DIABETES PREVENTION AND CARDIOVASCULAR RISK REDUCTION IN PRIMARY CARE PRACTICE

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Despite extensive research demonstrating that moderate lifestyle changes can reduce risk for Type 2 diabetes and cardiovascular disease these two chronic conditions continue to account for an overwhelming amount of morbidity and mortality worldwide. Translation of successful prevention and risk reduction research into "real world" settings faces many challenges, while strategies for implementation are lacking. For many reasons, the primary care practice venue provides an ideal environment for provision of prevention services on a permanent basis.

The dissertation consists of three related projects; the first two examined the main components of diabetes prevention and cardiovascular disease risk reduction while the third investigated the relationship between perception of disease risk and lifestyle intervention performance. Because current practices of prevention screening are often haphazard and tend to overlook those in greatest need, the first project focused on risk identification through prevention screening in a systematic manner. Feasibility in the primary care practice setting as well as differences between those invited to attend prevention screening and those not invited was examined.

The second project investigated the effectiveness and feasibility of provision of a lifestyle change intervention in a primary care practice setting. The successful lifestyle intervention utilized in the Diabetes Prevention Program was modified for delivery in a group rather than

individual setting. The effectiveness of the intervention was evaluated through risk assessment measures collected before and after participation in the intervention.

Finally, motivation for making lifestyle changes remains a mystery and varies considerably from one individual to another. It has been hypothesized that perceived risk, i.e., the probability of developing a disease or condition may influence an individual's health behavior. Utilizing a modified version of the Risk Perception Survey for Developing Diabetes (RPS-DD) the final project examined baseline differences in responses as well as the relationship between perception of risk and subsequent performance in the group lifestyle intervention. Differences in risk perception before and after participation were also examined.

The projects are significant from a public health perspective in that they seek to begin to establish a foundation for implementation of diabetes prevention and cardiovascular risk reduction for the general population.

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PREFACE

As I write this, the holidays are quickly approaching and I am reminded of all that I am thankful for. I began this journey not knowing if I could actually complete what I set out to do; now that I have, there are many people that have helped me reach my goal. Firstly, if it weren't for Dr. Trevor Orchard who suggested that I work toward a doctoral degree at this point in my life, I might not have even considered it. He has provided guidance and assistance from the beginning and I am so very grateful for his continued support and direction. I also very much appreciate the other members of my committee, Drs. Andrea Kriska, Linda Siminerio, Maria Brooks and Lora Burke who have been so wonderfully helpful in so many ways.

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1.0 INTRODUCTION

Two insidious peas in a pod, type 2 diabetes (T2D) and cardiovascular disease (CVD) are devastating chronic illnesses that affect millions of people worldwide. Although distinct disease entities, T2D and CVD are often intertwined; in general, individuals afflicted with diabetes are two to four times more likely to develop CVD than the general population [1] with two-thirds to three-fourths dying of some sort of heart or blood vessel disease [2]. Despite research demonstrating that risk for T2D and CVD may be lowered through modest lifestyle changes, these conditions continue to wreak havoc on the health of millions and strategies to implement prevention in the "real world" are far from optimal.

1.1 OVERVIEW OF DISSERTATION

The focus of this dissertation is on the implementation of diabetes prevention and cardiovascular risk identification and reduction for patients in a primary care practice setting; it is presented in three related projects. The first project evaluated the identification of those at risk for T2D and CVD through utilization of a systematic, organized screening approach. The second assessed effectiveness and feasibility of a group lifestyle intervention delivered in a primary care practice setting, while the third project investigated the relationship between perception of risk for disease and performance in the group lifestyle intervention.

1.2 PUBLIC HEALTH SIGNIFICANCE

Currently over 20 million people or about 7% of the total U.S. population are estimated to have diabetes; about 14.6 million have been diagnosed and 6.2 million are unaware that they have the disease [3]. The sixth leading cause of death in the United States [4], diabetes is also the leading cause of new blindness in those aged 20-74 years of age, the leading cause of kidney failure, and a major cause of lower limb amputation [3]. In 2002, estimated direct diabetes costs were almost $92 billion; indirect costs including disability, work loss and early mortality were approximately $40 billion, creating a colossal total diabetes financial cost in the US of $132 billion dollars [5]. Type 1 diabetes, referred to in the past as "insulin-dependent" or "juvenile onset" diabetes accounts for approximately 5-10% of those diagnosed with diabetes. Type 2 diabetes, previously known as "non-insulin dependent" or "adult onset" diabetes is much more prevalent and accounts for approximately 90-95% of those with diagnosed diabetes [6].

Often walking side by side with diabetes, cardiovascular disease, including diseases of the heart, stroke and hypertension, directly accounts for over 37% of annual deaths or one out of every 2.7 deaths in the US; it is estimated that one in three adult Americans has some form of CVD [2]. A major complication of diabetes, CVD is the leading cause of death for those with diabetes; individuals with diabetes are 2-4 times more likely to have heart disease or suffer a stroke than those without diabetes [7]. In fact it has been shown that patients with diabetes and no previous history of myocardial infarction (MI) have the equivalent risk of MI as non-diabetic patients with previous MI [8]. CVD is the most costly complication of diabetes, accounting for more than $17 billion of the $91.8 billion in annual direct medical costs for diabetes in 2002 [5].

1.2.1 Risk States Prior to Diabetes Diagnosis

While it is obvious that CVD is of major concern after diabetes diagnosis, research has shown that cardiovascular risk factors are often present in the interim stages prior to diagnosis with T2D. In the San Antonio Heart Study, a population-based study of diabetes and CVD, cardiovascular risk factor status in initially non-diabetic Mexican Americans was studied. After 8 years of follow-up those individuals who subsequently developed T2D had higher levels of total and low-density lipoprotein (LDL) cholesterol, triglyceride, fasting glucose and insulin, 2-hour glucose, body mass index (BMI) and blood pressure, as well as lower levels of high-density (HDL) cholesterol than subjects who remained non-diabetic, leading the authors to conclude that "pre-diabetic subjects have an atherogenic pattern of risk factors (possibly caused by obesity, hyperglycemia, and especially hyperinsulinemia), which may be present for many years and may contribute to the risk of macrovascular disease as much as the duration of clinical diabetes itself" [9]. Data from the Nurse's Health Study also demonstrated a significantly increased risk for CVD beginning at least 15 years prior to diagnosis with T2D [10] while other studies have confirmed the relationship between elevated blood glucose levels and CVD in non-diabetic patients [11, 12]. Previously undiagnosed diabetes and impaired glucose tolerance have been found in patients with acute MI [13] and other studies have shown that diabetes and CVD risk factors are often intertwined in the risk for type 2 diabetes [9, 14] as well as CVD [15-17]. Recently this relationship was confirmed again in the Dutch Transient Ischemic Attack Trial where stroke risk in a large clinical trial investigating two different aspirin doses and atenolol versus placebo was examined. The authors found that the risk for stroke was almost doubled among people with impaired glucose tolerance when compared with those who had glucose levels within normal limits [18].

