were performed with STATA version 12.0 (248) and analysis were done separately for males and females.

RESULTS

Baseline characteristics of study participants

A total of 803 adults without diabetes at baseline records were included in the analysis. The baseline characteristics of participants are shown in Table 6.1. One hundred and ten participants (38

males and 72 females) were diagnosed as having new onset diabetes during the follow-up period of 12633.4 person-years. The median follow-up time was 18 years. The overall diabetes incidence rate was 8.7 (95% CI: 7.2-10.5) per 1000 person-years, 5.6 (95% CI: 4.1-7.7) per 1000 person-years for males and 12.2 (95% CI: 9.7-15.4) per 1000 person-years for females. Figure 6.1 shows the cumulative incidence of diabetes (%) according to WC quartiles for males and females respectively in the follow-up time. As WC increased, the cumulative incidence also increased to about 18% for males and 37.5% for females in WC Q4 during the follow-up period.

Participants that developed T2D at the end of the follow up period had mean age estimate of 37.5 years, mean WC estimate of 97.3 cm and mean BMI estimate of 27.5 kg/m^2. 25.7% of those who developed T2D were non-smokers while 44.0% were non-alcohol consumers.

Table 6.1 Baseline Characteristics of study participants initially free of diabetes in study community followed up for up to 20 years (1992- 2012)

	Males	**Females**
N	419	384
Age (18- 76 years)	32.1 (10.7)	35.0 (12.9)
Waist circumference (cm)	85.9 (12.3)	89.0 (14.5)
Body mass index (kg/m^2)	23.0 (4.4)	24.2 (6.0)
Waist-to-hip ratio	1.0 (0.1)	0.9 (0.1)
Smoking status		
Non-smokers	76 (18.3)	132 (35.1)
Smokers	339 (81.7)	244 (64.9)
Alcohol consumption		
Non-drinkers	58 (14.0)	237 (63.2)
Drinkers	357 (86.0)	138 (36.8)

*Data are means (standard deviation) for continuous variables or n (proportions-%) for dichotomous variables.

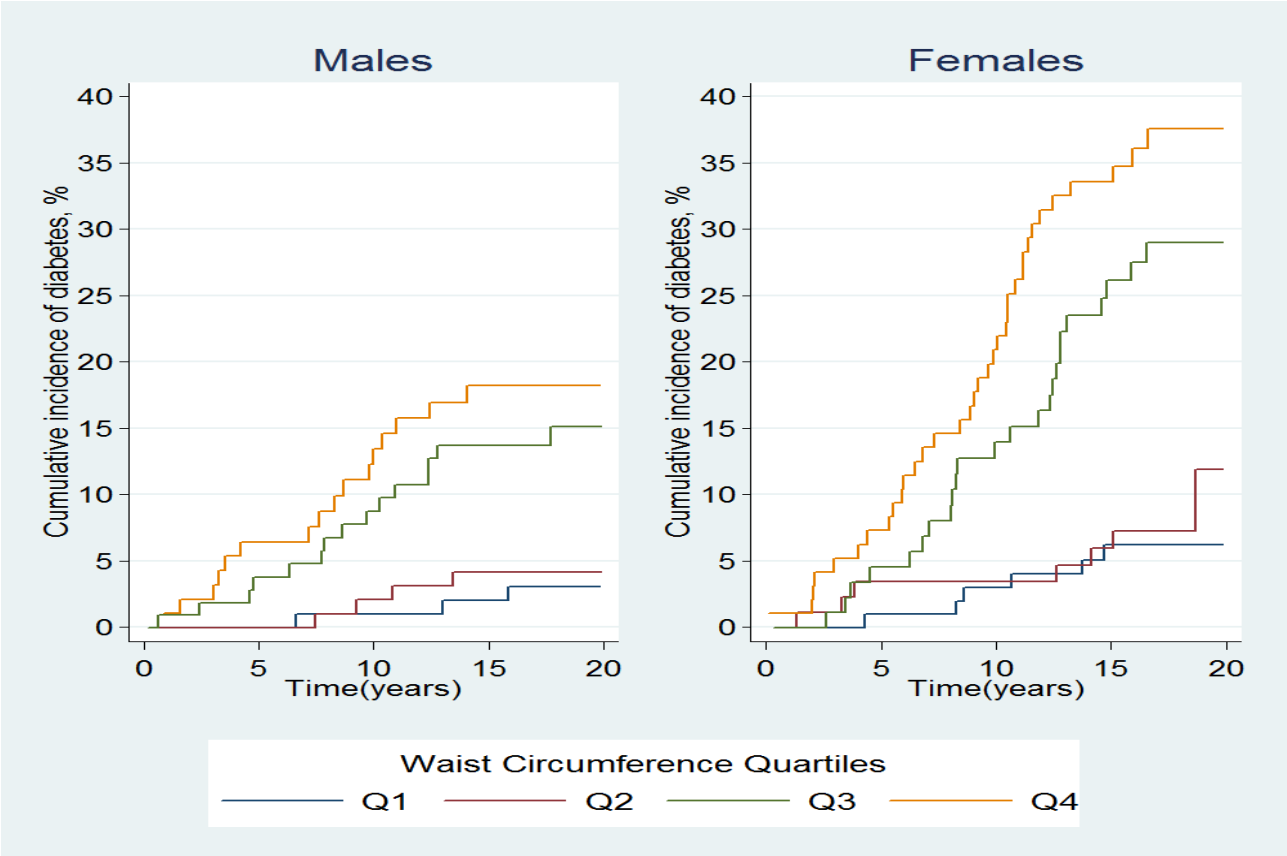

Figure 6.1 Gender-specific cumulative incidence of diabetes (%) by waist circumference quartiles

Association between WC and Type 2 diabetes

The crude HR for developing T2D with WC as a continuous variable was not significantly different between males and females. HR for 1 cm increase in WC was 1.04 (95% CI: 1.02-1.06, P<0 0001) for males and 1.05 (95% CI: 1.04-1.07, P<0.0001) for females. Crude and adjusted HRs for WC quartiles are shown in Table 6.2. The observed median follow-up times were 18.6, 18.2, 18.1 and 17.3 years for males and 18.2, 18.1, 16.8 and 15.9 years for females in WC quartiles Q1, Q2, Q3 and Q4 respectively.

Table 6.2 Crude and adjusted hazard ratios and 95% confidence intervals of association between T2D and WC quartiles

WC Quartiles	Crude HR (95%CI)	P-value	Adjusted HR (95%CI)	P-value
Males				
Q1	1	0.0002	1	0.0003
Q2	1.4 (0.3-6.2)		1.2 (0.3-5.8)	
Q3	4.9 (1.4-17.2)		4.1 (1.2-14.7)	
Q4	6.8 (2.0-23.2)		5.9 (1.6-21.4)	
Females				
Q1	1	<0.0001	1	<0.0001
Q2	1.4 (0.5-4.2)		1.4 (0.5-4.2)	
Q3	5.3 (2.1-12.9)		4.9 (2.0-12.3)	
Q4	7.6 (3.2-18.0)		7.2 (3.0-17.4)	

*Adjusted for age, smoking status and alcohol drinking status.
Waist circumference (WC). Quartile 1 (Q1). Quartile 2 (Q2). Quartile 3 (Q3). Quartile 4 (Q4).

The HR was 6.8 (95% CI: 2.0-23.4) for males in the highest (Q4) WC quartile compared to those in the lowest (Q1) WC quartile, with P=0.0002. After adjusting for confounding variables of age, smoking and alcohol status, this association remained statistically significant (HR= 5.9, 95% CI: 1.6-21.4, P=0.0003). The crude HR for females in Q4 WC quartile was HR= 7.6, (95% CI: 3.2-18.0, P<0.0001). Again, after adjusting for confounding variables, the association remained statistically significant for females, with HR= 7.2 (95% CI: 3.0-17.4, P<0.0001).

Table 6.3 shows the crude and adjusted HR of T2D corresponding to 1 standard deviation increase in WC, BMI and WHR (z-scores). The crude hazard ratio for males were 1.7 (95% CI: 1.3-2.2), 1.6 (95% CI: 1.2-2.1) and 1.3 (95% CI: 1.0-1.6) for WC, BMI and WHR respectively. For females, corresponding WC, BMI and WHR crude hazard ratios were 2.1 (95% CI: 1.7-2.6), 1.9 (95% CI: 1.6-2.4) and 1.3 (95% CI: 1.0-1.6). Associations remained statistically significant independently for WC and BMI in both genders after controlling for age, smoking and alcohol consumption. The interaction term between gender and WC was not statistically significant (P=0.22). Likewise, incorporating an interaction term between age and WC was not statistical significant (P=0.08).
The association of WC and T2D was mostly affected by age rather than smoking and alcohol consumption. Adjusting for age alone in the model testing for the association of WC and T2D resulted in HRs of 1.5(95%CI: 1.1-2.0) and 2.0(95%CI: 1.6-2.5) for males and females respectively. Each of the covariates had minimal impact on the association between BMI and T2D, and WHR and T2D (results not shown).

Table 6.3 Crude and adjusted WC, BMI and WHR z-scores and T2D hazards

	Crude HR (95%CI)	P-value	Adjusted HR (95%CI)	P-value
Males				
Waist circumference (cm)	1.7 (1.3-2.2)	<0.0001	1.7 (1.2-2.3)	0.001
Body mass index (kg/m^2)	1.6 (1.2-2.1)	<0.0001	1.6 (1.2-2.2)	<0.0001
Waist-to-hip ratio	1.3 (1.0-1.6)	0.03	1.3 (0.9-1.6)	0.17
Females				
Waist circumference (cm)	2.1 (1.7-2.6)	<0.0001	2.0 (1.6-2.5)	<0.0001
Body mass index (kg/m^2)	1.9 (1.6-2.4)	<0.0001	1.9 (1.6-2.5)	<0.0001
Waist-to-hip ratio	1.3 (1.0-1.6)	0.05	1.2 (1.0-1.5)	0.10

*Adjusted for age, smoking status and alcohol drinking status.
HR (Hazard ratio); 95%CI (95% confidence interval).

6.1.3 Absolute risk of diabetes by WC and age

$$Absolute\ risk\ (Males) = 1 - \exp\left[-\left\{exp(-8.8008 - (-0.0300 * WC - 0.0353 * Age)) * t_j\right\}^{1.1323}\right]$$

$$Absolute\ risk\ (Females) = 1 - \exp\left[-\left\{exp(-7.6955 - (-0.0369 * WC - 0.0066 * Age)) * t_j\right\}^{1.13307}\right]$$

Based on the coefficients of the final Weibull models above, we estimated 10-year absolute risks according to age and WC values. This was illustrated in Figures 6.2 & 6.3, showing a 10-year absolute diabetes risk (incidence of a first T2D event) of males and females respectively at different WC and age values. Diabetes risk increased with higher WC and older age. For males, the lowest diabetes risk (<=2%) was for those younger than 30 years with WC less than 73 cm. For females, those with WC less than 75 cm at any age presented the lowest diabetes risk (<=2%). Absolute diabetes risk of 32-34% was observed in males over 60 years with WC greater than 110 cm and for females over 55 years of age with WC greater than 113 cm.

