Indian Health Service

Guidelines for Care of Adults with Prediabetes and/or the Metabolic Syndrome in Clinical Settings

September 2008

Division of Diabetes Treatment and Prevention
5300 Homestead Rd
Albuquerque, NM 87110

Table of Contents

Figure

Tables

Executive Summary

The Indian Health Service (IHS) Division of Diabetes Treatment and Prevention, in conjunction with Area Diabetes Consultants, has developed these clinical guidelines for adults with prediabetes and/or the metabolic syndrome. Historically, patients who develop diabetes mellitus and/or cardiovascular disease (CVD) are frequently observed to possess a similar array of risk factors. These risk factors, which include dyslipidemia, hypertension and hyperglycemia, have been grouped into a syndrome with a pathogenesis hypothesized to be rooted in insulin resistance and central obesity (Reaven, 1988). Various labels referring to this constellation of risk factors have included Metabolic Syndrome, Insulin Resistance Syndrome, and Syndrome X. While the majority of individuals exhibiting this array of risk factors do not become frankly diabetic, they do have an increased risk of developing CVD and other adverse consequences associated with insulin resistance. Logically, one would want to implement a primary prevention strategy targeting prediabetes and metabolic syndrome to try and avoid these adverse consequences. However, in the case of metabolic syndrome, the labeling of the risk factors as a "syndrome" has been subject to some debate due to a lack of consensus on the definition and lack of understanding of the underlying pathogenesis (Kahn, et al., 2005). Despite the debate, CVD and diabetes persist as the number 1 and number 6 leading causes of death in the US, respectively (Mokdad, et al., 2004). The known risk factors, whether considered independently or as a cluster with a similar underlying pathogenesis, continue to drive the increasing rates of complications and mortality from these two chronic diseases. Consequently, IHS providers should aggressively target primary prevention strategies in addressing prediabetes and metabolic syndrome in American Indian and Alaskan Native populations where rates of CVD and diabetes exceed those seen in the general U.S. population (Kunitz, 2008).

The purpose of these guidelines is to outline a prevention strategy that can be used to help provide consistent, quality care to adults with prediabetes and metabolic syndrome. In testing for prediabetes, a fasting plasma glucose is recommended due to its simplicity and the opportunity it provides to check fasting lipids. Diagnosis and application of the test is illustrated in **Table 1.** Classification and Diagnosis of Impaired Glucose Homeostasis Diagnosis of metabolic syndrome, for the purposes of American Indian and Alaska Native populations, is based on the criteria defined by the Third Report of the Adult Treatment Panel (ATPIII). These criteria showed prognostic value in predicting CVD for both diabetic and non-diabetic participants in the Strong Heart Study (De Simone, et al., 2007) illustrates the criteria for diagnosing the metabolic syndrome. A patient that meets 3 or more of the criteria can be coded according to their prediabetes or metabolic syndrome diagnosis. The mainstay of treatment should be lifestyle change. The Diabetes Prevention Program showed up to a 58% reduction in the incidence of diabetes with diet, exercise and counseling in insulin resistant patients (Knowler, et al., 2002). Primary prevention through healthy eating and increased physical activity is essential in managing risk for both CVD and diabetes (Welty, et al., 2002). Recommendations for nutrition and exercise counseling are provided in **Appendix** A. Suggested Lifestyle Changes Counseling on Prediabetes and Metabolic Syndrome **Appendix B.** Nutrition Recommendations for Prediabetes and the Metabolic Syndrome and **Appendix C.** Overview of Guidelines for Exercise Testing and Prescription. Prior to initiation of any exercise regimen, the patient should be thoroughly evaluated and a determination made as to his/her level of CVD risk. An **American Indian and Alaska Native specific risk calculator** was developed using data from the Strong Heart Study (Lee, et al., 2006). IHS providers should use this calculator in determining the CVD

risk of individual patients. Prior to any prescribed exercise regimen patients at-risk for a cardiovascular event should be screened **(Table 3.** Criteria for Performing Stress Testing and Examples of Activity Intensity**).** Once, cleared for exercise, the FITT principle can assist in prescribing an exercise regimen **(Table 4.** Recommendations for Using the FITT Principle**).** In cases where lifestyle modification fails, medication is likely warranted. Weight loss that fails to achieve goal or that is not sustained may benefit from medication. Other evidence based prescription recommendations are also made for **Prediabetes** and **Cholesterol**.

Introduction

Prediabetes and metabolic syndrome are conditions that often present together, clinically, and share a common pathogenesis (Figure 1). Some of the linkages in the diagram may be debated and questioned in academic circles. However, much of the data out of the Strong Heart studies and others have shown that these linkages do exist for American Indian and Alaska Natives. Comprehensive management of a patient's cumulative "cardiometabolic risk" requires that the underlying risk factors be treated. Identifying individuals that have these conditions can be difficult. However, the impetus lies with the primary care provider to diagnose and treat these patients aggressively *before* they develop diabetes and/or cardiovascular disease (CVD) (Einhorn, et al., 2005). This is especially important among the American Indian and Alaska Native populations where the prevalence of metabolic syndrome exceeds that seen in the general population. Mortality rates among American Indians that have developed diabetes or CVD also exceed the rates seen in the general population (Kunitz, 2008). Therefore, early detection, treatment and periodic reassessment can help decrease one's cardiometabolic risk and improve overall health.

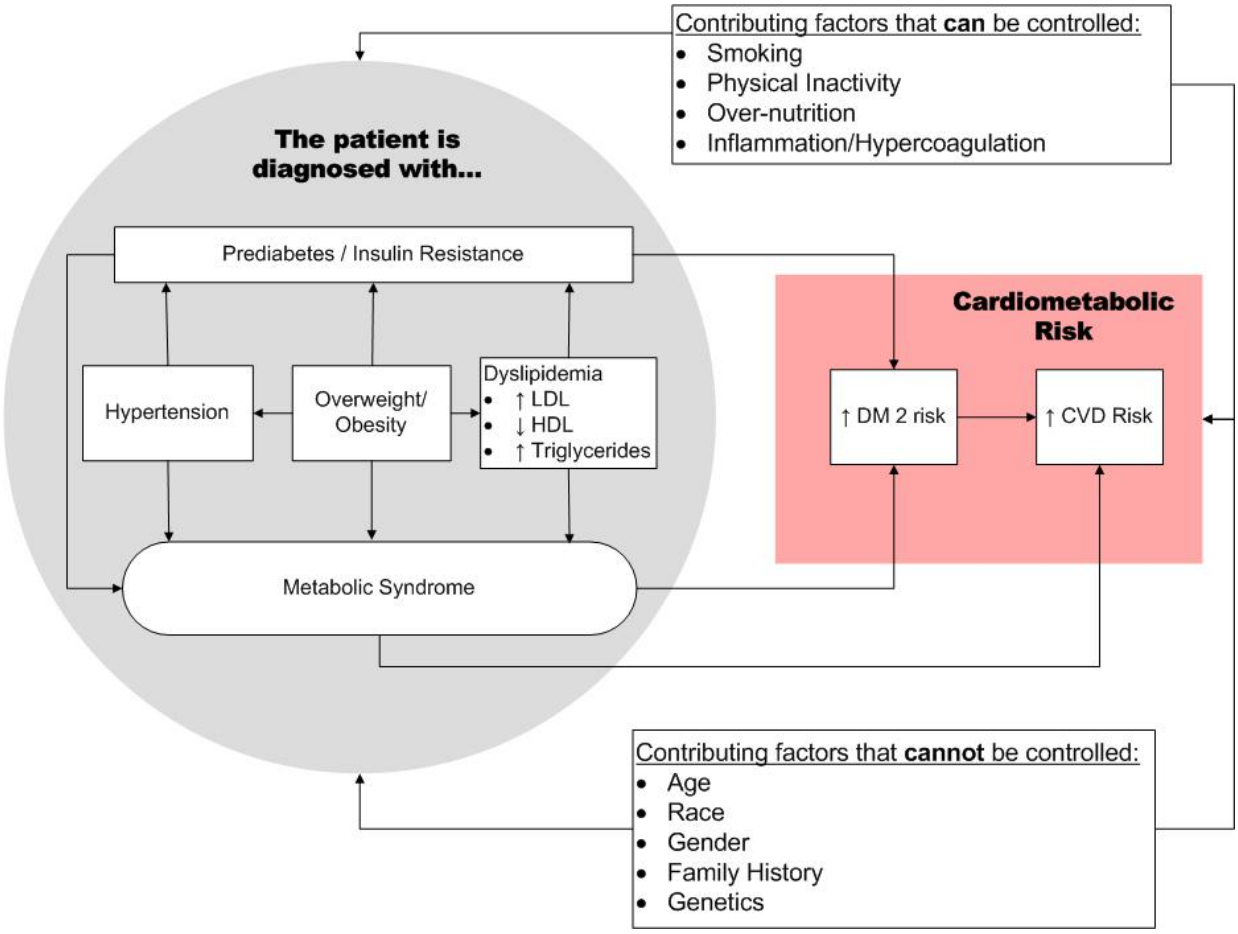

Figure 1- Factors Contributing to Cardiometabolic Risk

The importance of diagnosing prediabetes and metabolic syndrome lays in the fact that they help identify individuals at high risk for CVD and Type 2 diabetes (Zimmet & Alberti, 2005). Important aspects of these conditions include:

- The estimated prevalence of metabolic syndrome in American Indian and Alaska Native adult populations is 44% in men and 63% in women when using the ATP III criteria adopted by these guidelines (Russell, et al., 2007).
- Both prediabetes and metabolic syndrome confer high risk for the development of Type 2 diabetes.
- Recent clinical trials have demonstrated that progression to diabetes in high-risk individuals can be averted though behavioral lifestyle interventions (Knowler, et al., 2002).
- One of the key diagnostic indicators for the metabolic syndrome, obesity, is linked to the epidemic of diabetes in the American Indian and Alaska Native population. Morbidity and cost can be reduced more effectively through prevention than with treating the disease once diagnosed (Marrero, 2007).
- An analysis of American Indians diagnosed with metabolic syndrome according to ATP III criteria, revealed a significantly increased risk for combined fatal and nonfatal cardiovascular events (including coronary heart disease, stroke, and congestive heart failure) in both non-diabetic and diabetic patients. Non-diabetic American Indian patient with metabolic syndrome have a 30 to 40% higher new cardiovascular event rate (De Simone, et al., 2007).
- Another analysis looked at 172,573 individuals and found that patients with metabolic syndrome had a 54% greater risk of experiencing a cardiovascular event than someone without metabolic syndrome (Gami, et al., 2007).
- Detection and treatment efforts will focus on:
  - Identifying undiagnosed diabetes
  - Delaying the onset of diabetes through risk appropriate screening
  - Identifying undiagnosed hypertension
  - Identifying undiagnosed dyslipidemia
  - Diagnosing and treating obesity
  - Prevention through healthy lifestyle choices and medication when necessary

Prediabetes

Who Should Be Tested?

The American Diabetes Association recommends the following criteria for prediabetes screening in asymptomatic individuals (American Diabetes Association, 2008):

- Body mass index (BMI $\geq$ 25 kg/m^2) AND
- Member of a high-risk ethnic population

Therefore, all American Indian and Alaska Native patients who exceed the BMI cutoff should be screened for prediabetes. Screening should also be considered for this population with a normal BMI who have the following risk factors:

- Physical inactivity
- First-degree relative with diabetes
- Women who delivered a baby weighing >9 pounds or who have been diagnosed with gestational diabetes mellitus
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- High density lipoprotein (HDL) cholesterol level <35 mg/dl and/or a triglyceride level >250 mg/dl
- Women with polycystic ovarian syndrome (PCOS)
- Impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) on previous testing
- Other clinical conditions associated with insulin resistance (e.g. acanthosis nigricans)
- History of CVD
- History of weighing < 2500 grams at birth (low birth weight)

American Indian and Alaska Native patients with these risk factors classify as "high risk" and should be screened annually for prediabetes. Low risk patients should be tested every 1 to 3 years starting at age 35.

Classification and Tests

Prediabetes is a state of hyperglycemia that does not meet the diagnostic criteria for diabetes. Prediabetes can be diagnosed using either of the following classifications of impaired glucose homeostasis (Table 1):

Table 1. Classification and Diagnosis of Impaired Glucose Homeostasis

Classification	Tests Used	Diagnostic Values*
Impaired Glucose Tolerance (IGT)	75gm oral glucose tolerance test (OCCT), With test for plasma glucose after 2 hours	140 to 199mg/dl
Impaired Fasting Glucose (IFG)	Fasting plasma glucose (FPG) after an 8 hour fast	100 to 125mg/dl

***** According to the American Diabetes Association, 2007

A patient may have IFG, IGT, or both at the same time. However, either IFG or IGT may be used to diagnosis prediabetes. No one test is foolproof.

An FPG or OGTT may be used to screen for prediabetes. However it is impractical to conduct the OGTT for every patient in need of screening. An FPG is the preferred screening test (American Diabetes Association, 2007). The FPG is simple and convenient, and it provides an opportunity to check fasting lipids. An FPG test is best done in the morning after an 8-hour fast. Afternoon values, even after a similar fasting period, tend to be lower. Programs may consider adding a 2-hour OGTT if resources permit because it may identify additional cases of PD, as well as cases of diabetes among those with FPG in the PD range. Data from the Strong Heart Study have shown that anywhere from 37%-55.2% of AI's with diabetes diagnosed by OGTT (2hPG ≥200) had FPG <126 (Wang, et al., 2002). Therefore, programs with the resources to screen with OGTT may want to consider using the test to boost sensitivity for the detection of actual cases of diabetes.

Although casual blood glucose (CBG) or random blood glucose (RBG) screening may have a role in detecting people at risk for undiagnosed diabetes, especially in patients with symptoms, there are no cut points with acceptable predictive values for the detection of PD. Therefore, screening for PD with a CBG is not formally recommended at this time; however, we do recognize that some programs will perform screening with "finger stick" CBG glucose, in which case a value of ≥100 mg/dl (fasting or casual) and < 200 mg/dl (casual) is a reasonable threshold for further diagnostic testing.

An A1c is not recommended as a screening tool for prediabetes due to the test's poor ability to detect lower levels of hyperglycemia (U.S. Preventive Services Task Force, 2007). The addition of an A1c test does not add to the sensitivity of a FPG (American Diabetes Association, 2007). Strong Heart data have been used to look at using the A1c test to pick up new cases of diabetes missed by fasting blood glucose alone (Wang, et al., 2002). However, no defined cutoffs or recommendations have been made for using A1c for prediabetes screening. Similarly, a test for serum insulin levels does not aid in the diagnosis or management of prediabetes or metabolic syndrome and are not recommended.

Metabolic Syndrome

How Is It Diagnosed?

Several sets of criteria for metabolic syndrome have been proposed. The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria are the most clinically practical criteria and are therefore recommended for clinical use in the IHS (ATP III, 2002). Additionally, the ATP III criteria showed good prognostic value for CVD among a cohort of American Indians in The Strong Heart Study (De Simone, et al., 2007).

Table 2 presents information on the ATP IIII definition of metabolic syndrome. A diagnosis of metabolic syndrome requires three or more of the criteria listed in Table 2.

Table 2. ATP III Definition of Metabolic Syndrome

Factor	3 or more of the following
Abdominal Obesity*	Waist Circumference: > 40 inches (or 102 cm) for men > 35 inches (or 88 cm) for women
Triglycerides mg/dl	≥ 150mg/dl or on drug treatment for high TG
HDL, mg/dl	< 40mg/dl for men and < 50mg/dl for women, or on drug treatment for low HDL
Blood Pressure, mmHg	Systolic blood pressure (SBP) ≥ 135mmHg or diastolic blood pressure ≥ 85mmHg, or on drug treatment for HTN
Fasting glucose, mg/dl**	FPG, ≥ 100mg/dl

* The correlation of BMI with waist circumference is variable in patients with high or low muscle mass. Waist circumference is most valuable in detecting high-risk patients with BMI in the range of 25–35 kg/m^2. Most patients with BMI ≥ 35 kg/m^2 meet the metabolic syndrome waist circumference criteria, and the waist measurement is not necessary.
** Grundy, et al., 2005

To ensure that diabetes risk is adequately assessed, some metabolic syndrome clinic protocols have required IFG (or IGT) and a measure of central adiposity (waist circumference or BMI) to be two of the three risk factors.

ICD-9 Codes for Documenting Prediabetes and Metabolic Syndrome

Proper medical record documentation of these conditions can improve clinical care, improve public health surveillance, and help with insurance reimbursement. Although a full discussion of the documentation process is beyond the limits of these guidelines, the following list of ICD-9 codes is intended to help get you started on the documentation process. We encourage you to work closely with your coders to maximize the benefits that proper documentation can provide.

Prediabetes

If someone meets diagnostic criteria for diabetes, they should be coded as having diabetes, and these prediabetes codes should not be used.