The clustering of these conditions of risk including insulin resistance, dyslipidemia, obesity and hypertension has been referred to as syndrome X, insulin resistance syndrome and most commonly of late, metabolic syndrome. While definitions of and criteria for inclusion in this disorder have varied [19-24] and even its very existence as a syndrome has been debated [25], research has supported the conclusion that the grouping of these risk factors generally places an individual at greatly increased risk for diabetes and CVD [26-29]. This relationship was confirmed again recently in a large 8-year follow-up investigation using data from the Framingham Offspring study. The authors examined baseline and follow-up data for 3,323 middle-aged men and women and concluded that metabolic syndrome (following NCEP ATP III criteria) was associated with an increased risk for T2D and CVD in both sexes, accounting for approximately half of new T2D and up to one third of CVD in men in this cohort [30]. This connection appears to be not only related to overt CVD, but sub-clinical disease as well. Recently, the relationship between metabolic syndrome and atherosclerosis was examined in the French MONICA study, a study involving 1,153 individuals without clinical evidence of CVD. The association of metabolic syndrome, using WHO and NCEP definitions, with number of carotid and femoral plaques, carotid intima-media thickness (IMT) and pulse wave velocity (PWV) was studied; the authors found that the presence of the metabolic syndrome almost doubled the risk of sub-clinical atherosclerosis [31].

Obviously a public health problem of considerable magnitude, a resolution does not appear to be on the horizon. Current estimates from the Centers for Disease Control and Prevention suggest that about 54 million people in the US have pre-diabetes, thus are at higher risk for developing T2D, as well as heart disease and stroke [3]. It is anticipated that one in three Americans born in 2000 may develop diabetes in their lifetime, with minorities at even higher

risk [32]. These trends are already evident: from 1980-2004 the number of people in America with diabetes more than doubled from 5.8 million to 14.7 million [33], and parallel the overall increase in obesity [34]. In 1994 the majority of states in the U.S. had <5% diabetes prevalence, however in 2005 there is only one state with that rate and several are now exhibiting 8% prevalence and higher [35]. It has been projected that by the year 2030 there will be over 30 million people with diabetes in the U.S. and 366 million cases worldwide [36]. In addition to the increase in obesity, one of the most important demographic changes related to the increase in diabetes prevalence is the increase in the proportion of people age > age 65 [36]. Total national costs for diabetes have been estimated to reach $156 and $192 billion by the years 2010 and 2020 respectively, with predictions that the actual costs could be higher if health care outpaces the overall cost of living, or if the growing problem with obesity causes an increase in the prevalence of type 2 diabetes [5].

In 2002, the overall prevalence of the metabolic syndrome in adults in the US over age 20 years was 24%, with a considerable increase for age-specific groups: the prevalence in 50-year-old subjects was >30%, while the prevalence in subjects age 60 years and over was 40%. In addition, the prevalence was highest in Hispanics and lower in non-Hispanic whites and in African Americans [37]. Further evaluation using National Cholesterol Education Program Adult Treatment Panel III diagnostic criteria showed increases in the prevalence of metabolic syndrome. NHANES data from 1988-1994 showed the estimated unadjusted prevalence of metabolic syndrome in the US to be approximately 23%, while data from NHANES 1999-2000 showed a significant increase to 26.7% ($p= 0.043$). The age-adjusted prevalence increased by 23.5% among women ($p = 0.021$) and 2.2% among men ($p = 0.831$) [38].

1.2.2 Prevention

T2D and CVD are serious and persistent diseases which progress gradually, usually with little or no perceptible symptoms until they have succeeded in causing often irreversible damage to their victims' health. While it may not be obvious at first glance, the fact that these conditions share such a lengthy "incubation" period is actually a potential public health windfall as there is considerable evidence that T2D and CVD can be prevented or delayed. Lifestyle modification has been shown to be more effective in reducing risk for development of T2D and improving CVD risk status than medication in a number of studies. Results from the DaQuing Impaired Glucose Tolerance (IGT) and Diabetes study first provided evidence that diabetes risk could be reduced through improved diet and exercise in people with impaired glucose tolerance [39]. The Finnish Diabetes Prevention Study determined that risk for diabetes development was decreased by 58% in individuals at high-risk for diabetes using intensive individual lifestyle intervention including diet and activity modification [40]; recent results published demonstrate a sustained effect with continued reduction in diabetes risk [41]. In the US, the Diabetes Prevention Program (DPP) again demonstrated that diabetes risk can be reduced in at-risk patients with an intensive individual lifestyle modification program [42]. The lifestyle intervention implemented in the DPP was also found to reduce risk for metabolic syndrome [43] and to improve CVD risk factor status [44]. More recently lifestyle intervention including weight loss and increased physical activity was found to be effective in reducing coronary heart disease risk factors in a small group of obese older adults [45], while another recent investigation found weight loss induced by calorie restriction or exercise training improved glucose tolerance and insulin action in non-obese, healthy, middle-aged men and women [46].

Several studies have examined the use of pharmacological interventions for diabetes prevention with varied levels of success [42, 47-49]; more recently results from the DREAM trial exploring diabetes prevention potential for the thiazolidinedione (TZD) rosiglitazone and/or the ACE inhibitor ramipril were published. While ramipril demonstrated a significant increased regression to normoglycemia, it was not shown to have an effect on the primary end point-development of diabetes or death [50]. On the other hand, rosiglitazone demonstrated a 60% reduction in the frequency of the primary end point (incident diabetes or death) when compared to placebo [51]. Furthermore, several pharmacological intervention studies have shown positive results for prevention of CVD in patients with and without existing heart disease and/or diabetes [52-58]. Recently published results from the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid-Lowering Arm (ASCOT-LLA) demonstrated that for patients with T2D and well-controlled hypertension who did not have a history of CHD or greatly elevated cholesterol concentrations, the medication atorvastatin significantly reduced the risk of major cardiovascular events and procedures. The study found that the proportional reduction in risk was similar to that among participants who did not have diagnosed diabetes [59] .