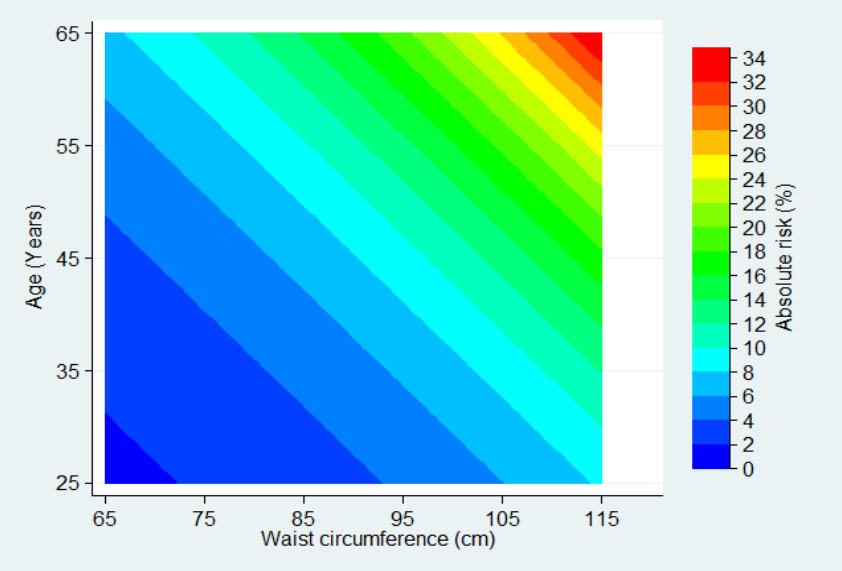

Figure 6.2 Absolute risk (%) of type 2 diabetes for males, using waist circumference (cm) and age (years)

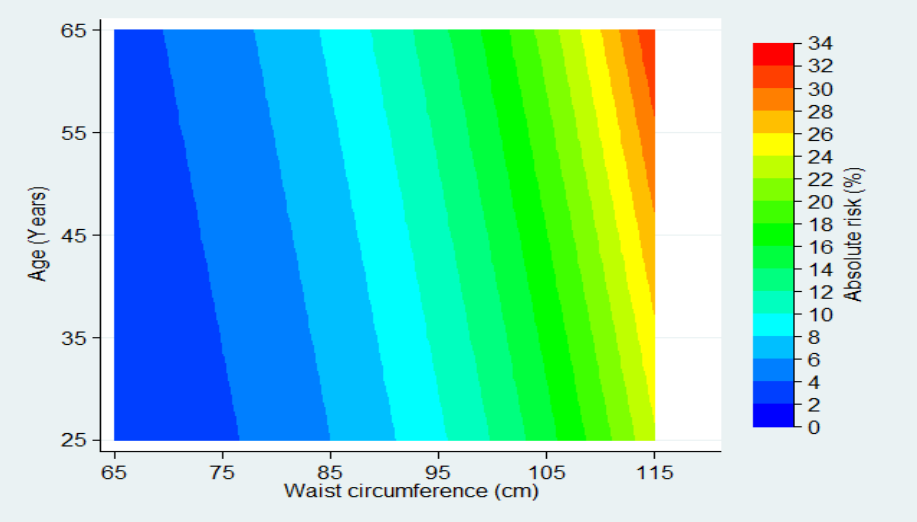

Figure 6.3 Absolute risk (%) of type 2 diabetes for females, using waist circumference (cm) and age (years)

DISCUSSION

Using long-term cohort data from a remote community, we have developed a simple model to estimate 10-year risk of T2D in an Aboriginal Australian community based on two variables: WC and age. The results are based on a maximum of 20 years follow-up (median, 18 years) and

ascertainment of T2D incidence cases. The values for the two predictors used can easily be obtained by individuals and in clinical practice. The absolute risk chart we developed is simple to use and understand. The availability of the simple tool to predict future risk of T2D should improve the understanding of WC on T2D risk and identify high-risk individuals based on WC and age. It can also serve as an adjunct for planning and conducting public health education programs for T2D and augment preventive strategies for Aboriginal communities.

Our approach based on the absolute risk method calculated from Weibull regression takes into account the synergetic effects of risk factors of disease of interest (272). This approach took into account the different follow-up time of all participants in the study to predict the risk of the disease. We have presented the prediction to a 10 year period as the goal of this study is to assess how risk of T2D change with WC values with a given age to assist in alerting individuals of the risk of T2D with increasing WC. While T2D is a complex multifactorial disease, and the cause originates from interactions among a number of risk genetic and environmental predictors, increased risk in Australia has been associated with increasing age, family history of diabetes, overweight (particularly with extra weight around the waist region), of indigenous Australian descent, lack of physical activity, unhealthy diet and high blood pressure (53). Unfortunately, we have no available data for family history of diabetes, physical activity and diet. The focus of this study was to calculate gender-specific absolute risk estimates for a community of Aboriginal Australians according to WC and age while adjusting for age, smoking and drinking in the multivariate analysis. Central obesity measured by WC has been known to increase the risk of T2D in the Australian Aboriginal population (9, 288). In the present study, we showed WC was a slightly better predictor of T2D than BMI and was much better at predicting T2D than WHR. This is consistent with the study conducted by Wang and Hoy (2004) in the same community presenting the odds ratio for diabetes after adjusting for age and sex to be 2.16, 1.80, 1.41, 1.81 and 1.84 for WC, BMI, weight, WHR, and hip circumference, respectively (9). As there are no WC cut-off points for Australian Aboriginals, we categorised WC into gender-specific quartiles for the analysis and presented a range for WC (65-115 cm) and age (25-65 years) for the prediction to enable easy use of the information from this study. Age has also been a commonly used single risk factor for detecting undiagnosed diabetes, more importantly, when used in addition to one or more risk factors such as obesity, family history of diabetes and hypertension, has the capacity to identify more individuals with undiagnosed diabetes (299). An Australian study assessed the relationship of increasing prevalence of diabetes with population ageing and obesity (300). They considered age group and BMI classification, and found that the greatest relative percentage increases over time were observed among those with normal BMI aged 60 years or older (148%), and those who were

obese and less than 60 years of age (139%). While BMI is mostly widely used in Australia, very few studies give reports of WC measured.

A previous Australian diabetes-prediction tool (Australian type 2 diabetes risk assessment tool-AUSDRISK) identified WC, age and ethnicity as risk factors in the prediction of incident diabetes (295, 296). However, Aboriginals in the AUSDRISK were grouped with Southern Europeans and Asians to generate a high-risk group which does not reflect a true representation of the level of diabetic risk among Aboriginals in Australia. Therefore, the validity and applicability of the tool to Aboriginals in Australia is questionable as they were derived from populations with different risk-factor profiles and ethnicities. The uniqueness of our study lies on our focus on one Aboriginal community; to estimate how the diabetes risk varies according to WC and age values, both have been reported as predictors of diabetes (8, 9).

In our study, the lowest T2D incidence was observed among persons in the lowest WC quartile, and we observed the strongest relationship between WC and T2D in the highest WC quartile. There was statistical significant association between WC and diabetes for both males and females in this population. Our estimates of cumulative incidence in Figure 6.1 suggest a high incidence of diabetes with high WC particularly among females (37.5%). Based on point estimates, our findings revealed females had higher WC values, and were at higher risk of T2D with increasing WC compared to males. The interaction terms incorporated among the variables used showed no statistical significance. A potential reason for this could be our relatively small sample size resulting in insufficient power to our study in detecting the interactions.

Strengths and limitations

Our study has a number of strengths. First, to our knowledge, this is the first diabetes prediction model specifically developed for an Aboriginal population in Australia. We focused on Aboriginals in a remote Aboriginal community where they were culturally homogenous (>80% ascertainment of the population). Also focusing on one Aboriginal community minimised the impact of heterogeneity in body habitus, as epidemiological studies on WC in the indigenous population of Australia have shown that there is substantial variation across communities (12). Second, the prospective study design used minimised systematic error introduced by the recall bias that cross-sectional and case-control studies are subject to. With a follow-up period of up to 20 years with high participation and follow-up rates, there was a robust ascertainment of diabetes events.

A few limitations of our study need to be acknowledged. First, T2D was only ascertained through recording of a T2D diagnosis reported among the diagnoses for a hospitalization episode. As most diabetes patients at the early stage or without any severe complications are usually managed without being hospitalized, it is likely that some people with diabetes were not hospitalised in the community during the study period, so the absolute risk presented in this study could underestimate the true risk in the population. Second, data on other important risk factors of diabetes such as physical activities, diet and family history of diabetes were not available. Therefore, we could only analyse on data available to us (age, WC, smoking, gender, alcohol consumption) in our analysis. Potential confounding effects of other variables (physical activities, family history of diabetes and diet) were not adjusted in the reported strong association between WC and diabetes risk in this study. Third, since our data were from one community, we were unable to generalise our findings about WC-associated absolute risks of T2D in other Australian Aboriginal communities. Due to our relatively small sample size (803 participants and 110 newly developed T2D), we could not assess internal validation by using subset of individuals from the study sample. However, our findings can be further replicated in other Aboriginal communities to assess the generalizability of our findings. Fourth, there may have been inaccuracies of WC measurements at baseline, resulting in the misclassification of participants into WC quartiles and attenuating the observed associations for WC.

CONCLUSION

We have constructed a simple tool for predicting the 10- year diabetes risk using WC and age as covariates, and this model focused on Aboriginals in an Australian remote community. This simple tool would assess how absolute risk of T2D changes with WC values. It is also helpful for identifying individuals at risk of T2D from high WC, and developing strategies for preventing diabetes in Aboriginal Australians. Our prediction tool will benefit from further validation with the inclusion of other important risk factors such as family history of diabetes, physical activity and diet.

CHAPTER 7

BODY MASS INDEX, WAIST CIRCUMFERENCE AND MORTALITY RISK AMONG ABORIGINAL PEOPLE IN A REMOTE AUSTRALIAN COMMUNITY

7.1 INTRODUCTION AND AIM

Epidemiological studies have shown that body mass index (BMI) and waist circumference (WC) are associated with risk of mortality in several populations of the world. However, there is scarcity of information on the associations of BMI and WC with mortality in the Aboriginal Australian population.

The aims of this chapter are:

1. To follow up on an earlier study conducted in the sample population to examine the association of BMI with the risk of mortality.
2. To assess the association of WC with all-cause mortality.
3. To examine which of BMI or WC has stronger association with all-cause mortality.

In this chapter, Section 7.2 provides a summary of my contributions to the study. Results from the study have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O, Hoy WE, Dong B, Wang Z. Body mass index and waist circumference as predictors of all-cause mortality in an Aboriginal Australian community. *Obesity Research & Clinical Practice* 2016. Doi: 10.1016/j.orcp.2016.06.003

7.2 CONTRIBUTION TO STUDY

Under the guidance of Dr Wang and Dr Hoy, I developed the analysis plan to examine the association between WC and all-cause mortality. I was responsible for the data management and I conducted the data analysis and interpreted the results in consultation with Dr Wang and Dr Hoy. I was responsible for writing the manuscript, taking into account the comments and suggestions of Dr Wang, Dr Hoy and Dr Dong.

ABSTRACT

Objective

Although elevated body mass index (BMI) and waist circumference (WC) have been identified as risk factors for mortality, data from the Australian Aboriginal communities are scarce. This study examined the associations of BMI and WC with all-cause mortality in an Australian Aboriginal community.

Methods

A total of 934 Aboriginal adults, aged 18 to 76 years, who participated in a community-wide screening program in Australia's Northern Territory from 1992 to 1998, were followed-up prospectively for up to 18 years for death outcomes. The hazard ratios for mortality were estimated by baseline BMI and WC. Age, sex, smoking and alcohol consumption status were adjusted for in multivariable analysis.

Results

In 14,750 person-years of follow-up, 216 deaths were recorded. For each standard deviation increase in BMI, the risk of all-cause mortality decreased by 9% (95% CI: 0.80-1.05); whereas for each SD increase in WC, the risk of all-cause mortality increased by 17% (95% CI: 1.03-1.33). The risk of mortality was lower in the 3rd BMI tertile compared to the 1st tertile for mortality after adjusting for WC, age, sex smoking and alcohol consumption. Risk of death was higher in WC tertile 3 compared to tertile 1 after adjusting for BMI, age, sex, smoking and alcohol consumption.

Conclusions

The risk of all-cause mortality among participants increased with higher WC, while participants with relatively higher BMI had a lower mortality risk. WC had stronger association with mortality than did BMI. The results indicate the importance of assessing WC measures in studies conducted in Aboriginal Australia.

Keywords: body mass index; waist circumference; all-cause mortality; Aboriginal people

INTRODUCTION

There is a significant gap in the life expectancy of Australian Aboriginal people compared to non-Aboriginals, estimated to be 10.6 years and 9.5 years lower for Aboriginal males and females respectively compared to their non-Indigenous counterparts (301). Although there is accumulating evidence pointing to the detrimental effects of high body mass index (BMI) and elevated waist circumference (WC) on mortality risk (302, 303), evidence is limited on the relationship of these two measures with mortality among Australian Aboriginal people. There have been reports that Aboriginal people have different body habitus profile which includes BMI and WC, in comparison to non-Aboriginals (12, 98). This Australian group have considerably higher WC measurements relative to their body weight, and particularly among females who have significantly higher WC estimates compared to non-Aboriginal females (12). Also, BMI and WC vary significantly in different Aboriginal communities (12). Therefore, there have been suggestions that generalising and stereotyping BMI and WC in Aboriginal people might not be appropriate due to the heterogeneity in the distribution and estimates of these measures in various Aboriginal communities (12, 98, 304). Furthermore, reports have indicated the currently advocated classification of BMI (overweight- 25.0 to 29.9 kg/m^2 and obesity- $\geq 30 kg/m^2$) (94) and WC (overweight- 94 for men and 80 cm for women, and obesity- 102 for men and 88 cm for women) (115) unsuitable for Aboriginal people (11, 98).