790.21 Impaired fasting glucose (IFG)
Fasting blood glucose 100–125 mg/dl

790.22 Impaired glucose tolerance (IGT)
2-hour OGTT value 140–199 mg/dl

790.29 Other abnormal glucose
Abnormal non-fasting glucose
Prediabetes, NOS (not otherwise specified)
Abnormal glucose, NOS

Metabolic Syndrome

This code can be used when people meet criteria for metabolic syndrome or any name used in a similar fashion (e.g., dysmetabolic syndrome, Syndrome X, etc.). The first time that the syndrome is documented, we recommend to code also for the individual components of the syndrome. Some will note that a person may have both diabetes and metabolic syndrome. In the IHS, we recommend that once a person is diagnosed with diabetes, the primary diagnosis should be diabetes and not metabolic syndrome.

277.7	Dysmetabolic Syndrome X (Metabolic Syndrome)

Commonly associated conditions:

272.4	Hyperlipidemia, NEC (not elsewhere classified) / NOS
401.9	Hypertension, NOS
278.00	Obesity, NOS
278.01	Morbid obesity
256.4	Polycystic ovaries
791.0	Proteinuria
701.2	Acquired acanthosis nigricans

Recommended Care for Patients with Prediabetes and Metabolic Syndrome

American Indian and Alaska Native patients with prediabetes and metabolic syndrome may have complex physical, psychological, and emotional needs. Patient self-management, education and multidisciplinary care coordination are essential to meet these needs. Services that teach, facilitate, and monitor lifestyle change for American Indian and Alaska Native patients should be made a priority in I/T/U clinics. Mitigating risk factors through lifestyle modification should, therefore, be the first goal in attempting to forestall the future development of Type 2 diabetes and CVD. Incorporating medication into a regimen that involves a healthy diet and exercise should be based on the level of calculated cardiovascular risk and the failure of lifestyle modification to give complete control of all risk factors.

Cardiovascular Risk Stratification

> **Key Point:** Calculate a 10-year CVD risk score for each patient at the time of metabolic syndrome and/or prediabetes diagnosis**.**

People with established diabetes are felt to have the equivalent of CVD and are treated accordingly. Patients with prediabetes and metabolic syndrome, however, do not appear to have the same CVD risk; although, a meta-analysis of the best available evidence suggests that people with metabolic syndrome are at some increased risk of cardiovascular events (Gami, et al., 2007). Quantifying this risk has traditionally been performed with The Framingham risk factor assessment. This tool, however, underestimates risk in American Indians and Alaska Natives. Fortunately, an analysis of data from The Strong Heart Study has yielded a formula for better

cardiovascular risk stratification (Lee, et al., 2006). This requires a calculation that can be performed through the following website:

http://strongheart.ouhsc.edu/chdcalculator/calculator.html

Unlike the Framingham risk calculator, this one is specifically designed to calculate cardiovascular risk for American Indians and Alaska Natives. It should be used to calculate cardiovascular risk among patients who are age 30 and older at the time the diagnosis of metabolic syndrome or any one of its components is made. If it is necessary to calculate the risk for a patient between the ages of 20-29 then the traditional Framingham risk calculator should be used.

http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=pub

The 10-year risk score allows the patient to be placed into one of the three following categories of risk to assist with treatment.

- Low Risk <10%
- Intermediate Risk 10-20%
- High Risk >20%

Goal 1: Risk Factor Control through Lifestyle Modification

The prime emphasis in the management of prediabetes and metabolic syndrome is to control the underlying, modifiable risk factors. These risk factors include obesity, hypertension, hypercholesterolemia, physical inactivity, and poor diet. The preferred method of control is through lifestyle change. When implemented effectively, lifestyle modification will reduce cardiometabolic risk. Many studies have clearly demonstrated that therapeutic lifestyle changes can significantly reduce the risk of developing diabetes and CVD.

Diabetes Prevention

There have been seven studies of lifestyle intervention for the prevention of diabetes showing an average risk reduction of 51% (Gillies, et al., 2007). One particular lifestyle intervention study, the Diabetes Prevention Program, gave all participants standard recommendations for lifestyle change and then randomized them to placebo, metformin, troglitazone or an intensive lifestyle modification program (Knowler, et al., 2002). The participants assigned to the intensive intervention arm received 16 sessions of one on one counseling with specific goals:

- Achieve and maintain a > 7% weight loss
- Fat gram goal of 25% of calories
- Calorie intake of 1200-1800 kcal/day
- 150 minutes per week of exercise

The group receiving lifestyle intervention was 58% less likely to develop diabetes than the placebo group. This was greater than the 31% risk reduction seen in the metformin arm.

Cardiovascular Disease Prevention

Lifestyle modification has also been shown to improve CVD risk factors and reduce coronary disease risk, as defined by the Framingham Heart Study, among patients without clinical manifestations of CVD (Ellsworth, et al., 2004). The 9 heart disease risk factors are:

- Being very overweight
- Cigarette smoking
- Diabetes
- Family History
- High blood pressure
- High cholesterol
- High fat diet
- Not exercising regularly
- Worry/anxiety/stress

Habits developed during young adulthood have a significant effect on these risk factors. Consequently, early diagnosis and intervention with education and lifestyle change is an important preventive strategy for coronary heart disease (Hubert, et al., 1987). This is particularly important among American Indian and Alaska Native populations where CVD is the leading cause of death and awareness of heart disease risk factors is low among certain subgroups. These groups include individuals with lower educational attainment, inhabitants of Arizona and southern North Dakota, men, and smokers (Schweigman, et al., 2006).

Lifestyle modification, provided through clinical education and counseling, for patients with prediabetes and metabolic syndrome can be an effective first step in preventing progression to the chronic disease state. Continuity-based group and individual support are key to helping people adopt and maintain healthy lifestyle changes (Appendix A. Suggested Lifestyle Changes Counseling on Prediabetes and Metabolic Syndrome .

Nutrition Counseling

The IHS highly recommends that weight management counseling be a multidisciplinary approach and include a registered dietitian or a public health nutritionist. All clinical providers should encourage healthier dietary choices. Appendix B. Nutrition Recommendations for Prediabetes and the Metabolic Syndrome provides information on the common nutrition recommendations. The recommendations incorporate the DASH diet which has shown potential benefits for the reduction of systolic blood pressure, diastolic blood pressure, total cholesterol and insulin resistance among patients with metabolic syndrome (Lien, et al., 2007).

Ideally, lifestyle changes should be made through a structured program. Such a program should emphasize goal setting, coaching and motivational interviewing, education and skills development, physical activity, self-monitoring, problem solving, behavior change (cognitive restructuring), stress and stimulus control, the importance of social support, and the utilization of community resources. In patients with hyperlipidemia a 4-session program comprised of these

elements was instrumental in lowering LDL and body weight (Hebert, et al., 1999). Another study found that 3 individualized dietitian visits of 1 hour each over an 8 week period had a beneficial effect in treating patients with hyperlipidemia (Sikand, et al., 2000). Proper nutrition counseling with regular participant contact and follow-up is a necessary intervention with significant cost savings in the long run (Delahanty, et al., 2001). Additionally, 87% of older Americans have either diabetes, hypertension, dyslipidemia or a combination of the three, in which nutrition interventions have been demonstrated to be effective in improving health and quality of life outcomes (Institute of Medicine Committee on Nutrition Services for Medicare Beneficiaries, 1999). Ensuring that patients over 55 years old receive medical nutrition therapy is a cost effective strategy in disease management (Sheils, et al., 1999).

Key Point: The initial weight loss goal should be to decrease body weight by 5-10%. Long term health benefits may be maximized with sustained weight loss of ≥10% of initial body weight. Sustaining modest reductions will significantly improve risk.

Key Point: Providers should refer patients to a registered dietitian (RD) or other qualified nutritionist for MNT. By ensuring individualized assessment, education, reassessment and follow- up providers can help patients achieve and maintain a healthy weight.

Exercise Guidelines

Exercise is a cornerstone of treatment for prediabetes and metabolic syndrome. Regular physical activity is essential for weight loss and has been shown to improve all of the elements that comprise metabolic syndrome (American College of Sports Medicine, 2001). In the case of hypertension, it has been shown that aerobic training reduces resting BP in both normotensive and hypertensive patients. Between the two, the decrease in BP appears to be more pronounced in hypertensive patients (American College of Sports Medicine, 2004).