1.2.3 Cost of Prevention

Because there is a lack of long-term data available from diabetes prevention research, the economic impact of prevention interventions are at the present time best assessed via computer simulation models. In 2003 Herman, et al., examined the costs associated with primary prevention of diabetes in the Diabetes Prevention Program and found both the metformin and lifestyle interventions to be associated with moderate incremental costs. Over three years, the direct medical cost of the metformin and lifestyle interventions were $2,542 per participant and

$2,789 per participant respectively, compared to a direct medical cost of $79 per participant for placebo. The authors estimated that from the perspective of a large health system, over three years, the cost of the metformin intervention in relation to the placebo intervention was $2,191 per participant and the cost of the lifestyle intervention was $2,269 per participant. Increased costs for the lifestyle intervention were associated with staff time for counseling and adherence monitoring, while the bulk of the cost for the metformin intervention was due to the cost of the medication itself. Costs for the lifestyle intervention decreased in each year and were 12% and 7% less than metformin in years 2 and 3. The authors speculated that the cost of the metformin intervention would decrease with the availability of less expensive formulations of generic metformin, while the costs of the lifestyle intervention could be reduced by improving the efficiency of staff time by using group visits. [60]. A later analysis examined more closely the cost effectiveness of the interventions from a health system perspective and found that when considering the interventions as being implemented in routine clinical practice and from a societal perspective, the lifestyle and metformin interventions cost $13,200 and $14,300, respectively, per case of diabetes delayed or prevented and $27,100 and $35,000 per quality-adjusted life-year (QALY) gained. The authors concluded that over the short term of three years, both the lifestyle and metformin interventions were effective in preventing or delaying T2D and were cost-effective from the perspective of a health system and society [61].

Another analysis in Canada used a Markov model to simulate the course of individuals with IGT under each of the following treatment strategies: acarbose, an intensive lifestyle modification program, metformin or no intervention to prevent progression to diabetes. The results of the model suggested that treatment of IGT in Canada was cost-effective and might generate savings. The authors determined that while the pharmacological treatments tended to

be less costly, intensive lifestyle modification if maintained, provided the greatest health benefits at reasonable incremental costs [62]. In later analyses examining the cost-effectiveness of lifestyle intervention and metformin in the DPP, Herman et al. attempted to project the costs, health outcomes and cost-effectiveness of the DPP lifestyle and metformin interventions in relation to the placebo intervention over a lifetime. Using a modified lifetime simulation model, the lifestyle and metformin interventions were estimated to delay the development of T2D by 11 and 3 years, respectively and to reduce the absolute incidence of diabetes by 20% and 8%, respectively when compared to placebo. The authors determined that the lifestyle intervention was highly cost-effective (cost per QALY approximately $1100) and that the metformin intervention was in a generally cost-effective range at $31,300 per QALY. In addition, as in the short term analysis completed earlier, when the interventions were implemented as they might be in routine clinical practice, the cost-effectiveness over a lifetime improved. The lifestyle intervention was found to be cost-saving in those < 45 years of age and cost-effective in all age groups, whereas metformin was found to be cost-effective for younger ages, but cost more than $100,000 per QALY for those older than 65 years. The authors reported that if costs were reduced by providing the intervention in a closed group of 10 patients and assuming a reduction of 20 or 50% in effectiveness as compared to the DPP, the lifestyle intervention was calculated to be cost-saving relative to placebo while the metformin intervention would cost about $6,600 to $21,000 per QALY. Thus, the lifestyle intervention, when compared to metformin was considerably more cost-effective and resulted in a greater reduction in the risk for diabetes development as well as improved health outcomes [63]. A more recent study examined whether the lifestyle intervention could be offered in such a way that would be beneficial from a health-payer perspective. The authors determined that when compared to usual care, providing the DPP

lifestyle intervention to eligible adults at age 50 could prevent 37% of new cases of diabetes before age 65 at a cost of $1,288 per QALY gained [64]. The authors concluded that by using cost-sharing strategies to implement the DPP lifestyle intervention for eligible people age 50-64, financial return on investment could be seen for private payers as well as a long-term benefit for Medicare.

In contrast, another analysis of the cost-effectiveness of the DPP interventions published later the same year using the Archimedes model found that when compared with not implementing any prevention program, the expected 30-year cost/QALY of the DPP lifestyle intervention from a health plan's perspective would be quite high, at about $143,000. The authors concluded that while "lifestyle modification is likely to have important effects on the morbidity and mortality of diabetes and should be recommended to all high-risk people…the lifestyle intervention utilized in the DPP may be too expensive to implement and other less expensive methods are needed" [65]. However, some have suggested that the discrepancies between the findings of these cost-effectiveness analyses may be related to different assumptions regarding the rate of glycemic progression in the Archimedes model (thus with underestimation of the long-term complications related to diabetes), the shortened time period utilized in the Archimedes model or lack of validity of the Archimedes model itself [66, 67].

1.2.4 Rationale for Translation to Primary Care Practice

While the rationale for diabetes prevention appears to be clear with both scientific and cost-effective evidence to support the concept, implementation of diabetes prevention in a 'real-world' setting is quite complex. Translational research to examine these factors as well as the effectiveness and feasibility of "real-world" diabetes prevention is lacking. For many reasons

the primary care practice venue provides an ideal environment for prevention administration on a permanent basis. Primary care practices employ persons that generally have the knowledge and background to receive training to become preventionists. In addition, patients look to primary care physicians and their staff for health information and advice when identified as being at risk. Furthermore patients are generally familiar with their primary care practice staff, routine, and location which could facilitate participation and retention. Finally, one of the most important aspects of prevention intervention includes follow-up regarding progress in the program, as well as coordination of follow-up care as required.

