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Utilization of a Metabolic Syndrome Index in Evaluating the Life in Balance Lifestyle Intervention for Prevention of Type 2 Diabetes among Urban American Indians and Alaska Natives

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UTILIZATION OF A METABOLIC SYNDROME INDEX IN EVALUATING THE
LIFE IN BALANCE LIFESTYLE INTERVENTION FOR PREVENTION
OF TYPE 2 DIABETES AMONG URBAN AMERICAN
INDIANS AND ALASKA NATIVES

by

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Bachelor of Science in Nursing
Shanghai Jiao Tong University, China
2006

A thesis submitted in partial fulfillment of
the requirements for the

Master of Public Health

**Department of Epidemiology and Biostatistics
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THE GRADUATE COLLEGE

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Hongbin Jin

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Utilization of a Metabolic Syndrome Index in Evaluating the Life in Balance Lifestyle Intervention for Prevention of Type 2 Diabetes among Urban American Indians and Alaska Natives

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ABSTRACT

Utilization of a Metabolic Syndrome Index in Evaluating the Life in BALANCE Lifestyle Intervention for Prevention of Type 2 Diabetes among Urban American Indians and Alaska Natives

by

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Background: A myriad of diabetes prevention programs modeled on the Diabetes Prevention Program (DPP) are carried out worldwide to fight against the current diabetes pandemic. The percentage of weight reduction is a widely used indicator to evaluate diabetes prevention programs. However, weight change alone may not fully reflect the efficacy of lifestyle intervention. A metabolic syndrome index is a promising novel scale for evaluation of diabetes prevention programs because it is a systematic, comprehensive, and stable indicator that reflects the metabolic risk reduction for diabetes and its complications at multiple levels and dimensions.

Methods: A total of 22 overweight and obese AI/ANs (age, 39.6 ± 10.4 years; BMI, 34.1 ± 6.3 kg/m²) at increased risk for developing type 2 diabetes residing in Las Vegas participated in the LIB program between April, 2010 and December, 2011. Metabolic syndrome was defined according to the American Heart Association and the National Heart, Lung, and Blood Institute criteria. Clinical measures were collected at three different points in time before and after the completion of the LIB lifestyle core curriculum and the end of post-program follow-up.

Results: Only 12 of the 22 participants completed the whole LIB program. Among the five metabolic syndrome components, only waist circumference demonstrated a significant correlation with weight. After a mean follow-up interval of 10.4 months, the metabolic syndrome index was reduced by 11% at the completion of the LIB program. The study population demonstrated significant decreased waist circumference and elevated HDL cholesterol. Triglycerides manifested the highest percentage change without statistical significance. No significant change was observed in blood pressure and fasting blood glucose.

Conclusions: These findings imply that the application of a metabolic syndrome index provides more detailed information than weight in evaluating diabetes prevention programs by analyzing pre-post changes in multiple diabetes markers, particularly when the target population has normal to slightly elevated BMI. Additionally, the changes in metabolic syndrome components outline the characteristics of diabetes prevention programs, showing great potential for helping public health professionals to individualize and optimize program curriculums for different target populations. Promotion of metabolic syndrome index in diabetes research will establish a unified criterion in evaluating diabetes prevention programs and facilitate efficacy comparison among different programs.

Key word: Diabetes; Metabolic syndrome; Prevention; Evaluation

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CHAPTER 1

INTRODUCTION

Percentage change from participants' starting weight is a widely used indicator to evaluate the efficacy of diabetes prevention programs (Ali, Echouffo-Tcheugui, & Williamson, 2012). Weight loss is a direct consequence of diet modification and exercise which are the two most common constructs in diabetes prevention programs. Yet, weight change alone may not fully reflect the efficacy of lifestyle intervention in terms of improving prediabetes conditions and reducing the risk of developing type 2 diabetes and its complications. Additionally, the accuracy and reliability of weight change is insufficient, since it can be affected by many confounding factors.

Metabolic syndrome, which is associated with central obesity and insulin resistance, has been demonstrated as a reliable predictor of type 2 diabetes in many epidemiological studies (Lorenzo, Okoloise, Williams, Stern, & Haffner, 2003; Wilson, D'Agostino, Parise, Sullivan, & Meigs, 2005; Mannucci et al., 2008; Wassink, Van Der Graaf, Soedamah-Muthu, Spiering, & Visseren, 2008). The presence of metabolic syndrome accounts for approximately half of the population attributable risk for diabetes (Wilson et al., 2005). Previous research studies have shown that, independent of weight loss, symptoms of metabolic syndrome can be reduced by lifestyle intervention (Christ, Iannello, Iannello, & Grimm, 2004; Okura et al., 2007; Muzio, Mondazzi, Harris, Sommariva, & Branchi, 2007; Meckling & Sherfey, 2007; Rector et al., 2007). However, the extent of improvement in each component of metabolic syndrome varied from project to project. A metabolic syndrome index is a multivariate parameter incorporating the

components of metabolic syndrome, which systematically, comprehensively and stably reflects the metabolic risk for diabetes and its complications.

From the perspective of epidemiology, population attributable risk is employed to describe risk reduction for a disease or an unhealthy condition objectively. However, a reduction in incidence cannot be measured without a control group. In this study, we propose to use a new concept – metabolic risk – in describing and quantifying the risk reduction caused by diabetes prevention programs. First, type 2 diabetes is a chronic metabolic disease. Research on metabolic risk factors for type 2 diabetes and its complications has greatly advanced in past decades and metabolic syndrome has been widely accepted as a predictor for type 2 diabetes and its complications. Second, metabolic risk for diabetes and its complications is generally attributable to environmental and behavioral factors. In other words, this type of risk, to some extent is separate from genetic risk and can be reduced by lifestyle intervention. The risk reduction in terms of the improvement in health status can be measured and quantified by a metabolic syndrome index. Additionally, adoption of metabolic risk is convenient for public health professionals because it is a direct reflection of the efficacy of diabetes prevention intervention.

To improve the evaluation methods for diabetes prevention programs to accurately and objectively reflect the metabolic risk reduction of developing type 2 diabetes and its complications, the metabolic syndrome index should be promoted as a preferred outcome indicator over weight loss for diabetes prevention programs.

Purpose of the Study

The purpose of this study is to utilize a novel indicator – the metabolic syndrome index – to evaluate the Life in BALANCE (LIB) lifestyle intervention for prevention of type 2 diabetes among urban American Indians and Alaska Natives (AI/AN) residing in Las Vegas. This study will promote the improvement of evaluation methods for diabetes prevention programs by creating a new scale to measure the magnitude of metabolic risk reduction for developing type 2 diabetes and its complications after intensive lifestyle intervention.

Research Question

Will the metabolic syndrome index be useful in evaluating the Life in BALANCE lifestyle intervention for prevention of type 2 diabetes among urban AI/ANs residing in Las Vegas?

Answering this question requires incorporating the following procedures in the study plan: 1) assess the change of the five components of metabolic syndrome and weight across the LIB program, 2) analyze the correlation between the five metabolic syndrome components and weight, and 3) assess the change of the metabolic syndrome index across the LIB program and compare with weight loss.