As recommended in the Diabetes Prevention Program, the goal is to exercise 150 minutes a week (e.g., a 30-minute walk, 5 days a week). An alternative strategy is to use a pedometer with the goal of 10,000 steps per day. More complex fitness formulas are not needed for the majority of people. If more vigorous exercise will be attempted, an exercise tolerance test, an exercise prescription, and/or supervision by a fitness professional may be indicated to avoid health risks, over-exertion, and injury (Galloway, et al., 2002). Patients will benefit from access to resources that can deliver an individualized exercise safety assessment and prescription. Consideration must be given to patient safety, physical limitations, accessibility to exercise activities, and the goals and interests of the patient.

Table 3 summarizes the criteria for performing stress testing prior to exercise to detect CHD in asymptomatic patients by the degree of exercise intensity in which they will be participating. Further information on current exercise testing criteria has been published by the ACSM (American College of Sports Medicine, 2006).

Table 3. Criteria for Performing Stress Testing and Examples of Activity Intensity

Activity Intensity Examples	Low Risk (<10%)	Intermediate Risk (10 to 20%)	High Risk (>20%)*
Low** - moderate paced walking, stretching, activities of daily living	Not necessary	Not necessary	Not necessary
Moderate * fast walking, jogging, swimming, biking	Not necessary	Not necessary, unless atypical CHD symptoms or sedentary	Recommended
Vigorous – interval training, fast running, weight lifting	Not necessary	Recommended	Recommended

* Level of risk refers to the 10-year CHD risk as predicted by the Strong Heart calculations (Lee, et al., 2006).
**Sedentary individuals may experience a higher physiologic response to a lower level of activity, and the heart rate should be monitored to ensure that it correlates with the prescribed activity.

After medical clearance has been documented, an exercise regimen should be prescribed. The **FITT** principle may be useful in developing an exercise prescription. FITT stands for:

- **F** is the frequency or the number of times of exercise each week.
- **I** is for intensity or amount of effort.
- **T** is for time is the total amount of time in one session.
- **T** is for type of exercise.

Table 4 provides recommendations for using the FITT principle for developing an exercise prescription.

Table 4. Recommendations for Using the FITT Principle

FITT	Fitness Level	Beginning	Goal
Frequency	Low-Moderate	3-5 days/week	5 days per week
Frequency	High	5-7 days/week	5-7 days per week
Intensity	Low-Moderate	Target heart rate - 50% maximum heart rate*	Target heart rate - 70% maximum heart rate
Intensity	High	Target heart rate - 70% maximum heart rate	Target heart rate - 85% maximum heart rate
Time	Low - Moderate	15-30 minutes	30 minutes
Time	High	30-60 minutes	30-60 minutes
Type	Low – Moderate	Intermittent** or Continuous***	Continuous
Type	High	Continuous	Continuous

*Maximum Heart Rare = 220-age, then multiply by the appropriate percentage to get the target heart rate.
** Intermittent exercises like handball, racquetball, volleyball, tennis, soccer, weight training
*** Continuous exercises like walking, running, cycling, swimming, rowing, hiking, cross country skiing

Incorporate 5–10 minutes of warm-up and cool-down during the exercise session:

- Warm-up by performing the aerobic exercise at low intensity (i.e., walking slowly and gradually increasing pace over 5–10 minutes).
- Cool-down by reducing the pace of exercise over 5–10 minutes, followed by easy stretching. To avoid injury, stretching should be done after the muscles have warmed up. Generally, stretching is best saved for the cool-down period.
- After establishing an aerobic program, consider adding resistance exercises (e.g., weight-lifting, therabands, etc.) for those without CVD, following provider approval and under the direction of a qualified individual. To minimize risk for injury, a weight lifting program should be individualized and under the direction of a qualified person.

Depression screening and treatment

Depressive symptoms have been associated with the induction of insulin resistance and the development of Type 2 diabetes (Golden, et al., 2008). Depression is associated with obesity promoting health behaviors such as physical inactivity and hypercaloric diets. Accordingly, we recommend that patients with prediabetes and metabolic syndrome be screened for depression and referred for further evaluation and counseling as indicated (see appendix for resources).

Tobacco cessation counseling,

Avoiding or quitting smoking may be the single most important intervention to reduce risk for CVD. In a recent large multinational study, smoking and abnormal lipids were the two most important risk factors for acute myocardial infarctions worldwide (Yusuf, et al., 2004). Oral tobacco use also increases risk for CVD by increasing blood pressure and lipid abnormalities.

Current tobacco use (smoking or oral tobacco) should be documented in the patient's chart and a referral made to a program for tobacco cessation counseling. The 5 provides information on a behavioral counseling framework as a useful strategy for engaging patients in smoking cessation discussions (U.S. Preventive Services Task Force, 2007). Resources for smoking cessation assistance are included in the appendix.

Key Point: 5-A behavioral counseling framework:

1. Ask about tobacco use.
2. Advise to quit through clear personalized messages.
3. Assess willingness to quit.
4. Assist to quit.
5. Arrange follow-up and support.

Goal 2: Risk Factor Control through Medication or Surgery

Patients who cannot obtain a 5-10% weight loss and/or normalize cardiometabolic risk factors with lifestyle change alone should be given long-term pharmacotherapy as an adjunct.

Prediabetes

Medication may have a role in preventing or delaying diabetes. Several currently available medications have been studied for the specific purpose of preventing diabetes.

In the Diabetes Prevention Program, metformin (850 mg twice daily) was found to be associated with sustained weight loss and prevention of Type 2 diabetes in individuals with the following characteristics (Knowler, et al., 2002):

- BMI ≥ 35 kg/m2
- Age < 60 years
- Fasting glucose 110–125 mg/dl

The DREAM trial randomized 5,269 patients with abnormal glucose to either rosiglitazone or placebo. Patients receiving rosiglitazone were 62% less likely to develop diabetes (The DREAM Trial Investigators, 2006). Despite the promise of preventing diabetes this class of drugs has a questionable safety profile and is currently under investigation for a possible association with increase cardiovascular events. The pioglitazone in the Prevention of Diabetes (PIPOD) and Actos Now for Prevention of Type 2 Diabetes (ACT-NOW) trials promise to shed some light on the safety and effectiveness of this class of drugs.

This is an emerging therapeutic intervention, and information is not yet adequate to know the long-term benefits and risks. The decision to use medication in this setting must be made on an individual basis and with the patient's full understanding. IHS providers should therefore focus on lifestyle interventions for the prevention of diabetes. If further glucose control is needed then either metformin or pioglitizone may be considered.

ACE inhibitors and ARB's may be useful in treating the patients with hypertension and prediabetes. See the section on blood pressure below.

Blood Pressure

Blood pressure (BP) should be measured at every visit starting at age 18 (U.S. Preventive Services Task Force, 2007). A diagnosis of HTN is made by documenting 2 or more serially elevated readings on 2 visits over a period of 1-2 weeks. However, elevated is defined by the JNC 7 as a systolic blood pressure >140 mmHg and/or a diastolic blood pressure >90 mmHg. Newer AHA guidelines recommend a goal of less than 130/80 mmHg for all patients with known coronary artery disease or a 10-year cardiovascular risk of 10% or greater (Rosendorff, et al., 2007). Therefore, any American Indian and Alaska Native patient diagnosed with metabolic syndrome and who has a 10-year cardiovascular risk of 10% or greater, according to the Strong Heart Calculator, should have their hypertension treated to a therapeutic goal of <130/80 mmHg. A goal of <130/80 mmHg should also be set for any patients with diabetes mellitus, chronic renal disease, coronary artery disease (CAD), CAD risk equivalents, carotid artery disease (carotid bruit, or abnormal carotid ultrasound or angiography), peripheral arterial disease and abdominal aortic aneurysm. If the above conditions do not exist and cardiovascular risk is < 10% then the therapeutic goal for treatment of hypertension should be set at <140/90 mmHg.

β-Blockers and thiazide diuretics should be avoided as initial agents in patients diagnosed with the metabolic syndrome due to an increased risk of provoking Type 2 diabetes. The AHA has removed β-Blockers as options for initial therapy (Rosendorff, et al., 2007). Additionally, the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) showed that a thiazide diuretic led to a significant increase in glucose intolerance (The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group, 2002).

Whenever possible, IHS providers should use an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) as first line therapy in American Indians and Alaska Natives with metabolic syndrome. Studies involving both medications have shown significant reductions in new cases of diabetes. Data from the Heart Outcomes Prevention Evaluation (HOPE) trial showed that patients who received ramipril had a 34% reduction in new diabetes (Yusuf, et al., 2001). Similar reductions were seen in the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) trial. There is potential in these medications for treatment of both hypertension and prediabetes. Ongoing studies such as the Telmisartan Reduction of IntraMyocellular fat (TRIM) study are looking at the ability of the medication to reduce intramuscular fat deposition thereby improving insulin sensitivity in the prediabetic state (Sharma, 2008).