1.3 STUDY GOALS

For the above noted reasons, a translational research investigation in a primary care practice setting was undertaken with a three-fold purpose: 1) to evaluate the efficacy and achievability of a prevention screening and risk identification program, 2) to examine the effectiveness and feasibility of a Diabetes Prevention Program based group lifestyle intervention program for at-risk subjects and 3) to investigate the relationship between perceived risk and performance in a lifestyle intervention program delivered in a primary care practice setting. To achieve these goals, data from the Screening, Training, Education and Prevention Services of the University of Pittsburgh (STEP UP) study was utilized. STEP UP was a prospective study which examined a structured screening program for identification of those at risk for T2D and CVD and also evaluated the delivery of a modified DPP lifestyle intervention in four primary care practices in Western Pennsylvania. Patients who were registered with the four practices and who were between the ages of 25-74 were invited for prevention screening using a computer driven

recruitment and screening program. Individuals without previously reported diagnosis of diabetes, with BMI $\geq$ 25kg/m^2 and at least three of five components of the metabolic syndrome (based on National Cholesterol Education Program Adult Treatment Panel III) [20] were eligible for the Group Lifestyle Balance (GLB) program, an adaptation of the individual lifestyle intervention utilized in the DPP. A total of 350 individuals attended screening, with 97 determined to be eligible for the intervention; subsequently 43 subjects identified through screening as well as an additional 8 individuals referred by their Primary Care Physician (PCP) enrolled in the intervention component of the project. Outcome measures included the collection of pre and post lipid profile and glucose (at least 2 hour fast requested), resting blood pressure, waist circumference and BMI; global risk was also assessed pre and post intervention. In addition, two surveys were administered before and after the intervention: a modified Risk Perception Survey for Developing Diabetes (mRPS-DD) and the CDC's 14-Item Health Related Quality of Life [68]. A third component of the project was the completion of a chart review of those subjects in the targeted screening group as well as another group who were not targeted for comparison.

Specifically the goals were as follow:

Paper 1: Evaluate the efficacy and achievability of a prevention screening and risk identification program.

a. It is hypothesized that a structured prevention screening program will facilitate the identification of those who are at risk for T2D and CVD in a primary care practice setting
b. Prevention screening will identify individuals with previously unknown risk states which will be confirmed via chart review.

Paper 2: Examine the effectiveness and feasibility of a Diabetes Prevention Program based group lifestyle intervention program for at-risk subjects.

a. It is hypothesized that participation in a modified DPP group lifestyle intervention will have beneficial effects upon weight and global CVD risk for those subjects taking part, as well as upon the other specific outcomes/measures collected including glucose, blood pressure, lipids and waist circumference.
b. Delivery of the Group Lifestyle Balance program will be feasible in a primary care practice setting.

Paper 3: Investigate the relationship between perceived risk and performance in a lifestyle intervention program delivered in a primary care practice setting.

a. It is hypothesized that elevated risk perception for diabetes development will be correlated with performance in the GLB program.

2.0 REVIEW OF LITERATURE

The review of literature encompasses a background of the classification and diagnosis of diabetes, type 2 diabetes and cardiovascular disease epidemiology and etiology as well as guidelines for prevention and the current state of diabetes prevention and cardiovascular risk reduction in primary care practice.

2.1 DIABETES MELLITUS

In very early times, diabetes mellitus was referred to as a condition of "honey urine" due to the fact that the urine of patients afflicted with diabetes often smelled and tasted sweet, like honey [69]. Well-known for thousands of years as a deadly disease, practitioners and scientists first recognized and later understood the signs, symptoms and complications of diabetes; however causality has not been completely explained. Characterized by high blood glucose concentration (hyperglycemia) due to inefficient insulin secretion, target tissue insulin resistance or both, diabetes mellitus encompasses an assorted set of disorders.

2.1.1 Classification and Diagnosis

Guidelines for the diagnosis and classification of diabetes were established by the National Diabetes Data Group (NDDG) in the late 1970's [70] and were endorsed by the World Health Organization (WHO) in 1980 [71] and later by the WHO Study Group on Diabetes Mellitus [72]. Two major forms of diabetes mellitus were recognized, insulin-dependent diabetes mellitus (IDDM, type 1) and non-insulin dependent diabetes mellitus (NIDDM, type 2). These two conditions, though related by hyperglycemia, were noted to be heterogeneous with very different etiologic origins. In addition, three other classifications for diabetes mellitus were recognized (gestational diabetes, diabetes caused by malnutrition and other types of diabetes), as well as the condition called impaired glucose tolerance (IGT) in which the glucose levels in the oral glucose tolerance test (OGTT) were elevated but not in a range considered to be diagnostic of diabetes.

In 1995 an international Expert Committee was convened to examine the scientific literature available since establishment of the original classification and diagnosis of diabetes recommendations to determine if changes were necessary, and in 1997, the American Diabetes Association (ADA) published revised guidelines [73]. Of particular note regarding classification of diabetes, the terms IDDM and NIDDM were eliminated while the terms type 1 and type 2 diabetes mellitus were retained. In addition, the classification of gestational diabetes was continued however, based on scientific evidence the classification of diabetes caused by malnutrition was deleted. The category for IGT was retained and the intermediate corresponding stage for fasting glucose was called impaired fasting glucose (IFG). Furthermore, new criteria for diagnosis of diabetes were introduced and the level of fasting plasma glucose for diagnosis of diabetes was lowered from 140 mg/dl to 126 mg/dl, while IFG was defined between 110 mg/dl and 125 mg/dl. These guidelines were essentially confirmed subsequently by WHO, although

diagnosis using the OGTT was the mandated preference for diagnostic testing rather than the fasting plasma glucose [74]. In 2003 the ADA introduced the term "pre-diabetes" to encompass the conditions of IFG and/or IGT indicating increased risk for the development of diabetes [75]. The ranges for diagnosis with IFG and IGT were originally set at 110-125 mg/dL and 140-199 mg/dL respectively, the ADA lowered the cut point for IFG to 100 mg/dL in order to optimize sensitivity and specificity for predicting future diabetes [76]. It was also felt that by decreasing the lower limit of IFG, thus subsequently increasing the proportion of people with IFG, the proportion of those with IGT that could be identified with a fasting glucose test would also increase [76]. The WHO has not yet adopted this criterion.