Hypotheses

Hypothesis1

H₀: There is no significant difference between pre- and post-intervention waist circumferences among urban AI/ANs residing in Las Vegas.

H_A: There is significant difference between pre- and post-intervention waist circumferences among urban AI/ANs residing in Las Vegas.

H_{A1}: Post-intervention waist circumference is significantly less than pre-intervention waist circumference among urban AI/ANs residing in Las Vegas.

Note: This hypothesis will be repeated for systolic blood pressure, diastolic blood pressure, triglycerides, HDL cholesterol, and fasting blood glucose.

Rationale: Previous research studies have indicated that the five components of metabolic syndrome respond differently to different lifestyle intervention designs (Christ et al., 2004; Okura et al., 2007; Muzio et al., 2007; Meckling & Sherfey, 2007; Rector et al., 2007). To a great extent, the design of a lifestyle intervention curriculum predetermines its efficacy. Therefore, the first step of this study is to determine whether the LIB program has reduced the symptoms of metabolic syndrome and the magnitude of the reductions.

Every program has its strengths and weaknesses, and not every component will necessarily demonstrate a statistically significant improvement. However, it is good to know what a program's strengths so that health professionals can choose the most effective program. By using a metabolic syndrome index, the magnitude of the change in the five components can serve as a program's "resume" by outlining the effect of each characteristic of a program.

Hypothesis 2

H₀: There is no significant correlation between waist circumference and weight among urban AI/ANs residing in Las Vegas.

H_A: There is significant correlation between waist circumference and weight among urban AI/ANs residing in Las Vegas.

Note: This hypothesis will be repeated for systolic blood pressure, diastolic blood pressure, triglycerides, HDL cholesterol, and fasting blood glucose.

Rationale: Theoretically, obesity is connected with the five components of metabolic syndrome directly or indirectly; however, the strength of their relationships varies. If a metabolic syndrome component is not correlated with weight, the risk for diabetes and its complications caused by the component cannot be fully revealed by weight.

Many research studies have indicated that waist circumference is highly correlated with body weight, but central obesity characterized by excess accumulation of abdominal fat is a stronger predictor for diabetes (Feller, Boeing, & Pischon, 2010). If the remaining four metabolic syndrome components are not significantly correlated with weight, the risk reduction caused by them cannot be reflected by weight loss alone. This would support the idea that a metabolic syndrome index is more systematic than weight loss in evaluating diabetes prevention programs. The hypothetical relationship between weight and metabolic syndrome is illustrated in Figure 1.

Hypothesis 3

H₀: There is no significant difference between pre- and post-intervention metabolic syndrome indexes among urban AI/ANs residing in Las Vegas.

H_A: There is significant difference between pre- and post-intervention metabolic syndrome indexes among urban AI/ANs residing in Las Vegas.

H_{A1}: Post-intervention metabolic syndrome index is significantly less than pre-intervention metabolic syndrome index among urban AI/ANs residing in Las Vegas.

Rationale: The method to calculate the metabolic syndrome index will be presented in detail in the methods section. This step is to test whether the metabolic syndrome index has been decreased through the LIB lifestyle intervention. The magnitude of reduction (percentage change) represents the amount of metabolic risk for diabetes and its complications that has been reduced.

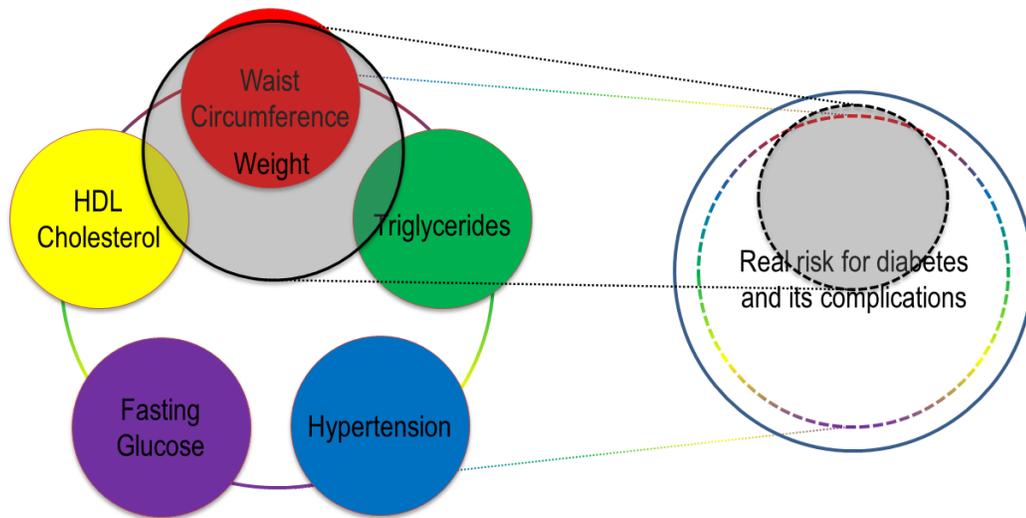


Figure 1. Hypothetical Relationship between Weight and Metabolic Syndrome in Reflecting the Real Risk for Diabetes and Its Complications

Significance of the Study

This study will establish a better indicator than weight loss for evaluating diabetes prevention program outcomes, which systematically, comprehensively and stably quantifies the risk reduction for diabetes and its complications caused by lifestyle intervention. Metabolic syndrome reflects more facets of risk for diabetes and its complications than weight loss and a metabolic syndrome index incorporates this cluster

of metabolic risk factors and integrates them into one scale. Lastly, by applying the metabolic syndrome index, a program “resume” will be created to facilitate program-to-program comparisons, which will greatly enhance the researchers’ ability to select an intervention program better suited to their study population with increased efficacy.

CHAPTER 2

REVIEW OF RELATED LITERATURE

Type 2 Diabetes

Diabetes is a global public health crisis affecting all socioeconomic classes and all races (Caprio et al, 2008). Diabetes is a common, disabling, and deadly disease with an increasing health and financial burden on individuals and countries. According to the Center for Disease Control and Prevention (CDC, 2011), in 2010 approximately 8.3% of the U.S. population (25.8 million) had diabetes and 35% of U.S. adults aged 20 years or older (79 million) had prediabetes, a condition in which blood glucose levels are higher than normal but not yet meet the diagnostic criteria for diabetes (ADA, 2012). Diabetes is the ninth leading cause of death worldwide (WHO, 2008) and the seventh leading cause of death in the United States (CDC, 2009).

The risk of death in people with diabetes is about twice as that in people without diabetes (CDC, 2011), which can be largely attributed to the diabetes-related complications. In addition to the risk of death, long-term complications such as heart disease, stroke, hypertension, diabetic retinopathy, and amputation drastically increase medical expenses and severely undermine the life quality of diabetes patients. A recent estimate reported that the U.S. national economic burden of prediabetes and diabetes reached \$218 billion in 2007 (Dall et al., 2010).

Type 2 diabetes is a chronic disease characterized by increased blood glucose levels that result from either insufficient insulin production or insulin resistance, a condition where cells ignore the insulin. It is a multifactorial disease caused by both genetic factors as well as non-genetic factors that result from individual behavior and

environment (Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2003). For example, some specific genes are associated with glucose homeostasis and regulate the magnitude of the effects of lifestyle choices such as physical activity (Lakka et al., 2004).