Patients with a systolic BP of 120–139 mm Hg and/or a diastolic BP of 80–89 mm Hg are said to have pre-hypertension. Lifestyle interventions should be implemented in these patients at this stage to help prevent or delay the development of hypertension.

Key Point: Hypertension Therapeutic Goals:

- If cardiovascular risk is <10%, treat to <140/90 mmHg.
- If cardiovascular risk is ≥10%, treat to <130/80 mmHg.

Key Point: Avoid β-Blockers and thiazide diuretics as first-line therapy. Initial therapy should include an ACEI or an ARB.

Cholesterol

Lipid testing should be done annually. Fasting lipoprotein (total cholesterol, low-density lipoprotein (LDL) cholesterol, HDL cholesterol, and TG) should be obtained after a 9–12-hour fast. Additional testing may be needed to adjust pharmacologic therapy. In most laboratories, LDL cholesterol is calculated from a formula that is not valid when the TG level is above 400 mg/dl. In this circumstance, a "direct LDL" assay is an alternative measurement.

Low-Density Lipoprotein Cholesterol

The LDL targets vary based on assessment of CHD risk factors and are further modified by calculation of the patient's 10-year risk for CHD as determined by the Strong Heart Risk Calculator. Currently, the mainstay of therapy for lowering LDL is an HMG CoA reductase inhibitor (statin). The lipid lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOTT) showed that daily Atorvastatin 10mg reduced both nonfatal and fatal MI by 36% in a population of patients at only moderate cardiovascular risk (Sever, et al., 2003). The Stop

All patients with the metabolic syndrome who have failed intensive efforts at lifestyle modification and who fall within an intermediate level of risk or greater should be considered for statin therapy. Those patients at intermediate 10-year risk should be treated to a goal of < 130 mg/dl or an optional goal of < 100 mg/dl. Those patients at high risk should be treated to a goal of < 100 mg/dl or an optional goal of < 70 mg/dl. Decision to treat to the optional goal should be based on the patient's ability to tolerate the treatment.

Key Point: LDL goals**:**

- **Intermediate risk level,** the goal is <130mg/dl optional goal is <100 mg/dl.
- **Hgh risk level,** the goal is <100 mg/dl optional goal <70 mg/dl.

Non-High Density Lipoprotein Cholesterol and Triglyceride

After assurance that LDL cholesterol targets have been met, it is appropriate to consider non-HDL cholesterol and TG.

Non-HDL cholesterol is a strong predictor of CHD risk, and is the total cholesterol minus the HDL cholesterol. It represents all of the atherogenic particles (VLDLs and small dense LDL). The non-HDL cholesterol target value is generally 30 mg/dl higher than the LDL cholesterol target values. Non-HDL cholesterol is particularly useful when LDL cholesterol cannot be calculated due to elevated TG or when lipid specimens are collected in the non-fasting state. Consider the non-HDL cholesterol as a proxy for the LDL. As such, a statin remains the treatment of choice.

If the TG level is ≥ 500 mg/dl, the patient is at risk for pancreatitis and pharmacotherapy should be instituted.

When the TG level is 200–499 mg/dl, the non-HDL cholesterol value should be determined. Treatment of TG, including use of pharmacologic agents, should be done until the non-HDL cholesterol target has been achieved.

When the TG level is borderline high (150–199 mg/dl), lifestyle modification should be emphasized. Calculation of the non-HDL cholesterol value is not required, but may be useful.

The recommended therapies for triglycerides include fibrates, such as gemfibrozil, and Omega-3 fatty acids. The benefits of fibrates were seen in the Helsinki Heart Study where there was a reduction in first myocardial infarction or cardiac death of 66% among patients randomized to gemfibrozil vs. placebo (Manninen, et al., 1992**)**. This dramatic decrease was seen among patients with triglyceride levels of 200 mg/dl or more and HDL levels of less than 42 mg/dl.

Combined statin and fibrate therapy can provide tighter control. However, one will incur a greater risk of myalgias and rhabdomyolysis with statin and gemfibrozil (Lopid). In instances where combination therapy is necessary, fenofibrate (Tricor) should be used. The benefit of statin-fibrate therapy in reducing adverse cardiovascular outcomes is currently under investigation in the ACCORD trial.

Omega-3 fatty acids have also been shown to be useful in treating hypertriglyceridemia in insulin resistant patients on statin therapy (Chan, et al., 2002). Lovaza is a new FDA approved supplement that can be prescribed as an adjunct to triglyceride management. The purity of OTC fish oil supplements is questionable and no recommendations can be made as to their use in triglyceride management.

> **Key Points:** Improvements in triglyceride, LDL and HDL have been reported with combination statin-fibrate therapy. Fenofibrate (Tricor) does not affect the metabolism of the statins and may reduce the risk of myalgias when combo therapy is necessary.

High Density Lipoprotein Cholesterol

Although research suggests that raising HDL cholesterol will reduce CHD risk, the evidence is insufficient to specify a goal of therapy (Canner, et al., 1986). However, we recommend that isolated low HDL cholesterol levels be acted upon in those with CHD or CHD risk equivalents after reaching LDL cholesterol goals. Niacin may be considered as adjunctive therapy for American Indians and Alaska Natives with the metabolic syndrome who have low HDL despite lifestyle modification and therapy with statins or fibrates (Blaha, et al., 2008).

Anti-platelet therapy

Anti-platelet therapy has known benefits in patients who have CHD and those at risk for CHD and thus applies to people with PREDIABETES and Metabolic syndrome. Patients with a 10-year risk probability for CHD $\geq$ 10% should be considered as candidates for anti-platelet therapy with the benefits of taking aspirin weighed against the risks of bleeding. Aspirin doses of 75 to 81mg are recommended and typically cause fewer side effects like bleeding. Higher doses afford no greater benefit and are associated with increased risk of GI bleeding (Campbell, et al., 2007).

> **Key Point:** A daily baby aspirin (81 mg) is recommended for patients with 10-year CVD risk $\geq$ 10%.

Weight Loss

In the lifestyle intervention arm of the DPP, 38% of participants initially classified as having the metabolic syndrome no longer had the syndrome after achieving a 7% reduction of body weight (Orchard, et al., 2005). Another study saw the prevalence of the metabolic syndrome decline by 44% and 48% for lifestyle change only and lifestyle change plus sibutramine, respectively **(**Phelan, et al., 2007). Small reductions in body weight can lead to substantial reduction in cardiometabolic risk. However, it is sustaining this degree of weight loss that challenges both

the patients and the care provider. Patients who fail to maintain weight loss through lifestyle change alone may benefit from either medication or surgery.

Medication

Drugs for weight loss can be divided into two categories: appetite suppressants and nutrient absorption inhibitors. The drugs (Table 5) when combined with lifestyle modification, can achieve an additional 5-10% weight loss (Halford, 2006). The long term cardiovascular outcomes associated with taking the medications are currently unknown and are under investigation. However, in the case of the only two medications approved for long term use, benefits have been shown in regards to treatment of the metabolic syndrome. The Sibutramine Trial of Obesity Reduction and Maintenance (STORM) showed that sibutramine induced weight loss and improved metabolic syndrome traits, such as triglycerides, HDL, waist circumference and insulin over a 2 year period (James, et al., 2000). Clinical trials have also shown that orlistat, in conjunction with diet, facilitate and sustains weight loss over a 2 year period (Hauptman, et al., 2000). All weight loss drugs show a beneficial effect on numerous metabolic risk factors.

Table 5. Pharmacotherapy for Weight Loss

Drug	Dose	Frequency	Mechanism	Therapy Duration	Side Effects
Phentermine (Generic)	15mg, 30 mg	One capsule po qd	Norepinephrine reuptake inhibitor, induces satiety	Short term	Modest increases in BP and pulse rate
Sibutramine (Meridia)	5mg, 10 mg, 15 mg	One capsule po qd	Norepinephrine and serotonin reuptake inhibitor, induces satiety	Long term	Modest increases in BP and pulse rate
Orlistat (Xenical)	120mg	One capsule po tid	Reduces fat absorption by binding pancreatic lipases	Long term	Loose oily stools that typically decrease with continued treatment
Rimonabant (Acomplia)*	20 g	One tab po qd	Blocks CB-1 receptor,	Unknown	Depression

* Available in Europe, not in the U.S. It is included as an emerging therapy.