Currently there are four generally recognized categories of diabetes: type 1 diabetes, type 2 diabetes, gestational diabetes mellitus (GDM) and diabetes of other specific types including genetic defects of the β-cell or with insulin action, diseases of the exocrine pancreas, endocrinopathies, drug or chemical induced diabetes and infections causing diabetes [77]. In contrast to previous terminology, current classification of diabetes is based on pathogenic processes rather than age at onset or treatment modality. Diagnosis of diabetes is based on a fasting plasma glucose greater than 125mg/dl or 2-hour post load glucose during an OGTT greater than 199mg/dl with either test requiring confirmation on a separate day in the absence of unequivocal hyperglycemia. In addition, the diagnosis of diabetes may be made based on a random or casual glucose greater than 199 mg/dl with diabetes symptoms, although it is recommended that the test be repeated for confirmation [6]. The use of the hemoglobin A1c (HbA1c) test is not currently recommended for diagnosis, although some have suggested its merit. GDM is diagnosed using the OGTT with either a 100g or 75g glucose load [78].

2.1.2 Type 1 Diabetes

Type 1 diabetes (T1D) accounts for approximately 5-10% of those with diabetes and as previously mentioned was known as "insulin dependent" or "juvenile onset" diabetes [6]; it has also been referred to as type 1a diabetes [79] and accounts for > 90% of all cases of T1D [80]. T1D is characterized by autoimmune destruction of the β-cells of the pancreas typically leading to absolute insulin deficiency, with subsequent exogenous insulin therapy required [81]. The rate of β-cell destruction varies from quite rapid progression as typically seen in infants and children to a much slower process observed mainly in adults [6]. The result of an autoimmune process caused by a combination of genetic and environmental factors [81], T1D is usually diagnosed in children or young adults; however this condition can occur in people of all ages. A small number of those with T1D fall into a category of unknown etiology, with most being of African or Asian ancestry; this type of diabetes is referred to as idiopathic or T1Db diabetes [77]. Although these patients may have permanent insulinopenia and may be prone to ketoacidosis, they have no evidence of autoimmunity. Insulin dependency is variable with insulin replacement therapy being necessary at times but may not be a permanent component to care. Incidence of T1D is highest in the Scandinavian countries and lowest in China and parts of South America [80] In parallel with T2D, T1D appears to also be increasing worldwide both in high and low incidence populations [82], however not at the rate seen with T2D.

2.1.3 Type 2 Diabetes

T2D encompasses those with insulin resistance and insulin deficiency which is relative rather than absolute. The deficiency in β-cell function which occurs over time is not related to

autoimmune processes as in T1D; usually initially and often throughout a lifetime, many patients with T2D do not require insulin to survive [6]. Most patients with T2D are obese or overweight; more than 80% of all people diagnosed with T2D were overweight before the disease developed [83]. Secretion of insulin in T2D patients is defective and does not counteract insulin resistance. Thought in the past to affect adults only, T2D is now being diagnosed in children as well as adolescents [84]. T2D will be discussed in further detail below.

2.1.4 Gestational Diabetes and Other Types of Diabetes

Additional diabetes classifications include GDM as well as a general 'other' category for certain specific types of diabetes. GDM is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy"[6]. Both the National Diabetes Data Group (NDDG) and the World Health Organization (WHO) guidelines mandate that this classification is appropriate despite treatment during pregnancy or whether the condition persists after pregnancy. In the United States, GDM occurs in about 4% of pregnancies, resulting in approximately 135,000 cases annually [6]. Gestational diabetes is more common among women who are African American, Hispanic/Latino American or American Indian and for those who are obese and/or have a family history of diabetes. For women afflicted with GDM, approximately 5% to 10% of women with gestational diabetes are found to have T2D after pregnancy, and women who have had gestational diabetes have a 20% to 50% chance of developing diabetes in the next 5–10 years [3].

Other specific and less common types of diabetes include those whose origins are found in specific genetic defects in insulin secretion or action, diseases of the exocrine pancreas such as pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis and fibrocalculous

pancreatopathy [85] and endocrinopathies including acromegaly, Cushing's syndrome and hormone secreting tumors of thyroid, pancreas, adrenal glands [86]. One subtype of diabetes, maturity onset diabetes of the young (MODY) is characterized by autosomal dominant inheritance, early onset of hyperglycemia, and impairment of insulin secretion [85]. Diabetes has also been related to certain specific genetic syndromes such as Down syndrome, Kleinfelter syndrome and Turner syndrome [87]. Certain viral infections such as congenital rubella, cytomegalovirus and coxsackie have been implicated in the destruction of pancreatic islets. Finally, in some cases certain drugs including nicotinic acid, glucocorticoids, thyroid hormone, thiazides and beta blockers have been associated with development of diabetes [85].

2.2 TYPE 2 DIABETES

2.2.1 Epidemiology

While there are several types of diabetes, the lion's share is attributable to T2D [6]. With a prevalence rate in 2005 of about 9.6% and affecting over 20 million adults age 20 and older in the United States, diabetes represents a significant health concern for our nation [3]. Worldwide prevalence of diabetes continues to increase as well; the prevalence of diabetes for all age groups was estimated at 2.8% in 2000 and predicted to rise to 4.4% in 2030 [36]. These increases are attributable to several factors including the aging population, increased survival rates, urbanization, sedentary lifestyles and continued and increasing rates of obesity. In the US, prevalence of diabetes is projected to increase to 14.5% in 2031 with 37.7 million adults having

diagnosed or undiagnosed diabetes [88]. As previously noted, T2D accounts for approximately 90-95% of all diabetes, thus is the major contributing factor driving these increasing numbers [6].

Prevalence varies with race and ethnicity; in the US, non-Hispanic whites exhibit the lowest prevalence of diabetes (8.7%). Individuals of Hispanic descent have higher rates of diabetes prevalence; Mexican Americans, the largest Hispanic/Latino subgroup in the US, are 1.7 times more likely to have diabetes as non-Hispanic whites [3]. It has been predicted that the prevalence of diabetes in this particular population could be potentially overwhelming in the future [36]. Adult non-Hispanic blacks are estimated to have a prevalence of 13.3%, affecting about 3.2 million people and are 1.8 times more likely to have diabetes than non-Hispanic whites [3]. Data is not available for the total prevalence of diagnosed and undiagnosed diabetes for Asian Americans or Pacific Islanders. However, in California, Asians were 1.5 times more likely to have diagnosed diabetes than non-Hispanic whites, while in Hawaii, Asians, Native Hawaiians and other Pacific Islanders age 20 and older were 2 times more likely to have diagnosed diabetes [3]. Finally, American Indians and Alaska Natives are estimated to have the highest prevalence of diabetes with a prevalence rate of approximately 15.1% and are 2.2 times more likely to have T2D than non-Hispanic whites [89]. Prevalence increases with age, with those in the oldest age groups having the highest rates [90]. Approximately 10.3 million people, (20.9%) aged 60 and older have diabetes [3]. In addition, in the US diabetes is somewhat more prevalent in men than women, affecting approximately 10% of all men age 20 and older compared to 8% of women in the same age group [3], however worldwide estimates for 2003 and 2025 show a higher rate for females of about 10% [1].