A number of epidemiological studies have reported on the association of BMI with all-cause mortality in some Asian populations (305, 306), the United States (307, 308) and in Australia (309). In addition, there have been studies linking high WC to a high risk of death in some other populations (72, 310-313). Furthermore, a few studies have assessed the relationship of both BMI and WC with the risk of death (312, 314-316), albeit in predominately European populations. Previously, Wang and Hoy in a 9-year follow-up period of Aboriginal people in a remote community in Australia's Northern Territory, observed that BMI was inversely associated with all-cause mortality; higher BMI was associated with lower mortality risks over the low and modest range of BMIs (309). The present study has taken a step further to assess the relationships of BMI and WC with all-cause mortality, using a follow-up time of up to 18 years in the same Aboriginal population. We sought to examine if there are changes to the inverse association between BMI and all-cause mortality with a longer follow-up time. Furthermore, we assessed the association of WC with all-cause mortality, and the combined associations of BMI and WC and mortality in the Aboriginal community. Understanding the role of BMI and WC in the risk of death might provide insights and assist in targeting appropriate strategies for individual communities and groups.

METHODS

Study participants

The original cohort consisted of 1490 people that participated in a community-wide screening program from 1992 to 1998 in a remote Northern Territory (NT) Aboriginal community in Australia. The NT is a federal Australian territory in the centre and central northern regions. Baseline data was collected through interview questionnaires at the community screening program where participants underwent anthropometric measurements (weight, height and WC), and provided some basic information such as age, sex, smoking (smokers and non-smokers) and alcohol consumption (drinkers and non-drinkers) status. Further details of the baseline examinations have been described elsewhere (8). Of the original baseline cohort, 514 were children (age<18 years), and 42 adult individuals did not have baseline WC and BMI measures, and these were not included in the study. In total, the study included 934 (474 males and 460 females) adult participants (aged ≥ 18 years) who had BMI and WC measurements at baseline, whose course was followed up for up to 18 years, to December 2010. This adult cohort represented over 85% of all adults in the study community (317). A unique study identification number was given to each study participant record at the start of the study.

Outcome variable

End point was all-cause mortality, defined as all deaths during the follow-up period from January 1992 to December 2010. The mortality data was collected through community networks and death registry records, and deaths were ascertained from records at the local clinics and hospital records.

Measurements

BMI was calculated as baseline weight divided by baseline height squared (kg/m^2). Baseline WC was measured in centimetres (cm) between the lowest ribs and the iliac crest using a tape measure. All measurements were single measurements made by one field worker and two Aboriginal health workers. As the currently recommended BMI and WC thresholds have been suggested to be inappropriate for Aboriginal people in Australia (11, 98), participants were categorised by baseline BMI and WC into sex-specific tertiles to make them comparable for the purpose of the analysis. BMI tertiles for males were as follows: (tertile 1= 14.20-20.98 kg/m^2, tertile 2= 20.99-25.10 kg/m^2 and tertile 3= 25.11-41.80 kg/m^2). BMI tertiles for females were as follows: (tertile 1= 13.58-21.14 kg/m^2, tertile 2= 22.22-27.12 kg/m^2 and tertile 3= 27.14-43.74 kg/m^2). WC tertiles for males were as follows: (tertile 1= 63-80 cm, tertile 2= 81-90 cm, tertile 3= 93-138 cm). WC tertiles for females were as follows: (tertile 1= 60-83 cm, tertile 2= 84-98 cm, tertile 3= 99-135 cm). Variables such as

age, sex (male/female), smoking (smokers, non-smokers) and alcohol consumption (drinkers, non-drinkers) obtained at baseline examination were covariates in this study.

Ethical Standards

All participants gave written informed consent prior to the start of the baseline examination. This original baseline database was approved by the Aboriginal community and Ethics Committee of the Menzies School of Health Research and Territory Health Services. The project was approved by the Behavioural and Social Science Ethical Review Committee of the University of Queensland (#2011001232).

Statistical analysis

Means (standard deviations) were calculated for continuous variables such as age, BMI and WC. Categorical variables, including smoking and alcohol consumption, were expressed as numbers (percentages). The Pearson's correlation co-efficient was used to evaluate the correlation between baseline BMI (kg/m^2) and WC (cm). The baseline and mortality datasets were merged after participants were de-identified. Participants were followed up from date of baseline examination till the date of death as recorded on mortality dataset. Those who died during the follow-up time were considered to have had the event, while those who had not reached the endpoint were considered 'censored' at the end of the follow up period (December 2010). Incident mortality rate (calculated per 1,000 person years of follow-up) for each baseline tertile of BMI and WC was obtained using the number of deaths divided by the person-years of follow-up. The Cox proportional hazards regression was used to present estimates of hazard ratios (HRs) with 95% confidence intervals (CIs) of mortality in relation to BMI and WC. Due to our relatively small sample size, sex was considered as a group, and was adjusted for in regression models. We converted original BMI and WC values into sex-specific z-scores thereby eliminating the differences in units to ensure that the magnitude of the HR results for both measures were directly comparable (262). Hazard ratio for each standard deviation change in BMI was 4.6 kg/m^2 for males and 5.9 kg/m^2 for females, and WC was 13 cm for males and 14.5 cm for females. HRs and their 95% confidence intervals of the risk of mortality associated with BMI alone, WC alone, and BMI and WC together were presented. HRs by BMI and WC tertiles were estimated while controlling for age, sex, smoking and alcohol consumption. BMI or WC was used as a continuous variable when adjusted for in multivariable models. The 1^{st} tertile of BMI and/or WC was used as the reference group for all analysis. Proportional hazards assumptions were tested on the basis of Schoenfeld residuals (318). Linear associations between BMI and WC and mortality were tested. An interaction term was included in the model to examine the difference between males and females in the association between BMI, WC and mortality (265).

Statistical significance was defined at the level of P<0.05 (two-tailed). Data analysis was conducted using Stata/SE 13.1 (319).

RESULTS

Baseline characteristics of study participants

Overall, 934 adult participants with BMI and WC measurements at baseline were followed up for up to 18 years and generated a total of 14,750 person-years. On average, baseline age, BMI and WC measurements were higher for females than males, as shown in Table 7.1. Males showed higher weight mean estimates compared to females. On average, males were about 10.7 cm taller than females. Males were more likely to smoke and consume alcohol than females. During the follow-up period, 216 deaths occurred. There were no statistical significant differences between males and females in the risk between BMI and mortality (P=0.83) and WC and mortality (P=0.48). The correlation between BMI and WC at baseline was 0.86 (P<0.05). Participants that died at the end of the follow up period had mean age estimate of 43.5 years, mean WC estimate of 90.9 cm and mean BMI estimate of 23.5 kg/m^2. 19.9% of those who died were non-smokers while 37.7% were non-alcohol consumers.

Table 7.1 Baseline characteristics of the study participants; 934 adults, aged 18 years and above by gender

	Males (n=474)		Females (n=460)	
	Mean	**SD**	**Mean**	**SD**
Age, years	33.6	11.5	36.4	13.1
Body mass index, (kg/m^2)	23.5	4.6	24.5	5.9
Waist circumference, (cm)	87.3	13.0	90.8	14.5
Weight, (kg)	69.3	14.8	63.5	15.9
Height, (cm)	171.6	6.3	160.9	5.8
	N	%	n	%
Tobacco smokers	376	80.0	300	66.4
Alcohol drinkers	397	84.5	156	34.6

SD= standard deviation

Associations of BMI, WC and all-cause mortality from results of z-scores

Table 7.2 presents mortality rates with study participants ordered according to sex-specific BMI and WC for deaths from all causes. The mortality rates varied across BMI tertiles and the highest rates

were observed in the 2nd BMI tertile. On the other hand, rates of all-cause mortality increased as WC increased with the highest rate in the WC 3rd tertile.

Table 7.2 Rates (95% confidence intervals) for all-cause mortality by baseline sex-specific tertiles of BMI and WC

	Deaths	Rate	95% Confidence Interval
Body mass index			
1st tertile	77	15.8	12.6-19.7
2nd tertile	80	16.7	13.4-20.7
3rd tertile	59	11.7	9.0-15.0
Waist circumference			
1st tertile	56	10.9	8.4-14.2
2nd tertile	77	15.8	12.6-19.7
3rd tertile	83	17.5	14.1-21.7

*Rates are in 1000 person-years
Note: BMI tertiles for males were as follows: (tertile 1= 14.20-20.98 kg/m^2, tertile 2= 20.99-25.10 kg/m^2 and tertile 3= 25.11-41.80 kg/m^2). BMI tertiles for females were as follows: (tertile 1= 13.58-21.14 kg/m^2, tertile 2= 22.22-27.12 kg/m^2 and tertile 3= 27.14-43.74 kg/m^2). WC tertiles for males were as follows: (tertile 1= 63-80 cm, tertile 2= 81-90 cm, tertile 3= 93-138 cm). WC tertiles for females were as follows: (tertile 1= 60-83 cm, tertile 2= 84-98 cm, tertile 3= 99-135 cm).

The hazards regression that had independent and combined analysis of BMI and WC z-scores assessing which had the stronger association with mortality are shown in Table 7.3. In the model conducted that included BMI only, while crude results showed no statistically significant association between BMI and mortality, adjusted analysis for all covariates showed an inverse relationship between BMI and all-cause mortality. In the model conducted on the sample that included WC only, crude results showed increase in the risk of death as WC increased and result was statistically significant; however, after adjustment for all the covariates, there was no statistical significance in the association between WC and mortality. Age, rather than smoking or alcohol consumption had the greatest impact on the association between BMI and mortality, HR= 0.81 (95%CI: 0.70-0.93, P<0.05), and the association between WC and mortality HR= 0.95 (95%CI: 0.82-1.09) (Results not included in tables).

The results of the z-scores showed higher HR for WC than BMI. When BMI and WC were combined in the model, BMI was inversely associated with mortality, while the risk of all-cause mortality increased as WC increased, and results were statistically significant in both crude and adjusted analyses.

Table 7.3 Hazard ratios (95% confidence intervals) for all-cause mortality by baseline sex-specific z-scores of BMI and WC

			BMI and WC	
	BMI	WC	BMI	WC
Mortality	**HR(95%CI)**	**HR(95%CI)**	**HR(95%CI)**	**HR(95%CI)**
Crude	0.91(0.80-1.05)	1.17(1.03-1.33) *	0.46(0.37-0.58) *	2.22(1.79-2.75) *
Adjusted	0.85(0.73-0.99) *	0.98(0.85-1.14)	0.60(0.46-0.79) *	1.50(1.15-1.94) *

Note: BMI and WC were included in models as continuous variables, and hazard ratios were computed for each standard deviation change in BMI and WC.
Adjusted for age, sex, smoking and alcohol consumption status
*Statistically significant (P<0.05)

Table 7.4 shows the crude and adjusted hazard ratios for all-cause mortality by BMI and WC tertiles. After adjusting for WC as a continuous variable, the risk of mortality was lower in the 3rd BMI tertile compared to the 1st. When BMI, WC (continuous variable), age, sex, smoking and alcohol consumption status were included in the same regression model, the risk of death was lower in the 3rd BMI tertile compared to the 1st tertile.

On the other hand, with adjustment for BMI as a continuous variable, risk of death was higher in the 3rd WC tertile compared to the 1st tertile, and results were statistically significant. After including WC, BMI (continuous variable), age, sex, smoking and alcohol consumption status in the same multivariable analysis, the risk of death was higher in the 3rd WC tertile compared to the 1st tertile.