Bariatric Surgery

Bariatric surgery is an approved treatment for obesity when other measures have failed. Patients who are eligible for surgery have shown reversal or control of their metabolic syndrome through surgically induced weight loss (Batsis, et al., 2008). When therapeutic options have been exhausted in morbidly obese patients, surgical consultation should be considered for bariatric surgery. The Division of Diabetes Treatment and Prevention acknowledges that many communities may not have the capacity and the resources to provide bariatric surgery and/or the crucial follow-up in the postoperative period. It should be emphasized that the recommendation is made based on the current literature. Any decision to pursue bariatric surgery should be made after careful discussion with the patient in the context of risks vs. benefits that are appropriate for the respective community.

Key Point: Consider surgical consultation for American Indian and Alaska Natives with a persistent BMI ≥35 who have failed to control prediabetes or metabolic syndrome with aggressive lifestyle modification and medications.

Other Tests in the Course of Routine Care

Insulin

Although useful in research settings or in certain specific clinical situations, the routine testing of an insulin level is not recommended.

Markers of systemic inflammation

There is interest in the role of the inflammation system in the development of diabetes and CVD. However, it is not clear how the measurement of these markers changes clinical management. Therefore, the routine use of these markers is not recommended.

Ovarian-Pituitary Axis hormones

The decision to measure leutinizing hormone and/or follicle stimulating hormone (LH/FSH) should be based on clinical history and exam findings suggesting disturbances of this hormonal system.

Thyroid function

The decision to evaluate thyroid stimulating hormone should be based on clinical history and exam findings suggesting disturbances of this hormonal system.

Microalbuminuria

Measurement of urine microalbuminuria may be useful because it is a strong predictor of CVD, may change BP targets, and influence choice of anti-hypertensive agents.

A1c

At this time, A1c or other glycosylated protein measurement has no role in the diagnostic or clinical management of Prediabetes or metabolic syndrome.

Appendix A. Suggested Lifestyle Changes Counseling on Prediabetes and Metabolic Syndrome

Typical Recommendation	Suggested Lifestyle Changes
Moderate weight loss (7–10% reduction in starting weight or, on average, 20–25 pound weight loss over 6 months)	Caloric intake should be reduced by 250–1,000 calories per day to produce the recommended goal of ½–2 pounds weight loss per week. Calorie reduction should be realistic and achievable and based on an individualized assessment, weight history, dietary intake, physical activity, and weight loss goals. The National Heart, Lung, and Blood Institute recommends the following daily calorie intake: • For men: 1,200–1,600 kcal/day. (Also for women who exercise and who weigh > 165 pounds). • For women: 1,000–1,200 kcal/day (most women). • If client is hungry, you may want to increase calories by 100–200/day. • Activity/Exercise: 30–60 minutes/day most days of the week. **Weight loss and maintenance is difficult to achieve without exercise and activity.**
Reduce calorie and modify fat intake (Less saturated fats)	Establish mutually agreed upon goals: • Eat smaller portions. • Drink more water and little or no sugar-containing beverages each day. • Choose leaner cuts of beef and pork. • Eat white meat of turkey, chicken, and wild game more often. • Eat fish high in omega-3 fatty acids, no more than 12 ounces per week. • Increase intake of whole fruits and vegetables. • Choose whole grains like rolled oats, barley, bran, and 100% whole grain bread instead of refined, processed carbohydrates like baked products made with white flour. • Choose low-fat or no-fat dairy products. • Use unsaturated vegetable oils that are liquid at room temperature like olive, canola, peanut, safflower, sunflower, corn, soybean, and cottonseed oils, and use soft-tub, squeeze, or spray margarine. • Eat at regular mealtimes. • Use low-fat food preparation (grilling, broiling, boiling, steaming, etc.). • Eat breakfast. • Reduce frequency of eating out, especially in fast food restaurants.
Patient "self-monitoring" records	Document food intake, physical activity, and feelings. Awareness is a key step in changing behavior. Food and activity diaries help a person become more aware of current lifestyle habits to identify small changes to make toward achieving healthier lifestyle habits.
Education	Education topics focusing on, but not limited to: Healthy Food Choices: • Choosing meals and snacks from a variety of foods. • Types of fats (less saturated fat). • Types of carbohydrates (more whole grains and fiber). Healthy Food Preparation: • Appropriate portion sizes. • Understanding the food label. • Recipe modification. Psychology of Eating Habits: • Understanding physical cues of hunger and fullness. • Setting goals. • Enlisting support. • Rewarding yourself.

Appendix B. Nutrition Recommendations for Prediabetes and the Metabolic Syndrome*

Total Calories (Energy)	Balance energy intake and expenditure to prevent weight gain or lose weight. Must evaluate patient's readiness for change and consider patient's cultural background and usual eating habits.
Protein	Approximately 15% of total calories or 0.8 g/kg body weight/day.
Cholesterol	< 200 g (fats of animal origin).
Saturated Fat	< 7% of total calories: Fats of animal origin and trans fats (see below).
Trans Fatty Acids	Reduce intake by avoiding products with hydrogenated and partially hydrogenated oils, such as stick margarine, vegetable shortening, and commercial bakery and deep fried foods and snacks.
Polyunsaturated Fat	Up to 10% of total calories: Safflower, sunflower, and corn oils.
Monounsaturated Fat	Up to 20% of total calories: Avocados; olives; olive, peanut, and canola oils; nuts, such as almonds, pecans, hazelnuts, walnuts, and peanuts (1 oz, 5 times/week).
Total Fat	25–35% of total calories (TG > 500mg/d, reduce fat intake to 15%).
Carbohydrate**	50–60% of total calories: Reduce consumption of sugar and refined, low-fiber carbohydrate foods. Recommend 5–9 servings of whole fruits, vegetables, and 3 or more servings of whole grains. There is a strong positive association between a high glycemic load (GL) and risk for CHD. GL = glycemic index (GI) % x grams of carbohydrate per serving A low GI/GL diet includes high fiber; whole grain cereals and breads made with oats, barley, bran, and whole seeds; and all types of whole fruits and vegetables (except potatoes). For more information, visit the following website: www.glycemicindex.com. ** If the effect of the high carbohydrate diet elevates TG and lowers HDL (atherogenic dyslipidemia), recommend isocalorically-substituting monounsaturated fats for carbohydrate foods (e.g., omit 1 slice bread, and add 3 tsp olive oil or 12 whole almonds).
Fiber	20–30 g/day (Encourage 10–25 g/day soluble fiber: Whole grains, rolled oats, oat bran, barley, dried beans, peas, legumes, and most fruits and vegetables.)
Plant Stanols/Sterol	2g/day: Benecol and Take Control margarine (~ 2 servings/day).
Soy Products	25g/day: Textured soy protein, tofu, tempeh, soy milk, etc.
Omega-3 Fatty Acids	Eat up to 12 ounces/week of a variety of fish and shellfish low in mercury, such as salmon, Atlantic herring, sardines, and cod. Limit albacore tuna and fish from local lakes, rivers, and coastal waters, such as Rainbow Trout to 6 ounces/week. Avoid shark, swordfish, king mackerel, and tilefish. Children and pregnant and nursing mothers are at highest risk of excessive mercury exposure. For more detailed information on mercury in fish and shellfish visit the following websites: www.cfsan.fda.gov/seafood1.html or www.epa.gov/ost/fish. Other sources include: Flaxseed; flaxseed, canola, and soybean oils; raw soybeans; walnuts; and fish oil supplement ~ 900 mg/day. Omega-3 fatty acid supplements may be most beneficial in treatment of severe hypertriglyceridemia.
Vitamins/Minerals	Folate: ≥ 400 mcg/day: Enriched cereal grains, bread and bread products, and dark green leafy vegetables. Vitamin B-6: 1.3 mg/dl/day: Fortified grains, organ meats, and soy-based meat substitutes. Vitamin E: 12 IU women, 15 IU men: Olive oil, wheat germ, nuts, and seeds.
Considerations for Hypertension (DASH Diet)	Calcium: 1,200–1,500 mg/day: Low-fat dairy products (recommend 3 c skim or 1% milk daily). Potassium: 3,500 mg/day: Fruits, vegetables, and whole grains. Magnesium: 400 mg/day: Lean meat, fish and poultry, dry beans, peas and lentils, nuts, seeds, whole grains, and dark green vegetables. Sodium: ≤ 2,400 mg/day
Alcohol	If alcohol is consumed, limit to 2 drinks/day for men and 1 drink/day for women.