Approximately 1.5 million new cases of T2D were diagnosed in adults aged 20 years and older in the year 2005; these numbers are expected to climb as problems with obesity increase [3]. This number has risen considerably from National Health Interview Survey data from 1990-92 which estimated approximately 625,000 new cases of diabetes each year [90]. Although T2D often affects middle-aged individuals, thus was previously known as adult-onset diabetes, more recently it has been diagnosed in adolescents and even children [84]. In 2002, diabetes was the sixth leading cause of death reported on death certificates in the U.S. According to death certificate reports, diabetes contributed to a total of 224,092 deaths [3]. Overall, individuals with diabetes have twice the risk for death as people of similar age without diabetes.

Very often symptoms are not present until T2D has progressed considerably and half or more may only be diagnosed concurrently with the initial presentation of a complication of the disease. In fact it is estimated that about 20% of patients with T2D have evidence of diabetic retinopathy at diagnosis with diabetes due to the long pre-clinical period often observed prior to diagnosis [90]. When present, symptoms of T2D may include a lack of energy, increased hunger, weight loss, polyuria and polydipsia, blurred vision, irritation and damage to the nerves causing pain, infections and/or slow healing of wounds. Other symptoms may include sexual function problems such as impotence in men or decreased vaginal lubrication with painful intercourse in women, and mood changes [83]. Over time, chronic hyperglycemia causes long-term damage to the organs of the body. Organs affected include the heart, eyes, kidneys, nerves and blood vessels [6]. The majority of complications arising from diabetes are due to the damage which occurs to blood vessels and are classified as macrovascular or microvascular in nature. Macrovascular complications are related generally to accelerated atherosclerosis affecting the coronary, carotid and femoral arteries, while microvascular complications are

associated with the retina, kidney and nervous system [91]. Macrovascular complications account for the majority of morbidity and mortality associated with T2D (add Diabetes in America references), while microvascular complications may lead to blindness, renal failure and neuropathy.

2.2.2 Etiology

T2D is a condition causing hyperglycemia due to insulin resistance and/or insulin deficiency which may be absolute or only partial. The underlying mechanism may be due to an islet defect associated with increased peripheral resistance to the action of insulin which results in decreased peripheral glucose uptake, or may be due to increased hepatic glucose output [81]. In many populations T2D is characterized not only by insulin resistance but also by insulinopenia (loss of β-cell function) [91]; over time the production of insulin is decreased eventually causing uncontrolled hyperglycemia. In general, T2D onset is usually insidious occurring slowly and without symptoms over a long period of time, however in certain cases it has been known to progress fairly rapidly. As discussed previously, CVD risk factors often develop during this long period of asymptomatic hyperglycemia while other complications such as retinopathy may also be occurring in early but harmful stages of progression [92] .

There is no single cause of T2D and it is apparent that demographic, genetic, and behavioral and lifestyle risk factors are all part of the complexity of the individual development of T2D [6]. Demographic risk factors include age, ethnicity and gender. Development of T2D in the past before age 30 was rare, however, it was estimated that for 1999-2000 approximately 7% of adolescents had impaired fasting glucose [93] and diagnosis with T2D is now beginning to be seen more frequently in this age group [84]. Risk for development of T2D continues to

increase rapidly with age and is highly prevalent in the oldest age populations in the US [94]. As mentioned above, rates of diabetes development between ethnicities vary considerably between certain groups; in the US, T2D is more prevalent in minority populations. Risk for development of T2D is similar for both genders, however in adolescents, the prevalence of IFG was found to be higher in boys than in girls (10% vs. 4%) [93] and in the most recent analysis of NHANES data, a significant increase in diagnosed diabetes was seen for men but not for women [94].

As noted, T2D is a heterogeneous disorder and thus not easily explained by one pathophysiological pathway or mechanism. Due to considerable variations in prevalence in different areas around the world the question concerning nature versus nurture has arisen, i.e. is the primary cause of T2D related to genetic influences, environmental factors, or both? Genetic or familial contributions have been noted in several populations including the North Dakota and Pima Indians [95]; other family studies have been conducted which have shown genetic as well as environmental influences. One study of twins in which one had T2D and the other did not found the concordance for abnormal glucose tolerance to be significantly different between monozygotic and dizygotic twin pairs, thus concluding that genetic predisposition is important in the development of abnormal glucose tolerance but that non-genetic factors might play a significant role in determining whether a genetically predisposed subject will progress to overt T2D [96]. Similarly, several other twin studies have suggested a genetic predisposition for glucose abnormality, however the importance of environmental factors is also stressed [97-100]. Genes which have been shown to be associated with T2D include Gc genotype gene located on chromosome 4, HLA gene on chromosome 6, lipoprotein antigen gene on chromosome 6, insulin gene polymorphism on chromosome 11, apo-lipoprotein genes on chromosomes 2 and 11,

glucose transporter genes on chromosomes 1 and 12, haptoglobulin gene on chromosome 16, and insulin receptor gene on chromosome 19 [101]. Although these genes have been found in various populations and are most likely essential components for development of T2D, their existence does not fully explain the onset of the disease. The appearance of the disease is probably due to a combination of environmental effects which activate a certain genetic predisposition.