Minorities such as American Indian/Alaska Natives (AI/AN) suffer a disproportionately high burden of diabetes (Mokdad, Bowman, Enqlqau, & Vinicor, 1998). AI/ANs have the highest age-adjusted prevalence and incidence of diabetes among all U.S. racial and ethnic groups in spite of the fact that numerous programs funded by U.S. government have been conducted in AI/AN communities to prevent and treat diabetes since 1997 (CDC, 2003). The causes of astoundingly high prevalence rates of diabetes among AI/ANs and other high prevalence populations remain unclear, but the evident race/ethnicity disparities may be accounted for by genetic predisposition to some extent. Studies rooted in Neel's "thrifty genotype" hypothesis advocate that diabetes has a strong genetic basis (Neel, 1962 & 1999; Ritenbaugh & Goodby, 1989). Previous genetic research has shown that several genes such as maturity onset diabetes of the young (MODY) genes and atypical diabetes mellitus (ADM) genes significantly contribute to some rare forms of diabetes (Benyshek, 2001). However, recent research suggests that type 2 diabetes has multiple and complex etiologies and genetic factors do not play a dominant role in this etiological puzzle. Substantial evidence indicated that maternal glucose during pregnancy is significantly associated with abnormal glucose intolerance in adulthood. Both nutritional deficits and surplus during prenatal and perinatal periods lead to increased adipose deposition later in life and raise the risk for type 2 diabetes (Benyshek, 2007). On the other hand, various behavioral and

environmental risk factors play important roles in the development of diabetes as well. Healthy diet and regular physical activity have been linked with a reduced risk of developing type 2 diabetes in terms of reducing body adiposity, improving insulin resistance, and ameliorating glucose tolerance (Ross et al., 2000; Kelley & Goodpaster, 2001).

Type 2 diabetes is shaped by a multitude of factors that include genetics, developmental factors during key stages of early life, lifestyle choices, as well as socioeconomic barriers. From the perspective of chronic disease epidemiology, a group of risk factors associated with type 2 diabetes are aging, overweight or obesity, high blood pressure, high triglyceride level, low HDL cholesterol level, sedentary or inactive lifestyle, previous positive impaired fasting blood glucose or impaired glucose tolerance, high-fat diet, family history, ethnicity and race, and gestational diabetes or giving birth to a low birth weight (< 2.5 kg) or high birth weight (> 4.0 kg) baby (NDEP, 2012).

The Diabetes Prevention Program

Recently, the most inspiring achievement in diabetes research was the Diabetes Prevention Program (DPP, 2002) funded by the National Institute of Diabetes and Digestive and Kidney Diseases, which demonstrated that lifestyle changes and metformin treatment both reduced the incidence of diabetes in high risk population, but the lifestyle intervention, in particular was more effective in preventing or delaying the development of diabetes (Knowler et al., 2007).

A myriad of diabetes prevention programs modeled on the DPP are carried out worldwide to fight against the diabetes pandemic (WHO, 2012). These programs are

individualized for specific target populations and optimized for the best use of resources and budgets. Even though most of the programs are translational projects sharing classic constructs such as lifestyle intervention, diet modification and exercise, the reported efficacy of these programs differed dramatically due to different program designs and evaluation methods (Ali et al., 2012).

Weight Loss

Percentage change from participants' starting weight is a widely used indicator to assess and evaluate the efficacy of diabetes prevention programs (Ali et al., 2012). The DPP proclaimed that diabetes can be delayed or averted through systematic and intensive lifestyle intervention (Knowler et al., 2007). A follow-up study concluded that intervention to reduce diabetes should primarily target weight reduction (Hamman et al., 2006). However, even when weight is regained after the DPP, the risk reduction for diabetes resulting from lifestyle intervention can persist for at least 10 years (Knowler et al., 2009).

There are many reasons why weight loss is prevailing in diabetes prevention programs as the main outcome. First, weight loss is an easy and affordable parameter to be measured repeatedly across the whole program. Second, weight loss is a predictable consequence of diet modification and exercise which are the two most common constructs in diabetes prevention programs, and which generally manifests dose-response relationship. Furthermore, limited by the nature of their study designs and ethical issues, most diabetes prevention programs are not allowed to include a control group so that they

fail to measure the “real” risk reduction – the reduced diabetes incidence, which is more common in long-term cohort or experimental studies.

Overall, weight loss seems to be a rational alternative and has been adopted by many programs. However, weight loss alone may not fully reflect the efficacy of diabetes prevention programs in terms of improving prediabetes conditions and reducing the risk of developing type 2 diabetes and its complications. The Finnish Diabetes Prevention Study demonstrated that the risk of diabetes was reduced 58% through lifestyle intervention after a 3-year follow-up in spite of minimal weight loss. More important, the authors emphasized that exercising 4 hours per week reduced the risk of diabetes in participants without weight loss (Tuomilehto et al., 2001). Many research studies have confirmed that beneficial changes in type 2 diabetes incidence can be achieved independently of weight loss (Pan et al., 1997; Ramachandran et al., 2006). Furthermore, the accuracy and reliability of weight change is problematic. Loss of muscle and bone mass instead of fat loss are likely to happen due to unhealthy diet and exercise plans. Stress caused by dramatic lifestyle change without sufficient family support may also contribute to weight loss. Additionally, weight measurement can be affected by confounding factors such as food and fluid intake prior to the measurement.

Metabolic Syndrome

Metabolic syndrome was first recognized by Reaven in 1988 (Reaven, 1988) as a cluster of risk factors such as dyslipidemia, hypertension, and hyperglycemia for cardiovascular disease. Later, insulin resistance was introduced into metabolic syndrome which drastically expanded its application in diabetes research. Findings from the

Framingham Heart study showed that metabolic syndrome predicted 25% of all new cases of cardiovascular disease (Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004). The “common soil” hypothesis suggested that type 2 diabetes and cardiovascular diseases share pathogenetic pathways (Stern, 1995). It has been widely accepted that metabolic syndrome is a constellation of metabolic risk factors in a person which contribute to both atherosclerotic cardiovascular disease and type 2 diabetes (Grundy et al., 2004; Alberti, Zimmet & Shaw, 2005; Grundy et al., 2005). Several organizations such as the World Health Organization, the International Diabetes Foundation, and the American Heart Association have proposed diagnostic criteria for metabolic syndrome in the efforts to promote its clinical practice in predicting the risk of cardiovascular disease and type 2 diabetes (Alberti & Zimmet, 1998; Balkau & Charles, 1999; Grundy et al., 2004; Alberti et al., 2005; Grundy et al., 2005). Although there is no consensus criteria for metabolic syndrome, hyperglycemia, hypertension, obesity, and dyslipidemia have been accepted as major components for this multiplex risk syndrome. These components connect with each other and constitute a network to comprehensively measure the risk for diabetes and its complications. Nonetheless, they are not inter-replaceable due to their independent roles in human metabolism.

Components of Metabolic Syndrome

Hyperglycemia (fasting blood glucose): Current research suggested that insulin resistance is the primary cause of metabolic syndrome (Deen, 2004), although the temporal sequence of insulin resistance and obesity is still unknown. However, insulin resistance will change the metabolism of carbohydrates and lipids (Shaw et al., 2005).