***Trial diet and exercise (12 weeks)**

Appendix C. Overview of Guidelines for Exercise Testing and Prescription

Reference	Frequency	Intensity	Time	Type	Exercise Treadmill Testing (ETT)
DPP Study	3–7 days	Low–moderate	150 min/wk	Aerobic	If history or symptoms suggestive of CVD *or* if man over 40 or woman post-menopausal not on hormone replacement therapy, ETT is indicated.
ACSM **Exercise and weight loss**	5–7 days	Moderate	Minimum: Aerobic 2.5 hr/wk Goal: 3.3–5 hr/wk, continuous. Intermittent for certain people.	Aerobic and resistance	No guidelines provided.
ACSM **Exercise and Hypertension**	5–7 days	Moderate	>30 min, continuous or accumulated aerobic physical activity/day.	Aerobic supplemented with resistance training	Dependent upon risk classification. Generally, if doing light exercise, no test needed.
Dr. Galloway **Exercise and Diabetes**	3–5 days	Low–moderate, depending upon complications present	>30 min, continuous with 5–10 min warm-up and cool-down.	Aerobic	Recommended if have 1+ risk factors (in presence of diabetes) or at physician's discretion. However, stress testing could provide opportunity to discover CAD before clinically manifested.
ACSM **Exercise and Type 2 Diabetes**	3–7 days, minimum cumulative of 1,000 kcal/wk	Low–moderate	>30–60 min, continuous or accumulated aerobic exercise/day.	Aerobic and resistance	Recommended if have diabetes and age > 35 years.
AHA **Exercise in prevention and treatment of CVD**	5–7 days	Moderate	>30 min	Aerobic	Questionable efficacy for healthy people. At the discretion of the physician for vigorous exercise in patients with known CVD.
ADA **Exercise and Diabetes**	No specifics	Depends on presence of complications	No specifics	Aerobic: Emphasized need for 5–10 min warm-up and cool-down.	Indicated if at high risk for CVD (gives guidelines). Physician discretion if exercise intensity will be <60% MHR.*

*MHR= Maximum heart rate. Preferably determined by maximal graded exercise test. Estimated by: (220 – age).
THR= Target heart rate. Determined by MHR and desired exercise intensity. Used in the exercise prescription.

Definitions for intensity (these vary somewhat in the literature):

Low: 20–40% MHR
Moderate: 40–70% MHR
High: >70% MHR

Appendix D. Online References

Blood cholesterol and lipids

The appendix of the *At-A-Glance: Quick Desk Reference* by the NCEP ATP III provides further information on the risk determination and treatment for elevated cholesterol levels. The quick reference guide, as well as the full report, are available at the following website:
http://www.nhlbi.nih.gov/guidelines/cholesterol/atglance.pdf

A risk assessment tool for estimating 10-year risk of developing hard CHD is available at the following website:
http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof

A similar risk assessment tool, based on Strong Heart data for American Indians, can be found at:
http://strongheart.ouhsc.edu/chdcalculator/calculator.html

Depression screening and treatment

National Institute of Mental Health
http://www.nimh.nih.gov

Diabetes prevention

American Diabetes Association
http://www.diabetes.org/

Diabetes Prevention Program
http://www.bsc.gwu.edu/dpp/index.htmlvdoc

National Diabetes Education Program
The Small Steps–Big Rewards Program's publication titled, *Your Game Plan for Preventing Type 2 Diabetes*: *Health Care Provider's Toolkit*, is available at the following website:
http://www.ndep.nih.gov/campaigns/SmallSteps/SmallSteps_index.htm

Exercise and nutrition

The American College of Sports Medicine's Position Statements are available at the following website:
http://www.acsm-msse.org/pt/re/msse/positionstandards.htm;jsessionid=lytbwdwctjc7hd2hwnymrgt3plrfchs7btx6q1nhyfmm2h4hztq2!526656812!181195628!8091!-1

American Heart Association
http://my.americanheart.org/portal/professional

Aim for a Healthy Weight Education Kit (for primary care providers)
http://www.nhlbi.nih.gov/health/prof/heart/obesity/aim_kit/index.htm

The American Medical Association's *Assessment and Management of Adult Obesity: A Primer for Physicians* is available at the following website:
http://www.ama-assn.org/ama/pub/category/10931.html

Hypertension

The physician reference card from the JNC 7 (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) is available at the following website: http://www.nhlbi.nih.gov/guidelines/hypertension/phycard.pdf

Tobacco cessation

American Lung Association's Freedom From Smoking Program
http://www.lungusa.org

American Cancer Society
http://www.cancer.org

References Cited

American College of Sports Medicine. (2006). *ACSM's Guidelines for Exercise Testing and Prescription* (7 ed.). Lippincott Williams & Wilkins.

American College of Sports Medicine. (2001). Appropriate intervention strategies for weight loss and prevention of weight regain for adults. *Medicine & Science in Sports & Exercise , 33* (12), 2145-2156.

American College of Sports Medicine. (2004). Exercise and Hypertension. *Medicine & Science in Sports & Exercise , 36* (3), 533-553.

American Diabetes Association. (2007). Diagnosis and classification of diabetes mellitus. *Diabetes Care , 30*, S68-S71.

American Diabetes Association. (2008). Standards of medical care in diabetes. Testing for pre-diabetes and diabetes in asymptomatic patients. *Diabetes Care , 31* (Suppl 1), S13-4.

ATPIII, N. (2002). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation , 106*, 3143-3421.

Balkau, B., Charles, M. A., Drivsholm, T., Borch-Johnsen, K., Wareham, N., Yudkin, J. S., et al. (2002). Frequency of the WHO metabolic syndrome in European cohorts, and an alternative definition of an insulin resistance syndrome. *Diabetes Metab , 28*, 364-376.

Batsis, J. A., Romero-Corral, A., Collazo-Clavell, M. L., Sarr, M. G., Somers, V. K., & Lopez-Jimenez, F. (2008). Effects of bariatric surgery on the metabolic syndrome: a population-based, long term controlled study. *Mayo Clinic Proceedings , 83* (8), 897-906.

Blaha, M. J., Bansal, S., Rouf, R., Golden, S. H., Blumenthal, R. S., & Defilippis, A. P. (2008). A practical ABCDE approach to the metabolic syndrome. *Mayo Clinic Proceedings , 83* (8), 932-943.

Campbell, C. L., Smyth, S., Montalescot, G., & Steinhubl, S. R. (2007). Aspirin dose for the prevention of cardiovascular disease: a systematic review. *JAMA , 297* (18), 2018-2024.

Canner, P. L., Berge, K. G., Wenger, N. K., Stamler, J., Friedman, L., Prineas, R. J., et al. (1986). Fifteen year mortality in coronary drug project patients: long-term benefit with niacin. *Journal of the American College of Cardiology , 8* (6), 1245-1255.

Chan, D. C., Watts, G. F., Barrett, H. R., Beilin, L. J., Redgrave, T. G., & Mori, T. A. (2002). Regulatory effects of HMG CoA reductase inhibitor and fish oils on apolipoprotein B-100 kinetics in insulin-resistant obese male subjects with dyslipidemia. *Diabetes , 51* (8), 2377-2386.

De Simone, G., Devereux, R. B., Chinali, M., Best, L. G., Lee, E. T., Galloway, J. M., et al. (2007). Prognostic impact of metabolic syndrome by different definitions in a population with high prevalence of obesity and diabetes. *Diabetes Care , 30* (7), 1851-1856.

Delahanty, L. M., Sonnenberg, L. M., Hayden, D., & Nathan, D. M. (2001). Clinical and cost outcomes of medical nutrition therapy for hypercholesterolemia: a controlled trial. *Journal of the American Dietetic Association , 101* (9), 1012-1016, 1021-1023.

Einhorn, D., Reaven, G. M., Cobin, R. H., Ford, E., Ganda, O. P., Handelsman, Y., et al. (2005, October 14). *American College of Endocrinology/American Association of Clinical Endocrinologists: Reaffirmation of the 2003 ACE Insulin Resistance Syndrome (IRS) Position Statement.* Retrieved from www.aace.com/pub/pdf/guidelines/irsstatement.pdf

Ellsworth, D. L., O'Dowd, S. C., Salami, B., Hochberg, A., Vernalis, M., Marshall, D., et al. (2004). Intensive lifestyle modification: impact on cardiovascular disease risk factors in subjects with and without clinical cardiovascular disease. *Preventive Cardiology , 7* (4), 168-175.