Table 7.4 Hazard ratios (95% confidence intervals) for all-cause mortality by baseline sex-specific tertiles of BMI and WC

	Crude		Adjusted[1]		Adjusted[2]	
	HR	**95% CI**	**HR**	**95%CI**	**HR**	**95% CI**
BMI						
1st tertile	1		1*		1*	
2nd tertile	1.05	0.77-1.43	0.66	0.47-0.94	0.69	0.48-0.98
3rd tertile	0.73	0.52-1.02	0.25	0.15-0.42	0.44	0.26-0.73
WC						
1st tertile	1		1*		1*	
2nd tertile	1.44	1.02-2.03	2.32	1.59-3.39	1.26	0.85-1.87
3rd tertile	1.58	1.13-2.22	4.57	2.80-7.46	2.03	1.22-3.39

Adjusted[1]: included BMI and WC in the multivariable analysis
Adjusted[2]: included BMI, WC, age, tobacco smoking status and alcohol consumption status in the multivariable analysis.
Note 1: adjusted BMI or WC was a continuous variable.
Note 2: BMI tertiles for males were as follows: (tertile 1= 14.20-20.98 kg/m^2, tertile 2= 20.99-25.10 kg/m^2 and tertile 3= 25.11-41.80 kg/m^2). BMI tertiles for females were as follows: (tertile 1= 13.58-21.14 kg/m^2, tertile 2= 22.22-27.12 kg/m^2 and tertile 3= 27.14-43.74 kg/m^2). WC tertiles for males were as follows: (tertile 1= 63-80 cm, tertile 2= 81-90 cm, tertile 3= 93-138 cm). WC tertiles for females were as follows: (tertile 1= 60-83 cm, tertile 2= 84-98 cm, tertile 3= 99-135 cm).
*Statistically significant (P<0.05)

DISCUSSION

The results of this study provide evidence that the risk of all-cause mortality increased with higher WC; whereas, higher BMI was associated with lower mortality risk after adjusting for WC. Furthermore, WC had stronger association with all-cause mortality than BMI. These findings have significant implications for Aboriginal people as WC has rarely been used to explore the risk of mortality in their communities.

Consistency with other studies

Our study confirms findings from prior investigations by Wang and Hoy in the study community that reported an inverse association between BMI and mortality, stating that individuals with relatively higher BMI had a lower risk of death (309). A large Australian cohort study- the Melbourne Longitudinal Studies on Healthy Ageing (MELSHA) with a sample of 1,000 men and women and 409 deaths, found low BMI was associated with a higher risk of death with adjusted HR= 2.15 (95% CI: 1.15-4.02) for BMI<18.5kg/m^2 using the second BMI group (18.5-24.9 kg/m^2) as the reference category (320). Although the MELSHA study was focused on the ageing population (+65 years) and participants were predominantly from English-speaking backgrounds and do not represent the Australian Aboriginal population, their result on low BMI and high risk of death was similar to the results of the present study. As BMI measures overall adiposity and cannot differentiate between weight from muscle and fat (321), it was difficult to speculate on mechanisms of our findings on low BMI and high mortality risk as we have no data on diet, physical activity and physical fitness which have been shown to be independent contributors to obesity-related mortality (322). Pre-existing illness has also been known to contribute to increased mortality risk among individuals with low BMI (308), so there is the possibility that individuals with low BMI at baseline had a history of existing disease that contributed to the increased risk of death observed among low BMI participants.

The association between high WC and increased risk of all-cause mortality have been reported in previous studies (72, 310). Recently, an Australian study used the Melbourne Collaborative Cohort Study (MCCS) to compare five adiposity measures as predictors of all-cause mortality (313). In their sample of 41,313 men and women aged 25 to 75 years and 2,822 deaths over the follow-up years, they reported 30% higher risk of all-cause mortality for the highest WC group for men (WC>102 cm) and women (WC>88 cm), and 30% and 20% higher death risk for the lowest BMI category (<23 kg/m^2) for men and women respectively. Using the second pre-defined sex-specific category as the referent group, they also found the highest risk of death for women was at the

highest WC quintile, HR= 1.5 (95% CI: 0.9-2.4). These results are consistent with our findings of higher risk of death associated with increasing WC and low BMI. However, participants of the MCCS were mainly Anglo-Celtic with about 25% southern Europeans (323) and generally do not represent the Aboriginal population.

While there are no proposed WC standards specifically for Aboriginal people, BMI ranging from 17 to 22 kg/m^2 has been suggested as normal instead of the currently used guidelines (94, 324). In the present study, BMI as well as WC were categorised into tertiles for the purpose of analysis to make them comparable and observe the trend and pattern of mortality. Although Australian Aboriginal people, particularly females tend to have a preference for abdominal fat (12, 149); interventions on weight loss need to be considered with caution. As high BMI showed lower risk of death from the findings of the present study, it seems a challenge proposing weight loss in a population where there is a likelihood, although unproven, that high WC is genetic (168), and reducing weight will likely further lower their BMI, which might increase the risk of mortality. The present result supports the presence of an "obesity paradox" where individuals with high BMI have a lower risk of dying than those with low BMI (325, 326). Future studies on BMI, WC and mortality in Aboriginal Australians should focus on a larger population to examine the relationship between the indices and mortality, and also examine changes in weight and the implication on independent BMI and/or WC associations with mortality.

Strengths and limitations

Strengths of this study include the prospective nature of the study design, population-based recruitment and use of a long-term 18-year mortality follow-up to assess the association BMI and WC have with all-cause mortality. Also, this study was based on data from an Aboriginal Australian population where little is known on the association of BMI, WC and mortality. In addition, we focused on one Aboriginal community with a high participation rate (over 85% of eligible community members were participants at the baseline screening examination). Due to variations in WC in different Aboriginal communities (12, 149), using data from one community improved the internal validity of our findings. However, this may also be a limitation to this study in terms of the generalizability of our findings to other Australian Aboriginal communities. The generalizability of the findings from this study should be further assessed in future studies. Despite the high participation rate in the study community, our sample size was still relatively limited. This could be a potential reason for the results regarding BMI, as results of the crude BMI and mortality analysis did not show a particular trend as the highest HR was found in the 2nd BMI tertile. However, after adjusting, the trend showed lower risk of death in the highest BMI tertile. Also, due to our limited

sample size, pre-existing diseases such as stroke, cancer and chronic obstructive pulmonary disease were not excluded. This could be a potential reason for the association of low BMI and increased risk of death observed in this study, with a possibility of history of pre-existing illnesses among the low BMI tertile. Furthermore, we do not have baseline data on physical fitness or activity and diet, so it is unclear if the protective association between BMI and mortality was paradoxically due to muscularity (321). Nevertheless, we were able to show the importance of WC measures by demonstrating the stronger relationship it has with mortality risk over BMI.

CONCLUSION

High WC was a risk factor for all-cause mortality in the study population. The risk of mortality was lower with high BMI after adjusting for WC. WC had stronger association with mortality compared to BMI. Our results underscore the importance of assessing WC measures in studies conducted in Aboriginal Australia. We recommend WC as a preferred obesity measurement to capture mortality-high risk individuals in the Aboriginal community.

CHAPTER 8

WAIST CIRCUMFERENCE VALUES EQUIVALENT TO BODY MASS INDEX POINTS FOR PREDICITING ABSOLUTE CARDIOVASCULAR DISEASE RISKS

8.1 INTRODUCTION AND AIMS

Despite the high risk of cardiovascular diseases (CVD) associated with elevated waist circumference (WC) in Aboriginal population, there is a lack of WC thresholds for identifying Aboriginal individuals at high risk of the disease. While the presently recommended WC cut-off points for overweight (≥94 cm for men, ≥80 cm for women) and obesity (≥102 cm for men, ≥88 cm for women) are suitable for Australians of European descent, the applicability for Aboriginal people have been questioned due to variations in WC profiles.

In this chapter, we aimed to evaluate WC values corresponding to body mass index (BMI) points with equal absolute CVD, coronary artery disease and heart failure risks in an Australian Aboriginal community. The WC values generated will assist future research by contributing to the evidence needed for the recommendation of waist circumference cut-off points appropriate to the Aboriginal Australian population.

In this chapter, Section 8.2 provides a summary of my contributions to the study. Results from the study have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O, Hoy WE, Wang Z. Waist circumference values equivalent to body mass index points for predicting absolute cardiovascular disease risks among adults in an Aboriginal community: a prospective cohort study. *BMJ Open* 2015. 5:e009185. doi:10.1136/bmjopen-2015-009185.

8.2 CONTRIBUTION TO THE STUDY

In addition to my contributions to linking baseline data to hospitalization data, I was responsible for the data management for this study. I conducted the analysis, produced the relevant tables and figure, and drafted the manuscript. Dr Wang and Dr Hoy contributed expertise by providing comments and suggestions to the final published article.

ABSTRACT

Objective

There have been suggestions that currently recommended waist circumference (WC) cut-off points for Australians of European origin may not be applicable to Aboriginal people who have different body habitus profiles. We aimed to generate equivalent WC values that correspond to body mass index (BMI) points for identifying absolute cardiovascular disease (CVD) risks.

Design

Prospective cohort study.

Setting

An Aboriginal community in Australia's Northern Territory.

Participants

From 1992 to 1998, 920 adults without CVD, with age, WC and BMI measurements were followed-up for up to 20 years.

Outcome measures

Incident CVD, coronary artery disease (CAD) and heart failure (HF) events during the follow-up period ascertained from hospitalization data. We generated WC values with 10-year absolute risks equivalent for the development of CVD as BMI values (20 to 34 kg/m^2) using the Weibull accelerated time-failure model.

Results

There were 211 incident cases of CVD over 13,669 person-years of follow up. At the average age of 35 years, WC values with absolute CVD, CAD and HF risks equivalent to BMI of 25 kg/m^2 were 91.5, 91.8 and 91.7 cm respectively for males, and corresponding WC values were 92.5, 92.7 and 93 cm for females. WC values with equal absolute CVD, CAD and HF risks to BMI of 30 kg/m^2 were 101.7, 103.1 and 102.6 cm respectively for males, and corresponding values were 99.2, 101.6 and 101.5 cm for females. Association between WC and CVD did not depend on gender (P=0.54).

Conclusions

WC ranging from 91 to 93 cm was equivalent to BMI 25 kg/m^2 for overweight, and 99 to 103 cm was equivalent to BMI of 30 kg/m^2 for obesity in terms of predicting 10-year absolute CVD risk.

Replicating the absolute risk method in other Aboriginal communities will further validate the WC values generated for future development of WC cut-off points for Aboriginal people.

INTRODUCTION

The importance of waist circumference (WC) in health assessment in relation to chronic diseases such as cardiovascular disease (CVD) prevention is well recognised in current guidelines and policies in Australia. These guidelines include the "National guide to a preventive health evaluation in Aboriginal and Torres Strait Islander peoples" by National Aboriginal Community Controlled Health Organisation (NACCHO), and the 'Clinical Practice Guidelines for the Management of Overweight and Obesity in Adults' by the National Health and Medical Research Council. The Central Australian Rural Practitioners Association (CARPA) Standard Treatment Manual recommends WC measures be included in all yearly Adult Health Checks (219). Although this is a major achievement in creating awareness of the importance of WC, which is often not the foremost focus of most studies assessing anthropometric indices, the previously mentioned guidelines have been unable to recommend WC cut-off points for Aboriginal people who have higher CVD risk (327) and have elevated WC (12) compared with non-Aboriginals in Australia. Recently, the Australian, States and Territories Government sponsored the Measure-Up Campaign targeted at measuring WC in an effort to reduce chronic disease risk for Australians by recommending WC cut-off levels of 94 and 102 cm for men and 80 and 88 cm for women derived from body mass index (BMI) of 25 and 30 kg/m^2, respectively. Despite their efforts in presenting these WC cut-offs in multilingual booklets for various ethnic Australian groups, the recommended thresholds were particularly relevant to populations of European origin and might not reflect the true health risk in Aboriginal people who differ in body composition from other Australians (11, 12, 149).

CVD has been reported as the leading cause of death among Aboriginal people who are 1.3 times as likely to develop the disease as other Australians (327). Elevated WC has been known to increase the risk of any CVD (8, 98, 155) , coronary artery disease (CAD) (328) and heart failure (HF) (329, 330). Aboriginal people, particularly females, have body composition characterised by relatively higher WC compared with non-Aboriginals, which has been associated with increased risk of CVD. (8, 98, 155) Although WC has been reported to have stronger association with CVD than BMI in Aboriginal communities (8), both WC and BMI are useful predictors of CVD (328, 331). Using a longitudinal follow-up study design, we aimed to evaluate WC values corresponding to BMI points with equal absolute CVD, CAD and HF risks in an Aboriginal community in Australia. The WC values generated will assist future research by contributing to the needed evidence for the recommendation of WC cut-off points applicable to the Aboriginal population.

METHODS

Study setting and participants

The study was a prospective cohort study which included two phases: the baseline and follow-up. At a baseline community screening programme conducted from 1992 to 1998 in a remote Aboriginal community in the Northern Territory of Australia, age as well as anthropometric indices such as WC, weight, height and BMI were recorded, details have been discussed elsewhere.(8)

A total of 976 adults (aged 18 years and above) participated in the baseline screening programme of whom 934 had records of age (years), as well as WC and BMI measurements. Out of the 934 adults, 920 were free from known CVD at baseline and were eligible for the present study. They represented over 90% of adults in the study sample. These 920 adults (468 males and 452 females) were included in the study and prospectively followed up for up to 20 years (until 31 May 2012) to identify hospital-diagnosed new incident cases of CVD through hospitalisation data obtained from public hospitals in the Northern Territory.