Dyslipidemia (triglycerides and HDL cholesterol): Hyperinsulinemia resulting from insulin resistance will lead to increased triglycerides and decreased HDL cholesterol (Shaw et al., 2005), which are common symptoms in type 2 diabetes patients (Moller & Kaufman, 2005; Alberti et al., 2006).

Hypertension (high systolic blood pressure and/or diastolic blood pressure): Hypertension has been strongly associated with both glucose intolerance and obesity. One research study suggested that hypertension is caused by hyperactive sympathetic nervous systems as a result of hyperglycemia (Shaw, Hall, & Williams, 2005).

Obesity (waist circumference): Obesity has been associated with insulin resistance, dyslipidemia and hypertension (Grundy et al., 2004) and contributes to the development of cardiovascular disease. Central obesity, in particular, strongly correlates with metabolic risk factors (Grundy et al., 2004; Wassink et al., 2008). Waist circumference is considered as an easy way to determine central obesity (Alberti et al., 2005).

Despite the fact that different criteria were adopted in epidemiological research, metabolic syndrome has been recognized as a precursor of cardiovascular disease and type 2 diabetes (Lorenzo et al., 2003; Wilson et al., 2005). Furthermore, several cohort studies have indicated that metabolic syndrome is a stronger predictor of type 2 diabetes than that of cardiovascular disease (Lorenzo et al., 2003; Wilson et al., 2005; Ford, Li, & Sattar, 2008), which accounts for approximately one fourth and half of the population-attributable risk for cardiovascular disease and diabetes respectively (Wilson et al., 2005). However, in light of the common pathophysiological pathways, cardiovascular disease becomes the primary complication of type 2 diabetes. In 2004, heart disease and stroke

were the top two complications of diabetes which accounted for 84% of deaths related to diabetes altogether (CDC, 2011).

To calculate the metabolic syndrome index, clinical cutoff values are required in this process. The criteria of clinical diagnosis of metabolic syndrome proposed by different organization are summarized in Appendix 1. In this study, the cutoff values from the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) criteria of metabolic syndrome were adopted. The criteria proposed by the European Group for Study of Insulin Resistance (EGIR) and American Association of Clinical Endocrinologists (AACE) were excluded from this study because they do not take patients with diabetes into account, which limits their application in diabetes prevention programs. The International Diabetes Foundation (IDF) criteria and AHA/NHLBI criteria are the updated versions for the World Health Organization (WHO) criteria and the National Cholesterol Education Program's Adult Treatment Panel III Report (NCEP) criteria respectively. The advantage of the IDF criteria is that it includes various waist circumference cutoff values which are specific to different ethnic groups. However, it doesn't provide reference values for AI/ANs and many research studies reported that the criteria of the NCEP are more effective in identifying subjects at risk for diabetes than the IDF criteria. Updates to the AHA/NHLBI criteria include lowering the fasting blood glucose threshold to 100 mg/dL, which is consistent with the prediabetes definition proposed by the American Diabetes Association.

Metabolic syndrome is an effective and efficient indicator in predicting the risk for developing diabetes and its complications. The question is whether metabolic syndrome is a sensitive and dynamic parameter in response to the risk reduction caused

by lifestyle intervention. A secondary analysis of the DPP found that both lifestyle intervention and metformin therapy reduced the development of the metabolic syndrome (Orchard, 2005). Further investigations by several studies found that the adoption of healthy diet and regular exercise, either alone or in combination can improve the components of the metabolic syndrome in some way (Christ et al., 2004; Okura et al., 2007; Muzio et al, 2007; Meckling & Sherfey, 2007; Rector et al., 2007). However, the improvement in the components of metabolic syndrome varied with different levels of intensity and combinations of interventions.

Rationale for the Metabolic Syndrome Index

The DPP provided a template for future diabetes prevention programs in establishing basic constructs and timeframes. However, different principles and study designs have been employed to individualize and optimize these programs. The DPP is a long-term experimental study (clinical trial) which allows the real risk for diabetes in terms of the incidence of diabetes to be observed. The highly successful study showed that a minimum of 7% weight loss or weight maintenance and a minimum of 150 minutes physical activity per week resulted in a 58% reduction in the incidence rate of diabetes (DPP, 2002). Unfortunately, most of the translational studies are short-term health promotion programs, which fail to measure the real risk reduction without controls. Many translational studies adopt the percentage of weight reduction as a targeted outcome in order to estimate the real risk reduction through comparison with the DPP. However, weight loss alone may not be able to reflect the effectiveness of these programs in terms of ignoring the characteristics in different program designs. For example, the percentage

of weight loss may be different between a program designed for individuals suffering from obesity and that of a program designed for individuals suffering from severe insulin resistance.

Lifestyle intervention for diabetes prevention programs is a multidimensional process with a series of health promotion strategies at multiple levels. The complexity of diabetes prevention programs necessitates a comprehensive and integrated indicator to evaluate their efficacy. Unlike the weight loss, the components of metabolic syndrome provide a multivariate parameter which covers more aspects of risk reduction caused by lifestyle intervention. A metabolic syndrome index is a systematic and comprehensive indicator that can be used to evaluate the efficacy of diabetes prevention programs because it measures risk reduction for diabetes and its complications at multiple levels and dimensions. A reduction in the metabolic syndrome index reflects the risk reduction for diabetes and its complications resulting from a diabetes prevention program, which makes program-to-program comparison possible. In addition, the five components of the metabolic syndrome index, to some extent represent different aspects of the risk for diabetes and its complications. The magnitude of change in the five components outlines the strengths and weaknesses of a program, which can serve as a useful reference for researchers to choose the best program for specific populations.

CHAPTER 3

METHODS

Calculation Method for the Metabolic Syndrome Index

A metabolic syndrome index is a five-point scale that assigns one point to each of the five metabolic syndrome components - waist circumference, blood pressure, triglycerides, high-density lipoprotein (HDL) cholesterol, and fasting blood glucose. The clinical cutoff values for this study were those from the metabolic syndrome criteria proposed by the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) in 2005 (Grundy et al., 2005).

The five components are assumed to be equally important for diabetes and its complications because each component is assigned one point only. The component equality is assured by the AHA/NHLBI definition, which is defined as the presence of any three or more of the following five components - central obesity (waist circumference > 102 cm for men, > 88 cm for women), elevated triglycerides (≥ 150 mg/dL), hypertension (systolic BP ≥ 130 mmHg, and/or diastolic BP ≥ 85 mmHg), raised fasting blood glucose (≥ 100 mg/dL), and reduced HDL cholesterol (< 40 mg/dL for men, < 50 mg/dL for women). By adjusting the clinical cutoff values, a balance is reached among the five components, guaranteeing that they contribute equally to a metabolic syndrome diagnosis.

One point will be counted if a component meets the clinical criteria above and a total score will be calculated as the metabolic syndrome index for each participant. A range from zero to five quantifies the metabolic risk for diabetes and its complications

which can be reduced by lifestyle intervention. A metabolic syndrome index should be measured at least twice (before and after intervention) in order to calculate the magnitude of the risk reduction potentially resulting from the intervention.