One theory that has attracted attention over the years is that of a "thrifty gene". The hypothesis is that in the past when humans were hunters and gatherers they exhibited a "thrifty" metabolism which made possible efficient storage of fat during so-called "feast" periods, and provided storage, or an energy buffer during periods of famine which was mediated by a "quick insulin trigger" [102]. This mechanism was beneficial for survival, however, as lifestyles have changed over time, has now become detrimental in a continual "feast" environment, leading to obesity and increased diabetes. There have been some investigations of birth weight and subsequent development of T2D which some have suggested support this theory [103-107]. These studies found a relationship between low birth weight and increased risk for T2D. Because low birth weight is highly associated with increased rates of mortality, these results could suggest that those with a genetic predisposition for diabetes have this "survival" or "thrifty" gene. Another theory put forth involves a 'thrifty phenotype" (Barker-Hales hypothesis) which proposes that a fetus develops alterations in the growth and function of tissues when in an adverse intrauterine environment by optimizing the use of a reduced nutrient supply to ensure survival. [108]. This under-nutrition in-utero is hypothesized to cause insulin-resistance and subsequent T2D later in life. Some studies have also found a relationship between high-birth weight, and both high and low birth weight and risk for T2D later in life [105, 109,

110]. In a very recent large meta-analysis of birth weight and risk for T2D, Harder, et al., determined that both high and low birth weight was associated with increased risk for T2D [111]. The authors suggested that the increased risk for high birth weight may be due to perinatal exposure to un-diagnosed and non-treated maternal hyperglycemia during pregnancy, as well as maternal overweight during pregnancy. They also postulated that for low birth weight, instead of a "thrifty gene" or "thrifty phenotype" being responsible for increased risk later in life, the relationship may be due to neonatal over-feeding and over-nutrition of low birth weight babies thus causing rapid neonatal weight gain. It has been suggested that over-nutrition during critical periods of life may lead to overweight and obesity later in life, which has been supported in at least one animal model [112]. These theories will require further research and investigation.

As noted above, both high and low birth weight appears to be related to development of T2D later in life, and in fact, overweight and obesity are widely recognized as the strongest environmental risk factors for T2D development. Defined as a BMI >30kg/m^2 [113] obesity has been shown to be very positively associated with the development of T2D in many studies [114-120]. Conversely and possibly related to the genetic factors discussed above, T2D has also been diagnosed in people who are not overweight and does not always develop in all who are obese [90], however in analyses carried out for World Health Report 2002, approximately 58% of diabetes and 21% of ischemic heart disease globally were attributable to a BMI above 21 kg/m2 [113]. The World Health Organization estimates that there are approximately 1.6 billion overweight individuals worldwide (age 15 and older) with at least 400 million considered to be obese. WHO further projects that the number of overweight adults worldwide will increase to approximately 2.3 billion by 2014 and more than 700 million will be obese. Of considerable concern, WHO estimates that there were at least 20 million children under the age of five years

old that were overweight globally in 2005 [113]. There does not appear to be any indication that the prevalence of overweight and obesity is decreasing; NHANES data showed that for children in the US aged 6 through 19 years in 1999-2002, 31% were at risk for overweight, while 16% were actually overweight [121]. Longitudinal data from the National Heart, Lung and Blood Institute Growth and Health Study (NGHS) demonstrate that rates of overweight in Caucasian girls increased through adolescence from 7% to 10% and from 17% to 24% in African-American girls [122].

As weight gain has also been associated with the development of diabetes, the above trend is particularly alarming. Prospective data from the Nurses Health Study confirmed the relationship between obesity and increased risk for development of T2D but also demonstrated that a weight gain of 7.0-10.9 kg after age 18 was associated with a twofold increase in the risk for diabetes [123]. In 1997, long-term patterns of weight change over about a 10 year period were examined in relation to incidence of diabetes in a national cohort of 8,545 adults in the U.S. from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. The results demonstrated increased risk with increased weight gain when compared to a stable weight; the authors found no evidence that the results differed by age, sex, or race and estimated that the population attributable risk was 27% for weight increases of 5 kg or more [124]. Additional results published in 2004 from the Health Professionals Follow-up Study also found a similar relationship. In this study, changes in body weight and body fat distribution and the subsequent risk of diabetes among 22,171 men over time was examined. The authors found that for every kilogram of weight gained, risk for diabetes increased by 7.3%, and that over 50% of the cases of diabetes in this group could be credited to a weight gain greater than 7kg [125].

In addition to general obesity, body fat distribution is another very important factor in the development of T2D as it is apparent that those with increased abdominal fat are at higher risk for T2D. Several studies have confirmed the association between increased central adiposity, including waist circumference, waist hip ratio and T2D development in both men and women [126-132]. One recent prospective study compared the ability of BMI, waist circumference (WC) and waist to hip ratio (WHR) to predict T2D development. The authors found both overall obesity and WC strongly and independently predicted T2D and determined that WC was a better predictor than WHR [133]. As has been shown for weight gain, changes in waist circumference are also related to increased risk. In the Health Professionals Follow-up Study mentioned above, in addition to confirming the relationship between weight gain and increased risk for T2D, an increased change in WC was also shown to be highly related to increased risk. When men who had increased WC by 14.6 cm or more were compared with men who had a stable WC, those with increased WC had 1.7 (95% confidence interval: 1.0, 2.8) times the risk of diabetes after controlling for weight gain [125]. Although some debate has arisen concerning waist measure cut-points, particularly in areas of ethnic differences, central adiposity is clearly an important component of T2D development and insulin resistance.

Another important environmental factor associated with T2D development is lack of physical activity. Physical activity has generally decreased in many populations in recent years due to advances in technology and lifestyle changes. Much research has suggested a relationship exists between sedentary lifestyle and risk for T2D, and vice versa [134-139]. One notable study examined the longitudinal relationship between physical activity, BMI and the development of type 2 diabetes in a high-risk Gila River Indian community from 1987 to 2000 [140]. A physical activity questionnaire that assessed past year leisure and occupation activity was