Anthropometric measurements

Baseline WC in centimetres was measured midway between the lower border of the ribs and the iliac crest. Baseline BMI was calculated as baseline weight (kilograms) divided by the square of baseline height (metres).

Outcomes measurements

The hospitalisation database included hospital and emergency admission records of individuals in the Northern Territory. The CVD cases during the follow-up period were determined from the hospitalisation records using the following International Classification of Diseases (ICD) codes. CVD outcomes were classified as hypertensive heart and renal diseases, coronary artery disease, pulmonary circulation, cardiac arrest, heart failure, myocardial infarction, stroke, cerebrovascular disease, diseases of arteries and veins, which were identified by patient hospitalization records using ICD-9 and ICD-10 codes presented in Table 8.1.

Table 8.1 ICD 9 and 10-AM codes for CVD, CAD and HF

Disease	ICD 9 code	ICD 10 code
CVD	402-404, 410-417, 427.5, 428, 430-459	I11-I13, I20-I28, I50, I60-I89
CAD	410-414	I20 to I25
HF	428	I50

Although, CVD comprised of CAD and HF, we further separated each of CAD and HF to assess their risks with BMI and WC. For the purpose of this study, we excluded rheumatic fever and diseases as well as hypotension, haemorrhoids and other CVDs, that WC has not been found to have a causal relationship. On the other hand, we included hypertensive heart disease and hypertensive renal disease due to their associations with the complications of high blood pressure to which BMI (332, 333) and elevated WC (205, 334) have been documented as risk factors. Death records were checked for CVD cases that were not recorded in the hospital data. The follow-up time for each participant was calculated from baseline screening to date of disease diagnosis according to the hospital record, or date of death, or end of follow-up, whichever occurred first. Over 82% of the study participants were hospitalised for any ailment during the follow-up period as evidenced by hospitalisation records; therefore, we are positive of a robust follow-up ascertainment.

Ethics statement

The protocol of the baseline screening programme was approved by the Ethics Committee of the Menzies School of Health Research and Territory Health Service, and the Aboriginal community. The Behavioural and Social Science Ethical Review Committee of the University of Queensland (#2011001232) gave approval of this study. All participants gave informed consent to participate.

Statistical analysis

Data were analysed separately for males and females. Mean and SD for continuous variables or frequency and percentages for categorical variables were calculated. The Weibull accelerated failure-time model was used to estimate the absolute CVD risk using the formula:

$$Absolute\ risk\ = 1 - \exp\left[-\left\{exp\left(-\beta_0 - X_j\,\beta_j\right) t_j\right\}^p\right]$$

where β_0 represented the baseline BMI or WC coefficient, β_j was the coefficient for covariates (BMI or WC and age), X_j represented the covariates, t = time and p= shape parameter (261).

The absolute risk method was employed to obtain estimates of equivalent WC values that corresponded to BMI values from 20 to 34 kg/m^2 for a 10-year CVD risk in males and females at the average age of 35 years. Interaction was tested for gender in relation to WC and risk of CVD using fractional polynomial regression (265). In addition, we independently assessed CAD and HF to obtain WC points from BMI with equivalent absolute risks. Statistical analyses were performed with STATA statistical software version 13.0 (319). The tests were two-tailed and we used $P<0.05$ as the level of statistical significance.

RESULTS

Characteristics of the participants

The study sample comprised 920 participants, including 452 (49%) females. Compared with males, the average age, WC and BMI were higher in females. Table 8.2 shows the baseline characteristics of the study participants. During an average follow-up time of 14.8 years, a total of 211 participants developed CVD. A total of 140 CAD and 81 HF incident cases were recorded. In general, a greater proportion of females than males had CVD (23.7-22.2%), CAD (15.7-14.7%) and HF (10.2-7.5%)

Table 8.2 Baseline characteristics of study participants

	Males (n=468)	Females (n=452)	Total (n=920)
Age, years-mean (SD)	33.5 (11.5)	36.2 (13.0)	35.0 (12.3)
WC, cm-mean (SD)	87.3 (13.1)	90.6 (14.5)	88.9 (13.9)
BMI, kg/m^2-mean (SD)	23.5 (4.6)	24.5 (5.9)	24.0 (5.3)
Any CVD outcome, n (%)	104 (22.2)	107 (23.7)	211 (22.9)
CAD, n (%)	69 (14.7)	71 (15.7)	140 (15.1)
HF, n (%)	35 (7.5)	46 (10.2)	81 (8.7)

Abbreviations: WC, waist circumference; CVD, cardiovascular disease; CAD, coronary artery disease; HF, heart failure; BMI, body mass index.

Results presented in Table 8.3 show the population profile of participants according to the study outcomes. Participants who developed CAD and HF were not different in age, WC and BMI estimates.

Table 8.3 Population profile of participants by CVD, CAD and HF

	CVD	CAD	HF
Age, years-mean (SD)	39.4(12.3)	40.1(11.8)	40.8(11.6)
WC, cm-mean (SD)	94.3(14.2)	96.0(13.9)	96.4(13.7)
BMI, kg/m^2-mean (SD)	25.3(5.7)	26.0(5.6)	25.9(6.0)
Sex- n (%)			
Males	104(49.3)	69(49.3)	35(43.2)
Females	107(50.7)	71(50.7)	46(56.8)

Abbreviations: WC, waist circumference; CVD, cardiovascular disease; CAD, coronary artery disease; HF, heart failure; BMI, body mass index.

Tables 8.4 and 8.5 show the estimated 10-year absolute CVD risks according to baseline BMI values of 20-34 kg/m^2 and corresponding WC values with equivalent risks, with age being fixed to

35 years, the average age of the study sample. For males, 10-years CVD absolute risk was 10.62% for BMI of 20 kg/m^2 compared with 21.47% for BMI of 34 kg/m^2. Corresponding values for WC associated with similar CVD risks in females were 11.97% and 17.46% for BMI of 20 and 34 kg/m^2 respectively. Similar patterns were observed for CAD and HF as shown in Tables 8.4 and 8.5. Figure 8.1 shows WC values corresponding to same absolute CVD risks with BMI points were similar for CVD, CAD and HF. The maximum differences for specific WC values generated ranged from -2.2 to +4.3 cm for CVD, CAD and HF.

For the currently recommended BMI for overweight at 25 kg/m^2, WC values with equivalent CVD risk were 91.5 cm (absolute risk=13.72%) and 92.5 cm (absolute risk=13.71%) for males and females respectively (Tables 8.4 and 8.5). For CAD, corresponding WC values to BMI of 25 kg/m^2 were 91.8 cm (absolute risk=6.07%) and 92.7 cm (absolute risk=7.42%) for males and females respectively. For HF, WC values with equal absolute risk with BMI of 25 kg/m^2 were 91.7 cm (absolute risk=3.24%) for males and 93.0 cm (absolute risk=3.99%) for females.

For the recommended BMI for obesity at 30 kg/m^2, WC values with the same CVD risk were 101.7 cm (absolute risk=17.64%) for males and 99.2 cm (absolute risk=15.70%) for females. For CAD, WC values with equal risk to BMI of 30 kg/m^2 were 103.1 cm (8.97%) and 101.6 cm (absolute risk=9.53%) for males and females respectively. For HF, corresponding WC values to BMI of 30 kg/m^2 for HF risk were 102.6 cm (absolute risk=4.45%) and 101.5 cm (absolute risk=5.12%) for males and females, respectively.

Table 8.4 Estimated absolute risks associated with CVD types using equivalent WC points corresponding to BMI values for males at the age of 35 years

Males	CVD		Coronary artery disease		Heart failure	
BMI (kg/m$^{2)}$	WC (cm)	AR (%)	WC (cm)	AR (%)	WC (cm)	AR (%)
20	81.3	10.62	80.5	4.09	81.0	2.37
21	83.3	11.18	82.8	4.43	83.1	2.52
22	85.4	11.77	85.0	4.79	85.2	2.68
23	87.4	12.39	87.3	5.19	87.5	2.86
24	89.4	13.04	89.5	5.61	89.6	3.05
25	91.5	13.72	91.8	6.07	91.7	3.24
26	93.5	14.43	94.1	6.57	93.9	3.45
27	95.6	15.19	96.3	7.10	96.1	3.68
28	97.6	15.97	98.6	7.68	98.3	3.92
29	99.7	16.79	100.8	8.29	100.4	4.17
30	101.7	17.64	103.1	8.97	102.6	4.45
31	103.8	18.54	105.4	9.69	104.7	4.73
32	105.8	19.47	107.6	10.46	106.9	5.03
33	107.8	20.45	109.9	11.29	109.1	5.36
34	109.9	21.47	112.1	12.18	111.2	5.70

Abbreviations: AR, absolute risk CVD, Cardiovascular disease; WC, waist circumference; BMI, Body mass index.

Table 8.5 Estimated absolute risks associated with CVD types using equivalent WC points corresponding to BMI values for females at the age of 35 years

Females	CVD		Coronary artery disease		Heart failure	
BMI (kg/m$^{2)}$	WC (cm)	AR (%)	WC (cm)	AR (%)	WC (cm)	AR (%)
20	85.9	11.97	83.7	5.74	84.1	3.11
21	87.3	12.30	85.5	6.04	86.1	3.27
22	88.6	12.64	87.3	6.36	87.8	3.43
23	90.0	12.99	89.0	6.70	89.5	3.61
24	91.2	13.35	90.9	7.05	91.2	3.79
25	92.5	13.71	92.7	7.42	93.0	3.99
26	93.9	14.09	94.4	7.79	94.6	4.19
27	95.2	14.48	96.3	8.20	96.4	4.41
28	96.5	14.87	98.0	8.62	98.1	4.64
29	97.8	15.27	99.8	9.06	99.8	4.88
30	99.2	15.70	101.6	9.53	101.5	5.12
31	100.5	16.12	103.4	10.02	103.2	5.38
32	101.9	16.55	105.2	10.54	104.9	5.66
33	103.2	16.99	107.0	11.07	106.7	5.95
34	104.5	17.46	108.8	11.64	108.4	6.25

Abbreviations: AR, absolute risk; CVD, cardiovascular disease; WC, waist circumference; BMI, Body mass index.

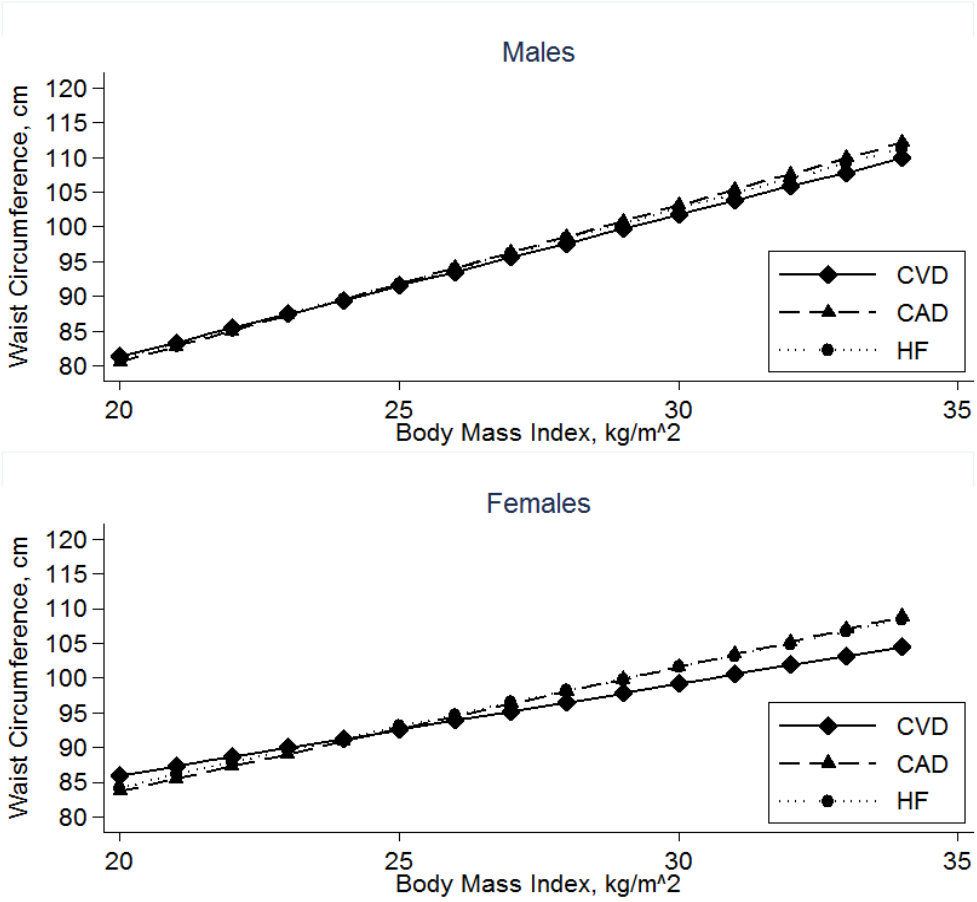

Figure 8.1 The body mass index and waist circumference relationship predicting equivalent 10-year absolute risk for CVD, CAD and HF at the age of 35 years

Note: CVD, cardiovascular disease; CAD, coronary artery disease; HF, heart failure.