Data Collection and Treatment

The Life in BALANCE (LIB) project, conducted by the University of Nevada, Las Vegas, was a community-based participatory research project to pilot a translational study that modeled the Diabetes Prevention Program (DPP) intensive lifestyle coaching intervention in urban American Indian/Alaska Native (AI/AN) population. AI/ANs suffer a disproportionately high burden of type 2 diabetes and the incidence has been escalating at an alarming rate since the early 1960s (Valway et al., 1993). Urban AI/AN populations, which account for 60% of AI/ANs, may confront a worse scenario because they are affected more by modernized lifestyles and benefit less from the health services provided by tribal reservations and the Indian Health Service (IHS). The LIB program provided an opportunity to study the full extent of the problem of diabetes in this underserved population and utilize a metabolic syndrome index in evaluating the LIB pilot study in urban AI/AN population.

The LIB project was a pre-experimental study (one group pre-test and post-test study). Non-clinical and clinical data were obtained from the LIB intensive lifestyle intervention pilot study. A secondary analysis was performed to answer the research question and hypotheses.

The LIB project was approved by the University of Nevada Las Vegas Institutional Review Board. All research activities were designed to have minimal risk to participants. Informed consent was required for all participants.

Target Population

The pilot study targeted urban AI/AN residents in Las Vegas, Nevada at increased risk for developing type 2 diabetes. Participants were recruited through community screenings, media announcements and referrals from other participants and/or project members. Six free community screenings were held at the Las Vegas Indian Center and Southern Nevada Native American Educational Coalition event in order to recruit qualified participants. The criteria for “increased risk” were defined as being overweight or obese and a glycosylated hemoglobin (HbA1c) level between 5.4% and 6.4% via a finger stick blood draw. Participants who met the inclusion criteria were informed about the LIB study and those who agreed to participate in would receive a 16-week core curriculum and regular follow-up.

Inclusion Criteria

1. Age 21 and older
2. Self-identified AI/AN ethnicity
3. Body mass index (BMI) ≥ 25 kg/m²
4. HbA1c between 5.4% and 6.4%

The LIB program was optimized and individualized for adult AI/ANs at high risk for type 2 diabetes. The presence of a BMI of 25 kg/m² and above (overweight) and a glycosylated hemoglobin level between 5.4% and 6.4% diagnosis were essential risk factors identifying high-risk potential participants for the study.

Exclusion Criteria

1. Major illness, myocardial infarction, symptoms of coronary heart disease, previous diabetes diagnosis, and pregnancy
2. Use of medication improving glucose tolerance (e.g., metformin)
3. Use of medication impairing glucose tolerance

The LIB program involved intensive lifestyle intervention which might be harmful for individuals with major illness or compromised health conditions. Individuals with previous diabetes diagnosis were excluded because the LIB program was designed to prevent the development of diabetes. Individuals using medications interfering glucose tolerance were excluded to avoid introducing a major confounding factor in this study.

Non-Clinical and Clinical Measures

Non-clinical data were obtained before and after the completion of the LIB lifestyle core curriculum. A baseline survey and a post-participation survey were conducted by lifestyle coaches.

Clinical measures were collected at three different points in time before and after the completion of the LIB lifestyle core curriculum and the end of post-program follow-up. All clinical procedures were followed standardized protocols and performed by trained clinical specialists. Clinical measures of interest included weight, waist circumference, blood pressure, triglycerides, HDL cholesterol, and fasting blood glucose.

Data Security

All survey data were secured with locked file cabinets and password protected computers at the American Indian Research and Education Center at University of Nevada Las Vegas. Biological samples were immediately analyzed and promptly

disposed afterward. All clinical data were stored in a secure digital database with restricted access. Each participant was assigned a unique identification number which disconnects the link between research data and participants' identifiable information. All participants' identifiable information was accessible to senior research team members only. Each member of the research team was required to complete the Collaborative Institutional Training Initiative (CITI) Human Subjects Protections training prior to conducting research activities with the LIB program. The principal investigator was responsible for supervising all data collection activities.

Data Management

All question choices and responses were numbered by different coding formats for further statistical analysis. Non-clinical and clinical data were compiled into Microsoft Excel spreadsheets. A data codebook was developed to code and decode data. Data cleaning, recoding, and statistical analysis were performed after the completion of data collection.

Statistical Methods

This study was a pilot study with a small sample size ($n=22$). Considering the magnitude of attrition rates (31.8% and 45.5% at the completion of the core curriculum and follow-up respectively), two separate group analyses were conducted for each test. The first one was to analyze only the participants who completed the entire LIB program. The second one was to analyze all the participants including those who dropped out before completing the program by employing a simple intention-to treat analysis (last observation carry-forward analysis). The purpose of the intention-to-treat analysis is to

avoid the effects of a high drop-out rate because it is reported that participants who completed a program are more likely to show expected change than those who dropped out, hence skewing the results towards positive outcomes. The results from the two analyses were reported independently and a comparison was done to reveal whether the positive change was a potential result from intervention. Variables of interest are summarized in Table 1.

Table 1. Variables of Interest

Variables	Type	Range	Values / Clinical Cut-off Values
Sex	Categorical	0 / 1	0 = Male 1 = Female
Age (years)	Continuous		
Education (%)	Categorical	0 / 1	0 = Without bachelor degree 1 = Bachelor degree or higher
Employment (%)	Categorical	0 / 1	0 = Unemployed 1 = Employed
Household income (%)	Categorical	0 / 1	0 = Less than \$ 50,000 per year 1 = 50,000 or greater per year
Weight (kg)	Continuous		
Waist circumference (cm)	Continuous		102 in men, 88 in women
Systolic blood pressure (mmHg)	Continuous		130
Diastolic blood pressure (mmHg)	Continuous		85
Triglycerides (mg/dL)	Continuous		150
HDL cholesterol (mg/dL)	Continuous		40 in men, 50 in women
Fasting blood glucose (mg/dL)	Continuous		100
Metabolic syndrome index	Categorical	0 - 5	

The SPSS statistical package (SPSS 19, IBM, Armonk, NY) was used for data analysis. All statistical tests were two-tailed. The overall statistical significance level was set to $\alpha = 0.05$.

Descriptive statistics was used to summarize the data. Mean, median and standard deviation were used to describe the central tendency and the dispersion for the variables of interest.

Both the histogram and Kolmogorov-Smirnov test indicated that the pilot data violated the normal distribution assumption, which cannot be corrected by data transformation. Therefore, nonparametric methods were employed in the data analysis.

The Wilcoxon signed-rank test and the Fisher's exact test were used to compare the differences of demographic information and baseline clinical measures between participants who completed the program and those who dropped out.

Hypothesis 1 and 3: The Friedman test was used to analyze the change of the variables of interest across the three time points. Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $p < 0.0167$. Intention-to-treat analysis was applied in this step.

Hypothesis 2: The Spearman's rank correlation coefficient was used to analyze the correlation between the components of metabolic syndrome and weight. Intention-to-treat analysis was applied in this step.

CHAPTER 4

RESULTS

A total of 22 (age, 39.6 ± 10.4 years; BMI, 34.1 ± 6.3 kg/m²) subjects were enrolled in this pilot study, 17 (77.3%) of them were female. Ten participants dropped out of the program before completion (dropout rate: 45.5%). The demographic information and baseline clinical data are summarized in Table 2. Based on subjects' characteristics at entry there were no significant differences in demographic information and clinical measures between those participants who completed the program and those who dropped out of the program.