Galloway, J. M., Clark, M. A., Brody, E. A., Malasky, B., Freund, N., & Holman, R. (2002). Appropriate exercise prescription for patients with diabetes mellitus. *The IHS Primary Care Provider , 27* (11), 221-225.

Gami, A. S., Witt, B. J., Howard, D. E., Erwin, P. J., Gami, L. A., Somers, V. K., et al. (2007). Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *Journal of the American College of Cardiology , 49* (4), 403-414.

Gillies, C. L., Abrams, K. R., Lambert, P. C., Cooper, N. J., Sutton, A. J., Hsu, R. T., et al. (2007). Pharmacologic and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *British Medical Journal , 334* (299), 1-9.

Golden, S. H., Lazo, M., Carnethon, M., Bertoni, A. G., Schreiner, P. J., Diez Roux, A. V., et al. (2008). Examining a bidirectional association between depressive symptoms and diabetes. *Journal of the American Medical Association , 299* (23), 2751-2759.

Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., et al. (2005). Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation , 112*, 2735-2752.

Halford, J. (2006). Pharmacotherapy for obesity. *Appetite , 46*, 6-10.

Hauptman, J., Lucas, C., Boldrin, M., Collins, H., & Segal, K. (2000). Orlistat in the long term treatment of obesity in primary care settings. *Archives of Family Medicine , 9*, 160-167.

Hebert, J. R., Ebbeling, c. B., Ockene, I. S., Ma, Y., Rider, L., Merriam, P., et al. (1999). A dietician delivered group nutrition program leads to redductions in dietary fat, serum cholesterol, and body weight: the Worcester area trial for counseling in hyperlipidemia (WATCH). *Journal of the American Dietetic Association , 99* (5), 544-552.

Howard, B. (2007). The metabolic syndrome in American Indians: The Strong Heart Study. *Journal of the Cardiometabolic Syndrome , 2*, 283-287.

Howard, B. V., Roman, M. J., Devereaux, R. B., Fleg, J. L., Galloway, J. M., Henderson, J. A., et al. (2008). Effect of lower targets for blood pressure and LDL cholesterol on atherosclerosis in diabetes. *JAMA , 299* (14), 1678-1689.

Hubert, H. B., Eaker, E. D., Garrison, R. J., & Castelli, W. P. (1987). Life-style correlates of risk factor change in young adults: an eight-year study of coronary heart disease risk factors in the Framingham offspring. *American Journal of Epidemiology , 125* (5), 812-831.

Institute of Medicine Committee on Nutrition Services for Medicare Beneficiaries. (1999). *The role of nutrition in maintaining health in the nation's elderly: evaluating coverage of nutrition services for the medicare population.* Washington DC: National Academy Press.

James, W., Astrup, A., & Finer, N. (2000). Effect of sibutramine on weight maintenance after weigt loss: a randomized trial. *Lancet , 356*, 2119-2125.

Kahn, R., Buse, J., Ferrannini, E., & Stern, M. (2005). The metabolic syndrome: time for a critical appraisal. *Diabetes Care , 28* (9), 2289-2304.

Knowler, W. C., Barnett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine , 346* (6), 393-403.

Kunitz, S. J. (2008). Changing patterns of mortality among Amerian Indians. *American Journal of Public Health , 98* (3), 404-411.

Lee, E. T., Howard, B. V., Wang, W., Welty, T. K., Galloway, J. M., Best, L. G., et al. (2006). Prediction of coronary heart disease in a population with high prevalence of diabetes and albuminuria. *Circulation , 113*, 2897-2905.

Lien, L. F., Brown, A. J., Ard, J. D., Loria, C., Erlinger, T. P., Feldstein, A. C., et al. (2007). Effects of PREMIER lifestyle modifications on participants with and without the metabolic syndrome. *Hypertension , 50*, 609-616.

Manninen, V., Tenkanen, L., Koskinen, P., Huttunen, J. K., Manttari, M., Heinonen, O. P., et al. (1992). Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study: implications for treatment. *Circulation , 85* (1), 37-45.

Marrero, D. G. (2007). Current knowledge of prevention of diabetes and obesity. *Making data count: measuring diabetes and obesity in the Indian Health System* (pp. 26-28). Tucson: IHS Division of Diabetes Treatment and Prevention.

Mokdad, A., Marks, J., Stroup, D., & Gerberding, J. (2004). Actual causes of death in the United States, 2000. *JAMA , 291* (10), 1238-1245.

Orchard, T. J., Temprosa, M., Goldberg, R., Haffner, S., Ratner, R., Santica, M., et al. (2005). The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. *Annals of Internal Medicine , 142* (8), 611-619.

Phelan, S., Wadden, T., Berkowitz, R., Sarwer, D., Womble, L., Cato, R., et al. (2007). Impact of weight loss on the metabolic syndrome. *International Journal of Obesity , 31*, 1442-1448.

Reaven, G. M. (1988). Role if insulin resistance in human disease. *Diabetes , 37*, 1595-1607.

Rosendorff, C., Black, H. R., Cannon, C. P., Gersh, B. J., Gore, J., Izzo, J. L., et al. (2007). Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the american heart association council for high blood pressure research and the councils on clinical cardiology and epidemiology and preventi. *Circulation , 115* (21), 2761-2788.

Russell, M., deSimone, G., Resnick, H. E., & Howard, B. V. (2007). The metabolic syndrome in American Indians: The Strong Heart Study. *Journal of the Cardiometabolic Syndrome , 2*, 283-287.

Schweigman, K., Eichner, J., Welty, T. K., & Zhang, Y. (2006). Cardiovascular disease risk factor awareness in American Indian communities: the Strong Heart Study. *Ethnicity and Disease , 16* (Summer), 647-652.

Scutchfield, F. D., & Keck, C. W. (2003). Concepts and Definitions of Public Health Practice. In *Principles of Public Health Practice* (p. 4). Albany, New York: Delmar Publishers.

Sever, P. S., Dahlof, B., Poulter, N. R., Wedel, H., Beevers, G., Caulfield, M., et al. (2003). Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower than average cholesterol concentrations, in the anglo-scandinavian cardiac outcomes trial- lipid lowering arm (ASCOTT-LLA). *Lancet , 361* (9364), 1149-1158.

Sharma, A. M. (2008). The value of current intervention for obesity. *Nature Clinical Practice Cardiovascular Medicine , 5* (Supplement 1), S3-S9.

Sheils, J. F., Rubin, R., & Stapleton, D. (1999). The estimated costs and savings of medical nutrtion therapy: the medicare population. *Journal of the American Dietetic Association , 99* (4), 428-435.

Sikand, G., Kashyap, M. L., Wong, N. D., & Hsu, J. C. (2000). Dietician intervention improves lipid values and saves medication costs in men with combined hyperlipidemia and a history of niacin noncompliance. *Journal of the American Dietetic Association , 100* (2), 218-224.

Taylor, A., Mercz, C., & Udelson, J. (2003). Executive summary- can therosclerosisi imaging techniques improve the detection of patients at risk for ischemic heart disease. *Journal of American College of Cardiology , 41* (11), 1860-1862.

The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. (2002). Major outcomes in high risk hypertensive patients randomized to angiotensin converting enzyme inhibitor or calcium channel blocker vs diuretic: the antihypertensive and lipid lowering treatment to prevent heart attack trial (ALLHAT). *JAMA , 288* (23), 2981-2997.

The DREAM Trial Investigators. (2006). Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet , 368* (9541), 1096-1105.

U.S. Preventive Services Task Force. (2007). *The guide to clinical preventive services.* AHRQ.

Wang, W., Lee, E. T., Fabsitz, R., Welty, T. K., & Howard, B. (2002). Using HBA1c to improve efficacy of the American Diabetes Association fasting plasma glucose criterion in screening for new type 2 diabetes in american indians: the Strong Heart Study. *Diabetes Care , 25*, 1365-1370.

Welty, T. K., Rhoades, D. A., Yeh, F., Lee, E. T., Cowan, L. D., Fabsitz, R. R., et al. (2002). Changes in cardiovascular disease risk factors among American Indians: the strong heart study. *Annals of Epidemiology , 12*, 97-106.

Yusuf, S., Gerstein, H., Hoogwer, B., Pogue, J., Bosch, J., Wolffenbuttel, B. H., et al. (2001). Ramipril and the development of diabetes. *JAMA , 286* (15), 1882-1885.

Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., et al. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet , 364* (9438), 937-952.

Zimmet, P. Z., & Alberti, G. (2005). The metabolic syndrome: perhaps an etiologic mystery but far from a myth- Where does the International Diabetes Federation stand? *Medscape Diabetes and Endocrinology , 7* (2).