The Weibull models below include coefficients used to estimate WC values from BMI points with equivalent absolute risks of CVD, CAD and HF.

Cardiovascular diseases (CVD)

For Males:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-6.3630 - (-0.0481 * BMI - 0.0336 * Age)) * t_j\right\}^{1.1380}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-7.1311 - (-0.0235 * WC - 0.0287 * Age)) * t_j\right\}^{1.1431}\right]$$

For Females:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-6.5302 - (-0.0306 * BMI - 0.0416 * Age)) * t_j\right\}^{0.9537}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-7.7402 - (-0.0230 * WC - 0.0376 * Age)) * t_j\right\}^{0.9578}\right]$$

Coronary artery disease (CAD)

For Males:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-5.7600 - (-0.0488 * BMI - 0.0162 * Age)) * t_j\right\}^{1.6587}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-6.3726 - (-0.0216 * WC - 0.0119 * Age)) * t_j\right\}^{1.6595}\right]$$

For Females:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-7.0271 - (-0.0472 * BMI - 0.0357 * Age)) * t_j\right\}^{1.1168}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-8.1433 - (-0.0264 * WC - 0.0313 * Age)) * t_j\right\}^{1.1159}\right]$$

Heart Failure (HF)

For Males:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-5.7964 - (-0.0391 * BMI - 0.0124 * Age)) * t_j\right\}^{1.6368}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-6.3449 - (-0.0181 * WC - 0.0083 * Age)) * t_j\right\}^{1.6333}\right]$$

For Females:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\left\{exp(-7.6541 - (-0.0434 * BMI - 0.0443 * Age)) * t_j\right\}^{1.1788}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\left\{exp(-8.8370 - (-0.0255 * WC - 0.0406 * Age)) * t_j\right\}^{1.1685}\right]$$

DISCUSSION

In our study of adults in an Aboriginal cohort, we have provided gender-specific WC values from corresponding BMI points with equivalent 10-year absolute CVD risk. WC with equivalent CVD risk as BMI of 25 kg/m^2 for males and females ranged from 91 to 93 cm, and varied from 99 to 103 cm for BMI of 30 kg/m^2. There were no significant differences between males and females in their association between WC and CVD risk. When assessing absolute risks for CAD and HF, we found that the absolute risk values for CAD and HF were lower than those for CVD. However, the WC values for those conditions equivalent to BMI values were not much different with a maximum difference of -2.2 to +4.3 cm. The absolute risks are convenient and useful for health education by health professionals and Aboriginal individuals. Furthermore, the absolute CVD risks associated with the estimated WC values in this study are useful contributions to the development of WC cut-offs for Aboriginal people in Australia.

Although Australian guidelines have made efforts to create awareness of the role of WC by recommending WC cut-off values as a health assessment tool to reduce the risk of chronic diseases (219), no consensus has emerged on the appropriate cut-offs for Aboriginal people, whose risk of CVD is higher than non-Aboriginals (335). Following the statement by Lear et al (2010) that the currently used WC cut-off points derived from European populations may not be appropriate for other ethnic populations (11), several population studies have provided evidence of WC cut-off points derived from BMI overweight and obesity thresholds to monitor the risk of developing chronic disease in adults. There have been no reports providing evidence of WC cut-off points for the Aboriginal population. The most commonly used methods for generating WC cut-off which involves optimising sensitivity and specificity whereby WC cut-off values are highly correlated with population mean values (13) might not be appropriate for Aboriginal people due to substantial variations of WC mean values among different Aboriginal communities (12). There have been suggestions on applying alternative methods, such as the absolute risk method (13) particularly in heterogeneous populations as Australia. Previously, the absolute risk method has been used to assess how risk of CVD changes with different WC values (155). In the present study, the absolute risk method was employed to generate WC values from BMI with equivalent absolute CVD risk. The WC values for overweight and central obesity from BMI determined in this study will contribute to evidence required for WC cut-off if the risk is considered high enough to take actions (13).

Although there have been earlier suggestions that the appropriate BMI range for Aboriginal people is between 17 and 22 kg/m^2, with increased risk of metabolic conditions above 22 kg/m^2, (93, 94) this is yet to be confirmed for in the population. In the present study, WC values equivalent to the

risk of CVD at BMI of 22 kg/m^2 were about 85 cm for males and 87-88 cm for females. A proportion of 69.7% (69.2% in males and 70.1% in females) CVD events occurred in individuals with BMI≥22 kg/m^2 (results not presented), indicating higher CVD events among individuals with and over this BMI threshold. Owing to the heterogeneity in body composition of Aboriginal people in different communities, further research is required to confirm the healthy BMI range for CVD in the population.

One important implication of the present study is that unique BMI and WC classifications is required for Aboriginal people as they are a diverse group with varying WC (12) and BMI estimates across gender and regions. Variations in BMI of Aboriginal people across Australian regions have potentially been attributed to differences in socio-economic and nutritional status (304, 336). Our study results were based on gender-specific BMI and WC measures of Aboriginal people in a community in the Northern Territory. Our observations of higher BMI and WC mean estimates among females compared with males are consistent with the observations made in an earlier study involving Aboriginal people in three remote communities in the Northern Territory (12). However, results of the study from remote communities in central Australia and north Queensland showed Aboriginal males in the cohort had slightly higher WC mean estimates than females (98). The WC cut-off values from European populations for overweight (94 cm in males and 80 cm in females) and obesity (102 cm in males and 88 cm in females) are 14 cm higher for males than for females. In our calculation of the 10-year absolute risks of CVD, we found that corresponding overweight WC for BMI (≥25 kg/m^2) ranged from 91 to 93 cm, and obesity from BMI (≥30 kg/m^2) ranged from 99 to 103 cm for males and females. The generated WC values for these BMI thresholds were relatively similar for males and females with differences ranging from 0.9 to 2.5 cm for CVD, CAD and HF. This suggests that analyses using the currently proposed categories of BMI and WC may not identify the appropriate WC range with sufficient degree of precision.

The main strength of the present study is that it is the first to provide WC values that correspond to equivalent BMI points for CVD risk in an Aboriginal population. Our choice of WC as a measure of adiposity was based on previous findings from recent studies in the same study population suggesting WC is a better predictor of CVD compared with BMI and WHR (155). Second, the prospective nature of our study enabled calculating absolute risk based on future CVD events which provided proof of the WC values generated from BMI points (115). Third, the data on which our results are based were derived from an Aboriginal community and are likely specific to this Northern Territory community. While this is advantageous due to population homogeneity, caution needs to be exercised when generalising findings to other Aboriginal communities due to heterogeneity of WC estimates in different Aboriginal communities. In addition, while over 80% of

eligible community members were involved in the baseline survey, our sample size was still limited. Further work could focus on validating the WC values generated in a larger Aboriginal sample or in more Aboriginal communities. Another limitation is the use of only hospital-diagnosed CVD which may present an incomplete and potentially biased assessment of incident CVD outcomes in the community. There is a possibility that participants could have accessed care in alternative healthcare facilities instead of the public hospitals, thereby underestimating the actual CVD numbers in the study population. However, we are confident that we captured a reliable number of CVD morbidity outcome representative of the study population as over 82% of participants were hospitalised during the follow-up period evidenced by hospital records for any ailment during the follow-up period. Future studies should include records from private and primary healthcare systems for more robust CVD outcomes.

CONCLUSION

Our study provides new and interesting observations of WC values with absolute risk of CVD equivalent to BMI values in an Aboriginal population. The association between WC and CVD in this study did not depend on gender. Our study suggests additional research using the absolute risk method in other Aboriginal communities will further validate the WC values generated in this study. Our findings provide valuable information to healthcare providers and evident contribution to expert committee members responsible for developing guidelines for WC cut-off points for Aboriginal people in Australia.

CHAPTER 9

WAIST CIRCUMFERENCE VALUES EQUIVALENT TO BODY MASS INDEX POINTS FOR PREDCITING ABSOLUTE TYPE 2 DIABETES RISKS

9.1 INTRODUCTION AND AIM

Based on the lack of waist circumference (WC) cut-off points for Australian Aboriginal people who suffer higher risk of Type 2 diabetes than non-Aboriginals, this chapter used data from the Tiwi Islands, of adult participants with body mass index (BMI) and WC values at baseline screening to present models to:

1. Evaluate WC values corresponding to BMI points with equal absolute Type 2 diabetes. The WC values generated will assist future research by contributing to the evidence needed for the recommendation of WC cut-off points appropriate to the Aboriginal Australian population.

In this chapter, Section 9.2 provides a summary of my contributions to the study. Results from the study have been published in a peer-reviewed journal. The reference for this publication is:

Adegbija O, Hoy WE, Wang Z. Corresponding waist circumference and body mass index values based on 10-year absolute Type 2 diabetes risk in an Australian Aboriginal community. *BMJ Open Diabetes Research and Care* 2015; 3:e000127. doi:10.1136/bmjdrc-2015-000127.

9.2 CONTRIBUTION TO THE STUDY

I was responsible for the data management and I conducted the data analysis and the results interpretation in consultation with Dr Wang and Dr Hoy. I was responsible for writing the manuscript, taking into account the comments and suggestions of Dr Wang and Dr Hoy.

ABSTRACT

Objective

There is a lack of waist circumference (WC) thresholds to identify Aboriginal individuals at high risk of Type 2 diabetes. We generated gender-specific WC values with equivalent 10-years absolute risk of Type 2 diabetes as body mass index (BMI) points in an Australian Aboriginal community to contribute to guidelines needed for establishing WC cut-off points for Aboriginals.

Research design and method

A cohort of 803 adult participants without Type 2 diabetes in an Aboriginal community was followed up for up to 20 years. We derived WC values with absolute risks equivalent for the development of Type 2 diabetes as BMI values (20 to 35 kg/m^2) using the Weibull accelerated failure-time model.

Results

After a mean follow-up of 15.7 years, 110 participants developed Type 2 diabetes. Absolute risk of Type 2 diabetes increased as WC increased, ranging from 3.52% (WC=77.5 cm) to 14.14% (WC=119.9 cm) in males, and 5.04% (WC=79.5 cm) to 24.25% (WC=113.7 cm) for females. In males, WC values with same absolute risks of Type 2 diabetes as BMI values were 77.5 cm for BMI=20 kg/m^2, 91.5 cm for BMI=25 kg/m^2 (overweight threshold), 105.7cm for BMI= 30 kg/m^2 (obesity threshold) and 119.9 cm for BMI=35 kg/m^2. In females, WC values were 79.5 cm for BMI=20 kg/m^2, 90.9cm for BMI=25 kg/m^2, 102.3cm for BMI=30 kg/m^2 and 113.7 cm for BMI=35 kg/m^2. Interaction between WC and gender was not statistically significant (P=0.53).

Conclusions

The absolute risk of Type 2 diabetes increased with higher WC measured at baseline screening. Males were not significantly different from females in the association between WC and Type 2 diabetes. Our findings are useful contributions for future establishment of WC cut-off points for identifying high risk individuals in Aboriginal people.