Table 2. Demographic Characteristics and Baseline Clinical Measures of the Study Population

Variables	Participants who completed the program (n=12)	Participants who dropped out (n=10)	p-value
Female (%)	83.33	70.00	0.624
Age (years)	38.58 ± 9.55	40.70 ± 11.81	0.923
Education (%)			0.074
Without bachelor degree	50.00	90.00	
Bachelor degree or higher	50.00	10.00	
Employment (%)			0.293
Unemployed	8.33	30.00	
Employed	91.67	70.00	
Household income (%)			1.000
< \$ 50,000	66.70	70.00	
≥ \$ 50,000	33.30	30.00	
Weight (kg)	96.67 ± 12.50	94.63 ± 28.64	0.381
Waist circumference (cm)	110.89 ± 11.40	113.00 ± 21.64	0.974
Triglycerides (mg/dL)	189.92 ± 109.41	152.10 ± 47.10	0.539

HDL cholesterol (mg/dL)	49.91 ± 15.42	48.00 ± 7.17	0.863
Fasting blood glucose (mg/dL)	107.17 ± 10.26	107.50 ± 6.40	0.923
Systolic BP (mmHg)	121.03 ± 14.49	116.99 ± 11.81	0.628
Diastolic BP (mmHg)	78.07 ± 11.08	74.70 ± 8.04	0.418

- Values shown are mean values ± standard deviation (SD).
- Results are based on the Wilcoxon signed-rank test and the Fisher's exact test.

After the LIB intensive lifestyle intervention, 12 completers demonstrated a statistically significant drop in weight (5.79%, $p=0.01$) with a range of -2.82% to 14.23%, in spite of the fact that two-thirds of them did not achieve the goal of a 7% weight loss. Metabolic syndrome symptoms were improved to different extents at completion. Of the five components, only waist circumference and HDL cholesterol demonstrated statistically significant improvements (5.79%, $p=0.01$ and 12.92% $p=0.007$). Waist circumference decreased steadily across the three time points, but HDL cholesterol did not start to rise until completing the core curriculum. Triglycerides had the largest reduction (15.89%), but the change was not statistically significant and with high variability. Systolic blood pressure decreased more than diastolic blood pressure. Fasting blood glucose showed very limited improvement after the program (Table 3.1 & 3.2).

Table 3.1. Comparison of Three Clinical Measures (n=12)

Variables	Baseline (1 st)	Completed core curriculum (2 nd)	Follow up (3 rd)	p-value	Change
Weight (kg)	96.67 ± 12.50	93.53 ± 12.44	91.07 ± 10.37	0.010*	- 5.79%
Waist circumference (cm)	110.89 ± 11.40	108.20 ± 11.66	106.08 ± 11.09	0.010*	- 4.34%
Triglycerides (mg/dL)	189.92 ± 109.41	158.42 ± 75.30	159.75 ± 72.14	0.717	- 15.89%
HDL cholesterol (mg/dL)	49.91 ± 15.42	48.64 ± 15.00	56.36 ± 14.62	0.007*	+ 12.92%
Fasting glucose (mg/dL)	107.17 ± 10.26	105.17 ± 7.94	106.75 ± 4.90	0.502	- 0.39%
Systolic BP (mmHg)	121.03 ± 14.49	117.00 ± 10.26	113.72 ± 10.25	0.338	- 6.04%
Diastolic BP (mmHg)	78.07 ± 11.08	78.71 ± 12.02	76.55 ± 11.82	0.779	- 1.95%

Table 3.2. Post Hoc Tests

Variables	1 st vs. 2 nd	1 st vs. 3 rd	2 nd vs. 3 rd
Weight (kg)	1 st > 2 nd , p = 0.003	1 st > 3 rd , p = 0.012	2 nd = 3 rd , p = 0.347
Waist circumference (cm)	1 st > 2 nd , p = 0.016	1 st = 3 rd , p = 0.050	2 nd = 3 rd , p = 0.230
HDL cholesterol (mg/dL)	1 st = 2 nd , p = 0.212	1 st = 3 rd , p = 0.045	2 nd < 3 rd , p = 0.004

- a. 1st refers to the first clinical measure before the LIB program; 2nd refers to the second clinical measure at the completion of the LIB core curriculum; 3rd refers to the third clinical measure at the end of follow-up.
- b. This procedure only included participants completing all three clinical measurements (n=12).
- c. Values shown are mean values ± standard deviation (SD).
- d. Results are based on the Friedman test.
- e. Post hoc results are based on the Wilcoxon signed-rank test with a Bonferroni correction (p < 0.0167); insignificant results are reported as equality, and no post hoc analysis was done.
- f. * indicates significant at 0.05.

The results from the intention-to-treat analysis were highly consistent with those from the original analysis (Table 4.1 & 4.2), indicating that positive findings did not result from removing the data of drop-outs. However, the results from the intention-to-treat analysis are not considered in the final results due to the risk of introducing bias and inflating type I error.

Table 4.1. Comparison of Three Clinical Measures with Intention-to-treat Analysis (n=22)

Variables	Baseline (1 st)	Completed core curriculum (2 nd)	Follow up (3 rd)	p-value	Change
Weight (kg)	95.74 ± 20.84	93.87 ± 20.90	92.53 ± 20.36	0.008*	- 3.35%
Waist circumference (cm)	111.85 ± 16.43	109.95 ± 16.96	108.79 ± 16.92	0.001*	- 2.74%
Triglycerides (mg/dL)	172.73 ± 87.14	151.18 ± 61.34	151.91 ± 59.41	0.581	- 12.05%
HDL cholesterol (mg/dL)	49.00 ± 11.67	48.91 ± 11.58	52.91 ± 11.89	0.002*	+ 7.98%
Fasting glucose (mg/dL)	107.32 ± 8.53	105.86 ± 6.98	106.73 ± 5.26	0.382	- 0.55%
Systolic BP (mmHg)	119.19 ± 13.19	115.46 ± 11.64	113.67 ± 11.51	0.245	- 4.63%
Diastolic BP (mmHg)	76.54 ± 9.74	75.71 ± 10.76	74.53 ± 10.35	0.368	- 2.63%

Table 4.2. Post Hoc Tests with Intention-to-treat Analysis (n=22)

Variables	1 st vs. 2 nd	1 st vs. 3 rd	2 nd vs. 3 rd
Weight (kg)	1 st > 2 nd , p = 0.005	1 st > 3 rd , p = 0.013	2 nd = 3 rd , p = 0.347
Waist circumference (cm)	1 st > 2 nd , p = 0.004	1 st > 3 rd , p = 0.013	2 nd = 3 rd , p = 0.230
HDL cholesterol (mg/dL)	1 st = 2 nd , p = 0.723	1 st < 3 rd , p = 0.010	2 nd < 3 rd , p = 0.004

- 1st refers to the first clinical measure before the LIB program; 2nd refers to the second clinical measure at the completion of the LIB core curriculum; 3rd refers to the third clinical measure at the end of follow-up.
- This procedure included all the participants (n=22).
- Values shown are mean values ± standard deviation (SD).
- Results are based on the Friedman test.
- Post hoc results are based on the Wilcoxon signed-rank test with a Bonferroni correction (p < 0.0167); insignificant results are reported as equality, and no post hoc analysis was done.
- * indicates significant at 0.05.

In the correlation analysis, a significant correlation between waist circumference and weight was detected, which is in line with the anticipated result. No other metabolic syndrome components were correlated to weight (Table 5).

Table 5. Correlation between Weight and Metabolic Syndrome Components (n=22)

	Waist circumference	Triglycerides	HDL cholesterol	Fasting glucose	Systolic BP	Diastolic BP
Weight						
Rho	0.733*	- 0.032	- 0.188	0.276	0.214	0.204
p-value	<0.001	0.825	0.201	0.055	0.139	0.160

- This procedure included all the participants (n=22) with censored data.
- Results are based on the Spearman's rank correlation coefficient.
- * indicates significant at 0.05.

The metabolic syndrome index had an 11% drop in total score for the participants completing the LIB program, which was not statistically significant. The decrease was not evident until the completion of the core curriculum (Table 6).

Table 6. Comparison of Three Metabolic Syndrome Index Measures (n=12)

Variables	Baseline (1st)	Completed core curriculum (2nd)	Follow up (3rd)	p-value	Change
Metabolic Syndrome Index	3.00 ± 1.41	3.00 ± 1.35	2.67 ± 0.99	0.256	- 11.00%

- a. 1st refers to the first clinical measure before the LIB program; 2nd refers to the second clinical measure at the completion of the LIB core curriculum; 3rd refers to the third clinical measure at the end of follow-up.
- b. This procedure only included participants completing all three clinical measurements (n=12).
- c. Values shown are mean values ± standard deviation (SD).
- d. Results are based on the Friedman test.

CHAPTER 5

DISCUSSION, LIMITATIONS, AND CONCLUSIONS

Discussion

A weight loss of 7% of initial body weight was set as the primary study goal for the LIB program, because it is deemed to be safe, effective, and feasible for participants to maintain over a long-term follow-up. Unfortunately, weight loss data failed to demonstrate the efficacy of the LIB program in minimizing the risk for diabetes because the 12 participants completing the program had an average weight loss of 5.79% at completion. Weight loss alone, however, cannot quantify the magnitude of risk reduction for diabetes and its complications. A metabolic syndrome index introduced a novel approach and an informative framework from which to evaluate LIB program outcomes.

In the present study a significant correlation was found between weight and waist circumference across the program spectrum. Weight and waist circumference are universal parameters in estimating general and abdominal obesity respectively. Abnormal body fat distribution, particularly around abdomen, is highly associated with an increased risk for diabetes, even if the BMI falls within the normal range (Schulze et al., 2006). A German research team pointed out that waist circumference gives a better prediction of diabetes risk than BMI because development of diabetes is influenced more by visceral fat tissue which is metabolically more active and produces more hormones and cytokines, and this relationship is more pronounced in people with normal BMI (Feller, Boeing, & Pischon, 2010). Statistically speaking, weight might be an inferior alternative to waist circumference ($r = 0.733$, $p < 0.001$), but it cannot take over the roles of other metabolic risk factors, which was evidenced by the non-significant correlation between weight and

triglycerides, HDL cholesterol, fasting glucose and blood pressure seen in the present study. Obesity plays a role in hyperinsulinemia, insulin resistance, dyslipidemia, and hypertension. However, the pathogenetic interactions do not allow obesity to serve a substitute for the other metabolic syndrome components. This inference is supported by the high prevalence of metabolic syndrome among individuals with normal to slightly elevated BMI (St-Onge, Janssen, & Heymsfield, 2004) and significant type 2 diabetes incidence reduction after lifestyle intervention with minimal weight loss (Tuomilehto et al., 2001).

The metabolic risk for diabetes and its complications has a multifaceted structure comprising environmental and behavioral factors. Lifestyle intervention for diabetes prevention programs works on these facets simultaneously with complex health promotion strategies. A metabolic syndrome index acts as a systematic and comprehensive indicator in evaluating the efficacy of lifestyle interventions by targeting the five principal metabolic factors. The results of the current study indicated that the LIB lifestyle intervention succeeded in lowering the metabolic risk for diabetes and its complications by 11% among the small pilot population. Since metabolic risk is an estimate of a modifiable proportion of the risk for diabetes and its complications, this parameter is more pragmatic for public health professionals by separating from non-modifiable risk like genetic predisposition or developmental metabolic programming. The value was higher than the percentage of weight loss, suggesting that a metabolic syndrome index covered more aspects of the risk for diabetes and its complications which cannot be revealed by weight alone.

The metabolic syndrome components responded differently to the LIB lifestyle intervention. Only waist circumference and HDL cholesterol demonstrated statistically significant improvement. Waist circumference manifested a significant correlation with weight. Both of them showed a significant reduction at the completion of the core curriculum, although this trend slowed down in the follow-up period. The core curriculum was the most structured phase of the LIB lifestyle intervention involving increased physical activity and decreased calorie and fat intake. All the participants were required to set individualized goals for weight loss and fat/calorie intake before the core curriculum and were encouraged to achieve these goals within 4 months. The early achievement of a significant reduction of waist circumference might be attributed to the presence of lifestyle coaches and an incentive package that included a free gym membership. With the guidance and supervision of the lifestyle coaches as well as accessible sports apparatus, participants were more prone to follow the scheduled exercise and diet plan. However, after removing extrinsic motivations, a self-managed and self-monitored plan was employed to reinforce the acquired positive behavioral changes in the follow-up period, which might have contributed to the deceleration of the waist circumference reduction. No weight and waist circumference regain occurred at the end of the follow-up period, indicating that the core curriculum was effective in helping participants master weight maintenance skills and the effect of the LIB lifestyle intervention persisted at least 35 weeks. Considering the efficiency of weight loss and waist circumference reduction seen during the core curriculum, an extension of the core curriculum may be helpful to achieve the original goal of a 7% weight loss.

HDL and triglycerides are two typical lipoproteins in diabetic dyslipidemia, although their responses to lifestyle interventions may differ. A 36-month clinical trial in Germany found that both diet alone and diet combined with exercise decreased triglyceride levels and increased HDL cholesterol values in participants with metabolic syndrome (Christ et al., 2004). Two similar studies in Italy and the United States found that no change occurred in HDL cholesterol from baseline after 5-month and 6-month lifestyle intervention respectively, regardless of a significant reduction in waist circumference and triglyceride levels (Muzio et al., 2007 & Rector et al., 2007). Results from the three studies suggest that triglycerides have a quick response to lifestyle intervention while HDL cholesterol demands a longer period to manifest observable positive change. In the present study, HDL cholesterol remained steady throughout the 16-week core curriculum, but a statistically significant elevation was observed during the follow-up period. No significant change was detected in triglycerides, but these showed the highest percentage of decrease which mainly occurred during the core curriculum. These findings are in concordance with the assumption above, indicating that elevation of HDL cholesterol has a long lag time and a 16-week ongoing LIB lifestyle intervention is effective to increase HDL cholesterol in the long term.