Keywords: waist circumference, body mass index, type 2 diabetes, absolute risk, Aboriginals

INTRODUCTION

Central obesity measured by waist circumference (WC) is a known and reported risk factor for Type 2 diabetes in the Aboriginal population (9, 10, 156). Risk thresholds for WC derived from body mass index (BMI) in predominantly European populations have been proposed for use in Australia. However, these standards might not necessarily be applicable to the Aboriginal population who experience a disproportionately greater burden of Type 2 diabetes (337, 338) and display a body habitus that is different from non-Aboriginals in Australia (12). Aboriginals, particularly females have a tendency for preferential abdominal fat deposition (12, 149), of which the cause is complex and multifactorial, and to which genetics, lifestyle, inflammation and infections have been suggested to be contributory (168). Although the International Diabetes Federation (IDF) has recommended that investigations be performed to determine WC cut-off values for clinical practice in different ethnic regions (339), there is no consensus on WC cut-off points to identify individuals at high risk of chronic diseases in Aboriginal Australians.

The conventional sensitivity and specificity approach used by most studies to determine cut-off values has been questioned and the absolute risk approach has been recommended (13). Furthermore, WC has been found to be a better predictor of Type 2 diabetes than BMI in the Aboriginal population (9, 156), which provides the basis for conducting this study. The present study aimed to estimate the absolute risks of Type 2 diabetes prospectively by following up participants without Type 2 diabetes at baseline examination to derive WC values with absolute risks of Type 2 diabetes equivalents to body mass index (BMI) points. The estimates generated from this study will contribute to the establishment of WC cut-off points to identify individuals at increased risk of developing Type 2 diabetes in the Aboriginal population.

METHODS

We conducted a prospective cohort study of adults (aged 18-76 years) using data collected during a community screening program (baseline screening) in an Aboriginal community in the Northern Territory of Australia. The baseline data of eligible participants included age, BMI and WC (8). WC was measured in centimetres halfway between the lowest ribs and the iliac crest, while BMI was calculated by participant's weight in kilograms divided by their height in meter-squared (kg/m^2). A total of 976 adults participated in the baseline community screening program from 1992 to 1998. Of the 976 adults, 803 had records of age (years), as well as BMI and WC measurements and were free from Type 2 diabetes at baseline. They represented over 80% of the adults in the study population. We followed up the eligible 803 adults on hospitalization records until 31 December, 2012 to

identify new incident Type 2 diabetes cases using the International Classification of Diseases (ICD) codes: 250 (ICD-9) and E11 (ICD-10). Our study outcome was hospital-diagnosed Type 2 diabetes before or by 31 December 2012. For participants identified with Type 2 diabetes, their follow-up time was calculated from the time of their baseline screening to their first episode of Type 2 diabetes according to the hospitalization records. Those who had not developed Type 2 diabetes by 31 December 2012 were 'censored'.

Participants volunteered for the baseline screening examinations, and written informed consent was obtained from each participant prior to the data collection. The Ethics Committee of the Menzies School of Health Research and Territory Health Service, and the Aboriginal community approved the original baseline datasets used for this study. The Behavioural and Social Science Ethical Review Committee of the University of Queensland (#2011001232) gave approval of this study.

Statistical analysis

Data were analysed and presented as means with SD and frequencies as appropriate. Interaction between gender and WC was assessed for their association with Type 2 diabetes using fractional polynomial regression. The Weibull accelerated failure-time model was used to estimate the absolute Type 2 diabetes risk using the formula:

$$Absolute\ risk\ = 1 - \exp\left[-\left\{exp\left(-\beta_0 - X_j\,\beta_j\right)\,t_j\right\}^p\right]$$

where β_0 represented the baseline BMI or WC coefficient, β_j was the coefficient for covariates (BMI or WC and age), X_j represented the covariates, t is the time and p the shape parameter (261).

The gender-specific estimates of equal WC values that corresponded in absolute risks to BMI values from 20 to 35 kg/m^2 for a 10-year risk for Type 2 diabetes, at a population average age of 35 years were obtained. All statistical analyses were performed using Stata statistical software V13.0 (319). Tests were two-tailed and a P-value of 0.05 was used to indicate statistical significance.

RESULTS

Our study included 803 participants (419 males and 384 females). The mean age at baseline was 32.1(SD 10.7) years for males and 35.0(SD 12.9) years for females. In females, the mean values of baseline WC (89.0 cm) and BMI (24.2 kg/m^2) were higher than in males (WC= 85.9 cm and BMI= 23.1 kg/m^2). Participants were followed up for 12,633.5 person-years with mean follow-up time of

15.7 years. There were 110 cases of incident Type 2 diabetes (38 males and 72 females) during the follow-up period.

Table 9.1 presents results of the WC values generated from BMI for a 10-year Type 2 diabetes absolute risk, at the average age of 35 years. Absolute risk of Type 2 diabetes increased with increasing WC values. The interaction between WC and gender showed no statistical significance (P=0.53). The absolute risk equations used to generate the values on table 9-1 are presented below:

For Males:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\{exp(-8.3367 - (-0.0855 * BMI - 0.0392 * Age)) * t_j\}^{1.1281}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\{exp(-8.8008 - (-0.0300 * WC - 0.0353 * Age)) * t_j\}^{1.1323}\right]$$

For Females:

$$Absolute\ risk\ (BMI) = 1 - \exp\left[-\{exp(-6.6145 - (-0.0837 * BMI - 0.0122 * Age)) * t_j\}^{1.3388}\right]$$

$$Absolute\ risk\ (WC) = 1 - \exp\left[-\{exp(-7.6955 - (-0.0369 * WC - 0.0066 * Age)) * t_j\}^{1.3307}\right]$$

In males, WC values with same absolute risks of Type 2 diabetes as BMI-specific values ranged from 77.5 cm for BMI of 20 kg/m^2 (absolute risk=3.52%) to 119.9 cm for BMI of 35 kg/m^2 (absolute risk=14.14%). Derived WC values of 91.5 and 105.7 cm had similar absolute risks of Type 2 diabetes with BMI of 25 (overweight threshold) and 30 kg/m^2 (obesity threshold) respectively. Likewise, for females, WC values ranged from 79.5 cm for BMI of 20 kg/m^2 (absolute risk=5.04%) to 113.7 cm for BMI of 35 kg/m^2 (absolute risk=24.25%). WC=90.9 and 102.3 cm had equivalent absolute Type 2 diabetes risk as BMI of 25 and 30 kg/m^2, respectively.

Table 9.1 Estimated 10-year gender-specific absolute risks of Type 2 diabetes using equivalent WC values corresponding to BMI points at the age of 35 years

	Males		Females	
BMI (kg/m^2)	**WC (cm)**	**AR (%)**	**WC (cm)**	**AR (%)**
20	77.5	3.52	79.5	5.04
21	80.0	3.87	81.8	5.62
22	83.0	4.25	84.1	6.27
23	85.8	4.67	86.4	6.99
24	88.7	5.14	88.7	7.78
25	91.5	5.64	90.9	8.66
26	94.4	6.20	93.2	9.63
27	97.2	6.80	95.5	10.72
28	100.0	7.46	97.8	11.91
29	102.9	8.19	100.1	13.22
30	105.7	8.98	102.3	14.67
31	108.5	9.84	104.6	16.26
32	111.4	10.79	106.9	18.00
33	114.2	11.81	109.2	19.91
34	117.1	12.93	111.5	21.99
35	119.9	14.14	113.7	24.25

AR, absolute risk; BMI, body mass index; WC, waist circumference.

DISCUSSION

The major findings in this study were the estimated WC values which were equivalent to BMI values from 20 to 35 kg/m^2 for predicting the absolute risks of Type 2 diabetes for Aboriginal people. Also of importance is the absolute Type 2 diabetes risk increased as WC increased, ranging from 3.52% (WC=77.5 cm) to 14.14% (WC=119.9 cm) in males and 5.04% (WC=79.5 cm) to 24.25% (WC=113.7 cm) in females. WC of 91.5 cm and 90.9 cm for males and females, respectively, corresponded with BMI of 25 kg/m^2 (overweight threshold), while WC of 105.7 cm in males and 102.3 cm in females corresponded with obesity threshold (BMI=30 kg/m^2). Although, on average, females had higher WC compared with males (approximately 3.1 cm mean difference) and the absolute risks tend to be higher in females for each derived WC than in males, the association between WC and Type 2 diabetes was not dependent on gender. While there appeared to be

widening difference between gender-derived WC at BMI>30 kg/m^2, with greater increase in males, interactions did not show statistical significance (results not shown). This could potentially be due to the fewer numbers of those with BMI above 30 kg/m^2 and incident Type 2 diabetes outcomes at that level.

There is limited evidence of contribution to the development of WC cut-offs for identifying individuals at high risk of chronic disease for Aboriginals in Australia. Although a few studies have shown the link between WC and Type 2 diabetes, we are not aware of any study that has determined using either cross-sectional or cohort design what levels of WC increased the risk of Type 2 diabetes among Aboriginals. Potential reasons for this lack may be due to the diversity in WC estimate levels existing in Aboriginal communities and the specific statistical technique required to testing this heterogeneity. This study has taken a step in overcoming these two challenges by making some contributions to whatever guidelines will be required in future research to attain this goal. There could be debates on the need for WC thresholds for Type 2 diabetes in the Aboriginal population as high WC appears to be a phenomenon with reported tendency for central obesity even at younger ages (340). However, the evidence linking WC with Type 2 diabetes is strong and consistent in the Aboriginal population (9, 10, 156). Furthermore, WC has been found to be a better predictor of Type 2 diabetes compared with BMI, waist-to-hip ratio, as well as weight and hip circumference in the Aboriginal population (9, 156). There have been reports evidenced by improved or completely normalized metabolic abnormalities of Type 2 diabetes among Aboriginals after a short reversion to traditional hunter-gatherer lifestyle which entailed high physical activity and low-fat diets resulting in weight loss (341). Although preventing excessive weight gain among Aboriginals is a complex process due to the strong link between poverty and obesity (342), the hypothesis that weight loss results in reduced WC, and also, controlling risk of complications that have been associated with risk of Type 2 diabetes are supported by trial studies outside Australia (343, 344). Therefore, operational definition of central obesity is important and necessary for health promotion in this population. As WC is easy to measure with no required calculations, unlike BMI, and has been found to have stronger association with Type 2 diabetes than BMI and other anthropometric indices (9, 156), establishment of threshold WC values in the Aboriginal population will be beneficial for individuals and healthcare workers to help reduce the prevalence of Type 2 diabetes among this Australian group.

As the Aboriginal Australian population is heterogeneous in their WC levels, varying from one community to another, future studies using the absolute risk approach should be assessed prospectively in other Aboriginal communities to examine the similarities or differences between males and females in the association between WC and Type 2 diabetes. Furthermore, the absolute

risk method used in this study would benefit the diverse Aboriginal population by demonstrating the applicability of our findings in WC-homogeneous communities.

The use of prospective study design with a long-term follow-up period is the main strength of this study. However, the findings from an Aboriginal community may not be generalizable to all communities due to the heterogeneity in WC levels among different Aboriginal groups. Replicating this study using the absolute risk method in other Aboriginal communities or larger Aboriginal groups will further confirm the generalizability of our findings.

CONCLUSION

The absolute risks of Type 2 diabetes increased as WC increased. For overweight defined as BMI of 25 kg/m^2, WC was 91.5 cm for males and 90.9 cm for females, while for obesity (BMI of 30 kg/m^2), WC were 105.7 and 102.3 cm for males and females respectively. Males and females did not differ remarkably in the relationship between WC and Type 2 diabetes. This similarity was also reflected in the derived WC estimates with equal absolute risks of Type 2 diabetes as corresponding overweight and obesity BMI values. The findings of this study will be useful for health professionals and public health workers when evaluating the risk of elevated WC in association with type 2 diabetes. Also, our results are important and useful for future research in the development of WC cut-off points in the Aboriginal population.

Main Message

1. Using the absolute risk method, we derived for overweight defined as BMI of 25 kg/m^2, WC of 91.5 cm for males and 90.9 cm for females; and for obesity (BMI of 30 kg/m^2), WC was 105.7 cm and 102.3 cm for males and females respectively.
2. There were no significant differences between males and females in the association of WC and Type 2 diabetes.
3. The generated WC values with similar risk as specific BMI points can contribute to the development of WC cut-off points for Aboriginals in Australia.

Research questions left to be answered as a result of this study include:

1. Are the values of WC derived in this study similar in other Aboriginal communities or in a larger Aboriginal study?
2. Are there gender differences in the relationship between WC and Type 2 diabetes in other Aboriginal communities?
3. Are the absolute risks of Type 2 diabetes for overweight and obese high enough for the establishment of waist circumference cut-off points for Australian Aboriginals?