Many studies have indicated that hypertension can be relieved through lifestyle intervention, especially in decreasing systolic blood pressure (Christ et al., 2004, Meckling et al., 2007). A smaller decrease was observed in diastolic blood pressure compared with systolic blood pressure in the present study, but neither was statistically significant. One possible explanation is that the average baseline blood pressure among our participants was within normal range (systolic BP: 119.19 ± 13.19 mmHg; diastolic

BP: 76.54 ± 9.74 mmHg), which might have limited the effect of the LIB lifestyle intervention in alleviating hypertension.

Hyperglycemia is one of the primary symptoms in individuals with prediabetes and diabetes. It is also the most intractable target in diabetes prevention programs. Diet and exercise are widely perceived to be beneficial for glycemic control. However, conflicting results on the effects of lifestyle intervention in improving hyperglycemia are common in clinical trials. In the present study, fasting blood glucose was not affected by the LIB lifestyle intervention. In addition, no sign of improvement in long-term glycemic control was observed, which was evidenced by stable glycosylated hemoglobin (HbA1c) levels (data not shown). This finding is consistent with a recent study in an overweight and obese female Canadian population, reporting that fasting blood glucose was not affected by diet and exercise regardless of a significant weight loss (Meckling et al., 2007). Moderate weight loss is beneficial in improving insulin resistance (Reaven, 2005). Previous studies have shown that a 10% weight loss lowers blood glucose and improves cardiovascular risk factors. It is possible that an average weight loss of less than 10% is not sufficient to trigger a detectable reduction of blood glucose. On the other hand, considerable evidence showed that isocaloric diet, low in fat and enriched in carbohydrates, will exacerbate insulin resistance. Replacing saturated fat with carbohydrates may increase daily blood glucose level because it requires more insulin to maintain glucose homeostasis, which is demanding in individuals with insulin resistance (Reaven, 2005). The LIB core curriculum emphasizes reducing fat and total calorie intake without a structured guide for dietary macronutrient content. High levels of carbohydrate intake might have counteracted the effect of weight loss in improving insulin resistance

and lowering blood glucose. The addition of a structured dietary macronutrient content guide in the LIB core curriculum may be effective in achieving more weight loss and an observable fasting blood glucose reduction.

In summary, the results indicate that the LIB program reduced the metabolic risk for diabetes and its complications by 11% in urban Native Americans living in Las Vegas with increased diabetes risk. The current LIB core curriculum is effective in decreasing waist circumference and elevating HDL cholesterol level. Further research is needed to investigate the effect of an extended and optimized core curriculum in strengthening the efficacy of the LIB program.

Limitations

Some limitations of this study have to be taken into account. First, this pilot study has a small sample size. Even the intention-to-treat analysis indicates that the positive changes may be attributable to the lifestyle intervention itself, but large variability resulting from a small sample size may mask some significant results. Second, the last follow-up visit was completed at either 8 months or 12 months after the first clinical measure, resulting in a follow-up period varied from 8.1 months to 12.8 months. Theoretically acquired positive behaviors gradually weaken over time without proper reinforcement. Participants who had an early follow-up visit might behave better than those who had a late follow-up visit, which might have influenced the last clinical measure. Third, due to the nature of secondary analysis, some important confounding factors cannot be included in this study. Social support is crucial in shaping and consolidating individuals' positive behaviors. Information like marital status was not

collected in the LIB pilot study, which might also contribute to a high dropout rate. Information on lifestyle choices like smoking and drinking was not collected as well, which play a role in increasing metabolic risk related to diabetes, which might have attenuated the effects of the LIB program.

Conclusions

In conclusion, findings from the present study imply that the application of the metabolic syndrome index provides more detailed information in addition to weight in evaluating diabetes prevention program outcomes by analyzing pre-post changes in multiple diabetes markers, particularly when the target population has normal to slight elevated BMI. It also serves as comparison for other evaluation tools used in diabetes prevention programs by reporting the amount of metabolic risk for diabetes and its complications that has been reduced. Additionally, the changes in metabolic syndrome components outline the characteristics of diabetes prevention programs, showing great potential for helping public health professionals to individualize and optimize program curriculums for different target populations. Promotion of metabolic syndrome index in diabetes research will establish a unified criterion in evaluating diabetes prevention programs and facilitate efficacy comparison among different programs.

APPENDIX 1

SUMMARY OF METABOLIC SYNDROME CRITERIA

Clinical Measure	WHO (1998)	EGIR (1999)	NCEP (2001)	AAACE (2003)	IDF (2005)	AHA/NHLBI (2005)
Insulin Resistance	IGT, IFG, T2DM, or lowered insulin sensitivity	Plasma insulin > 75 th percentile		IGT or IFG		
Obesity	WR > 0.9 in men WR > 0.85 in women and/or BMI > 30 kg/m ²	WC ≥ 94 cm in men WC ≥ 80 cm in women	WC ≥ 102 cm in men WC ≥ 88 cm in women	BMI ≥ 25 kg/m ²	Increased WC (population specific)	WC ≥ 102 cm in men WC ≥ 88 cm in women
Dyslipidemia	TG ≥ 150mg/dL and/or HDL-C < 35 mg/dL in men HDL-C < 39 mg/dL in women	TG ≥ 150mg/dL and/or HDL-C < 39 mg/dL in men or women	TG ≥ 150 mg/dL HDL-C < 40 mg/dL in men HDL-C < 50 mg/dL in women	TG ≥ 150mg/dL and/or HDL-C < 40 mg/dL in men HDL-C < 50 mg/dL in women	TG ≥ 150mg/dL HDL-C < 40 mg/dL in men HDL-C < 50 mg/dL in women	TG ≥ 150mg/dL HDL-C < 40 mg/dL in men HDL-C < 50 mg/dL in women
Hypertension	Systolic BP ≥ 140 mmHg or Diastolic BP ≥ 90 mmHg	Systolic BP ≥ 140 mmHg or Diastolic BP ≥ 90 mmHg	Systolic BP ≥ 130 mmHg or Diastolic BP ≥ 85 mmHg	Systolic BP ≥ 130 mmHg or Diastolic BP ≥ 85 mmHg	Systolic BP ≥ 130 mmHg or Diastolic BP ≥ 85 mmHg	Systolic BP ≥ 130 mmHg or Diastolic BP ≥ 85 mmHg
Hyperglycemia	IGT, IFG, or T2DM	IGT or IFG (but not diabetes)	FG ≥ 110 mg/dL	IGT or IFG (but not diabetes)	FG ≥ 100 mg/dL	FG ≥ 100 mg/dL
Other	Microalbuminuria			Other features of insulin resistance		
Diagnosis	Insulin resistance plus any 2 of the 5 features	Insulin resistance plus any 2 of the 4 features	Any 3 of the 5 features	Insulin resistance plus any 1 of the 5 features	Increased WC plus any 2 of the 4 features	Any 3 of the 5 features

IGT = Impaired glucose tolerance, IFG = Impaired fasting glycaemia, T2DM = Type 2 diabetes, WR = Waist-to-hip ratio, WC = Waist circumference, TG = Triglycerides, HDL-C = High-density lipoprotein cholesterol, FG = Fasting glucose, BP = Blood pressure

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