CHAPTER 10

THESIS DISCUSSION

The studies presented within this thesis assessed the waist circumference (WC) of Aboriginal Australians in relation to two major chronic diseases with high prevalence- cardiovascular disease (CVD) and Type 2 diabetes, and with mortality. In light of the scarce documented evidence on ethnic-appropriate WC cut-off points for identifying Aboriginal individuals at high risk of chronic diseases, two of the studies were designed to:

1. Create tools to examine changes in risks of CVD and Type 2 diabetes at different WC points using the absolute risk method, and
2. Identify WC values from body mass index (BMI) cut-off points predicting the same absolute risks of CVD and Type 2 diabetes

This final chapter summarises the main findings, discusses the strengths and limitations of the available data, and highlights further research that would be beneficial to clarify the generalizability of the findings in the Australian Aboriginal population.

Summary of key findings

Chapters 5 and 6 assessed the associations of WC with CVD and Type 2 diabetes among participants. These studies found that WC had statistically significant associations with CVD and Type 2 diabetes in the study population. Furthermore, WC compared to BMI or waist-to-hip ratio (WHR) had stronger associations with CVD in females, and Type 2 diabetes in males and females in the study population. In addition, these chapters showed that the 10-year absolute risk of CVD and Type 2 diabetes increased as WC increased. The studies highlighted the importance of WC in the Aboriginal community and presented simple tools for predicting future risk of CVD and Type 2 diabetes according to changes in WC at different ages.

Chapter 7 examined the relationship of BMI and WC with all-cause mortality. Results showed that WC was associated with the risk of all-cause mortality, and the risk of mortality increased as WC increased. In addition, WC compared to BMI had stronger associations with all-cause mortality.

Chapter 8 generated equivalent WC values from corresponding BMI points for the 10-year absolute risk of CVD, coronary artery disease (CAD) and heart failure (HF). Results of the study are as follows: at the average age of 35 years, WC values with absolute CVD, CAD and HF risks equivalent to BMI of 25 kg/m^2 were 91.5, 91.8 and 91.7 cm respectively for males, and corresponding WC values were 92.5, 92.7 and 93 cm for females. WC values with equal absolute

CVD, CAD and HF risks to BMI of 30 kg/m^2 were 101.7, 103.1 and 102.6 cm respectively for males, and corresponding values were 99.2, 101.6 and 101.5 cm for females.
Chapter 9 presented equivalent WC values from corresponding BMI points for the 10-year absolute risk of Type 2 diabetes. Derived WC for overweight (BMI of 25 kg/m^2) was 91.5 for males and 90.9 cm for females; and for obesity (BMI of 30 kg/m^2), derived WC values were 105.7 cm and 102.3 cm for males and females respectively. These predicted WC values are useful contributions to future guideline in the establishment of WC cut-off points for Aboriginal people.

Overall, there were no significant differences between males and females in their association between WC and risk of disease (CVD and Type 2 diabetes) and mortality. Furthermore, the derived WC representing overweight and obese did not differ much between males and females, as maximum differences ranged from -2 to 3.5 cm.

Consistency with other studies

Several studies conducted in and outside Australia, in Aboriginal and non-Aboriginal groups, have demonstrated the risk of CVD and Type 2 diabetes associated with elevated WC (8, 9, 170, 328). Prior to this research work, Wang and Hoy examined the relationship between WC and CVD and Type 2 diabetes (8, 9). Those results were based on cross-sectional studies with potential inherent limitations such as difficulty in establishing temporal association between exposure and outcome, but the findings suggest the importance of WC in the study community. Findings using prospective study design as used in this thesis would be considered more informative. McDermott et al followed up 225 Aboriginal adults for 6 years and found higher rates of Type 2 diabetes among those with high WC compared with lower WC, despite their small sample size (10).
A few studies have documented on the stronger associations of WC with CVD and Type 2 diabetes compared with BMI and/or WHR. In rural communities in the Far North Queensland of Australia, WC was better than BMI, but not as good as WHR in predicting cardio-metabolic risk factors which include diabetes (146). In a 7-year prospective study of Mexican-American, WC but not BMI or WHR was found to be the best predictor of diabetes (345). Pouliot et al concluded that WC rather than WHR is an important index in the assessment of CVD risk (170).
There is a shortage of studies on absolute risk of diseases using WC as an exposure variable alongside other factors; therefore, it was difficult to compare the findings on absolute risks. Nonetheless, some other studies have used other methods to present WC values that best reflected disease risk in some Aboriginal communities (146, 178). Bambrick in 2005 using the sensitivity and specificity method suggested that reducing WC threshold to ≥90 cm for men would better reflect

disease risk (178). Their suggested WC threshold is consistent with WC values (>91 cm) generated from BMI in chapters 8 & 9 from equivalent absolute risks for both CVD and Type 2 diabetes in males. Also, Li and McDermott used the ROC curve method in rural communities in north Queensland to generate optimal WC cut-off values for predicting cardio-metabolic risks, and results ranged from 87.5 to 91.2 cm (146). These findings are similar to the results of this thesis on WC generated from overweight BMI (25 kg/m^2). The world Health Organisation (WHO) recommended WC thresholds for identifying overweight and obese individuals indicate a difference of 14 cm between males and females (115). This thesis showed WC difference range of -2 to 3.5 cm between the genders, with no significant differences between males and females in the association between WC and disease outcome.

Strengths and limitations

Strengths

1. First, this is the first study to conduct a systematic review and meta-analysis comparing gender-specific WC of Aboriginals and non-Aboriginals in Australia.
2. Second, this is also the first study to present prediction models to assess changes in risk of CVD and Type 2 diabetes at different WC levels and age values using the absolute risk method in an Aboriginal Australian population.
3. Third, no other report has provided evidence of WC values derived from BMI points for any disease outcome as a contribution to future guidelines for generating WC cut-off points for Aboriginal people in Australia.
4. Fourth, this is also the first study in an Aboriginal Australian population to assess risk of all-cause mortality with WC as a risk factor.

Although some of the strengths of the population data utilized for analyses have been addressed in each of chapters 5, 6, 7, 8 and 9, a brief summary of the major strengths are:

1. The focus on Tiwi Islands where over 80% of the population are of Tiwi origin indicates homogeneity both culturally and ethnically, limiting bias due to heterogeneous body size composition
2. There was a good participation rate as over 80% of the eligible community members were involved in the baseline community screening survey
3. The prospective follow up of individuals with baseline WC to identify future CVD and Type 2 diabetes risks as well as deaths ascertained by hospitalization and mortality records

respectively, established a temporal relationship and limited the misclassification of exposure and outcome, thereby reducing the possibility of bias

4. The length of follow-up (up to 20 years) of this work allowed monitoring to ascertain as many incident outcome events as possible, ensuring a good number of events representative of the study population.

Limitations

The Tiwi Island Study Data

The endpoints were ascertained from hospitalization and mortality records, thus there is a possibility that this study focused on more severe end of disease spectrum. If some individuals with chronic disease did not present to the hospital, they would not have contributed to the study and would have been falsely classified as not having the endpoints. This would have underestimated the number of disease cases. This is especially likely for Type 2 diabetes, which is usually discovered and managed in outpatient clinic environment). However, with the long term follow-up, this study captured a good number of affected individuals, generating significant results. Furthermore, there is the probability of underestimated incidence because of the long lead time between development of Type 2 diabetes and hospitalisation.

The WC measurements used in this study were from individuals in one Aboriginal Island, and results may not generalise to the entire Aboriginal population. As mentioned in most of the studies, there is a significant heterogeneity in WC across Aboriginal communities and a one-size-fit-all estimate might not be representative. Further research will be necessary to assess the absolute risk of CVD and Type 2 diabetes according to WC levels in other Aboriginal communities.

With regards to the data, first, the sample size used is relatively small. There is the possibility that the indistinctive difference between males and females in the association between WC and outcomes is due to the limited sample size. Furthermore, the limited sample size could be responsible for the indistinctive association between BMI and mortality.

There is a potential for measurement bias in the WC measurements. Results may vary depending on persons carrying out the measurements.

Previous studies in other populations have linked WC with the risk of other chronic conditions such as sleep apnoea/ sleep disordered breathing (212), certain cancers (132, 346) and gall stone disease (210, 211). However, the hospitalization data included very few numbers these conditions. Therefore, we could not include them to fully address the spectrum of chronic illnesses associated with high WC.

Furthermore, important confounding factors such as physical activities, family history of diseases, education levels and socio-economic status were not available in the baseline data. Therefore, relevant factors such as age, smoking and alcohol consumption were controlled for in the analysis.

The use of baseline WC measurement in the prediction of future disease event gives no consideration for changes in WC over the follow-up time. This is unlikely to affect this study as the purpose was to relate WC measured at baseline with the future risk of a disease. Previous prospective studies have provided systematic comparisons of WC measured at baseline and development of chronic diseases related to central obesity after long follow-up periods (116, 347, 348).

Study Implications

Public health implications

Given the association of WC with chronic diseases among Aboriginal people, it is important that appropriate health promotion guidelines relating to WC be provided. The findings of this thesis have several significant implications. The results support the hypothesis that central obesity, for which WC is a marker, is associated with CVD and Type 2 diabetes. Also provided, were absolute risks of CVD and Type 2 diabetes according to different WC levels, and generated WC absolute risk values equivalent to disease risks corresponding to various BMI values. The absolute risk approach gave simple and easily-understood evidence for establishing helpful guidelines for Aboriginal people in the study community. Compared to males, females appeared to have higher WC and risk of CVD, Type 2 diabetes and mortality. However, results were not significantly different between both genders in the risks of WC and study outcomes. The 14 cm gap between males and females in the standard WC cut-off points (115) is significantly higher than the differences observed in the present study (-2 to 3.5 cm). The findings of this thesis suggest for males and females in the study population, WC of 91 to 93 cm for overweight BMI and WC of 99 to 102 cm for obese BMI for CVD; and WC of 91 cm for overweight BMI and WC of 102 to 105 cm for obese BMI for Type 2 diabetes.

Policy implications

The Measure-Up Campaign sponsored by the Australian Government aimed to reduce the risk of chronic diseases among Australians, and the central measurement of the Campaign for guiding the public to take actions was WC (349). The focus of the campaign was to create awareness of the need for healthy living by being physically active and healthier eating habits to maintain a healthy

WC. The WC thresholds recommended in the Campaign were 94/102 cm for men and 80/88 cm for women to indicate overweight and obesity. While the Campaign achieved its aim of impacting on the knowledge and behaviours relating WC measurement to healthy diet, the focus was on the general Australian public with no specific target for Aboriginal people. The present findings focuses on Aboriginal people and the WC results generated have the potential to contribute significantly to future policies in the Aboriginal population in the prevention of chronic diseases.

Also, as there is no previously established underlying biological link of WC to CVD and Type 2 diabetes, the earlier stated potential mechanisms in chapter 2 are important factors to consider in the relationship between high WC and these two chronic conditions in the study community.

Directions for future research

More deliberate focus on waist circumference in epidemiological studies

There are considerable opportunities for further research on the role of high WC in the development of CVD, Type 2 diabetes and other chronic conditions (gall bladder disease, sleep apnoea and cancers) as well as mortality in a larger Aboriginal Australia population. Additional research also needs to focus on WC in understanding the observed high levels among females in this Australian group. This should involve epidemiological studies on dietary patterns and physical activity levels while monitoring changes in WC and risk of chronic illnesses.

Further clarification on the use of the absolute risk method in other Aboriginal communities

Future studies examining WC in Aboriginal communities should employ the absolute risk method to assess the risk of disease while observing changes in WC, with a further step to provide WC points that correspond to BMI values with equivalent absolute disease risk. Results from other Aboriginal communities would contribute to the evidence required for future WC-threshold for Aboriginal people.

Further clarification on the role of other confounders on the relationship between WC and CVD and Type 2 diabetes

Potential confounders such as diet, physical activity, socio economic status and family history of disease should be considered in future studies assessing the relationship between WC and future risk of chronic diseases and mortality. Disentangling the effects of potential confounders and the role of potential effect modifiers such as pre-existing co-morbidities by stratified analyses should produce the direct effect of high WC.

Conclusions

The findings imply WC as a valuable factor in the chronic disease risk prediction models in the Aboriginal population. The results can potentially contribute to future development of guidelines and establishment of WC cut-off points in the Aboriginal Australia population. Furthermore, the findings can be used by general practitioners, Aboriginal health workers and other health professionals to communicate knowledge of the risk of high WC estimates associated with chronic diseases to individuals in the community via primary care. Ultimately, the WC and risk of disease tools developed could serve to raise awareness of morbidity and mortality outcomes of CVD and Type 2 diabetes in the Indigenous population.

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