administered to 1,728 non-diabetic Pima individuals age 15-59. Using the OGTT to determine diabetes diagnosis, over an average follow-up period of six years, the authors found that total activity was related to the development of T2D in both men and women, with women demonstrating a significant relationship between diabetes development and physical activity ($p<0.05$). Furthermore, the incidence of diabetes remained lower in the more active individuals across most categories of BMI for both men and women in this study. Another example is the Honolulu Heart Program, which prospectively followed 6,815 Japanese-American non-diabetic men age 45-68 years over a six-year period and found that increased activity was inversely related to decreased risk for T2D even when other mediating risk factors were adjusted for [141]. In another more recent investigation, 2,017 Finnish men and 2,352 Finnish women age 45-64 years with no previous history of diabetes were followed prospectively for 9.4 years. After adjusting for other risk factors such as age, study year, gender, blood pressure, smoking and education, level of physical activity was found to be inversely associated with risk for T2D. This relationship was persistent in those with both obesity and impaired glucose regulation, either obesity or impaired glucose regulation or with normal BMI and glucose regulation [142]. Another prospective study of middle-aged non-diabetic British men over a mean of 9.8 years found that men engaged in moderate levels of physical activity had a substantially reduced risk of diabetes, when compared to the physically inactive men, after adjustment for age and BMI. This association persisted in full multivariate analysis [143]. Another study using Nurses Health Study data, the "dose" of activity required for beneficial risk reductions was examined. The results suggested that more vigorous activity resulted in an increased risk reduction, but also confirmed that more moderate activities such as walking provided a reduction in risk as well [144]. Low levels of physical activity and increased risk for T2D have been shown in the elderly

population as well. Residents of East Boston age 65 years and older who were participating in the East Boston Health Project (one of four components of the National Institute on Aging-sponsored Established Populations for the Epidemiologic Study of the Elderly) were followed prospectively over two 3-year time periods. High BMI (>26kg/m^2) and low physical activity level were found to be significant predictors of T2D in a multiple regression model adjusting for age, gender, and blood pressure [145].

Although not as well studied, this relationship has been found in children and adolescents as well. One very recent small study examined 54 obese and lean children age 9-11.5. The results of the study suggested that elevated central adiposity and low levels of daily physical activity were the main predictors of insulin resistance in this population [146]. Thus, the important relationship between physical activity and risk for T2D exists across gender as well as various age groups and ethnicities; however, it does not appear that levels of physical activity are increasing. Using the Medical Expenditure Panel Survey, a nationally representative survey of the U.S. population, physical activity in those with diabetes and at risk for diabetes was examined for the year 2003. A total of 39% of adults with diabetes were physically active versus 58% of adults without diabetes [147].

One other obvious component of lifestyle risk includes diet. While the possibility that diet is involved in the development of T2D has been recognized for quite some time, the specific dietary components and processes involved have not been wholly identified. The theory that high-fat diets may contribute to the development of insulin-resistance and T2D has evolved from observations of increased risk for T2D in populations that have "Westernized" their diets, i.e. changed from diets rich in multiple fruits and vegetables, which were usually high in complex carbohydrate and fiber, to diets which are much higher in fat and lower in complex carbohydrate.

In many instances, later generations who have migrated to the U.S. or other western cultures have seen marked increases in rates of T2D. Studies comparing later generation migrated populations to those who remain in their homeland have found higher amounts of dietary fat in those who have migrated [148, 149]. Other research, both cross-sectional and prospective, has supported the concept of a high-fat diet, or high-fat low-carbohydrate diet being associated with the development of T2D [150, 151]. Additional evidence exists to suggest that it is not just the quantity but the quality of fat intake which is important in the development of T2D, with higher intakes of saturated fat and trans-fat potentially having an adverse effect on glucose metabolism [152].

Carbohydrates and fiber have also been identified as possibly playing a role in the development of T2D. There has been some evidence that high-complex carbohydrate, high-fiber diets may improve insulin sensitivity [153]; furthermore the quality of carbohydrate has received considerable attention lately as this may influence the rate of digestion and subsequent glucose response. The concept of glycemic index (GI) was developed in 1981 in an effort to quantify the glycemic responses induced by carbohydrates in different foods [154] and continues to be a nutritional tool as well as a viable hypothesis under continued investigation [155]. Research has supported the concept of a relationship between high glycemic load foods, low cereal fiber and increased risk for T2D [156-158] In a review of existing literature, Hu et al., concluded that a diet consisting of low GI carbohydrates and high in fiber could potentially reduce risk, while diets containing large amounts of higher GI foods may increase risk for T2D [152]. The authors admitted that the concept of GI has been controversial, but that GI may be useful when data bases are further developed and refined. The relationship between glycemic index, glycemic load and dietary fiber intake and the risk of T2D was examined prospectively over 8 years in a

large cohort of young women. Glycemic index was significantly associated with increased risk for T2D after adjustment for age, BMI, family history of diabetes, as well as other potential confounders, while cereal fiber intake was associated with a decreased risk of diabetes. Glycemic load was not significantly associated with risk for T2D. The authors concluded that a diet with high glycemic index foods and low fiber cereal was associated with increased risk for T2D [159].

In summary, it is apparent that a variety of components are involved in the development of T2D, and in fact all must be addressed in the reduction of risk for T2D. Findings from a large prospective study of 84,941 female nurses followed over a 16-year period from 1980 to 1996 exemplify the importance of considering all components of risk for T2D. All participants were free of diagnosed CVD, diabetes or cancer at baseline assessment; 3300 new cases of type 2 diabetes were found during the study time period. The authors found that overweight or obesity was the single most important predictor of T2D; after adjusting for BMI, other factors attributed to a significantly increased risk of diabetes were lack of exercise, a poor diet, current smoking, and abstinence from alcohol. The authors concluded that in this large cohort of middle-aged women, "a combination of several lifestyle factors, including maintaining a body-mass index of 25 or lower, eating a diet high in cereal fiber and polyunsaturated fat and low in saturated and trans fats and glycemic load, exercising regularly, abstaining from smoking, and consuming alcohol moderately, was associated with an incidence of type 2 diabetes that was approximately 90 percent lower than that found among women without these factors. These results suggest that in this population the majority of cases of type 2 diabetes could be avoided by behavior modification." [160].

2.3 CARDIOVASCULAR DISEASE

2.3.1 Epidemiology

Cardiovascular disease, which consists of hypertension, coronary heart disease (CDH), heart failure, stroke and congenital cardiovascular defects, remains the number one cause of death in the U.S., accounting for 36.3% of deaths in 2004, or 1 in every 2.8 deaths in the U.S. CHD accounts for over 50% of CVD mortality, followed by stroke at 17%. It is estimated that 1 in 3 adults in the U.S. have some form of CVD, with over half age 65 and older [161]. Data from the Framingham Research Study indicate that the lifetime risk for CVD is 2 in 3 for men and more than 1 in 2 for women at age 40 [161]. In the U.S., CVD prevalence in 2004 was highest in black females (49.0%) and black males (44.6%), followed by white males and females (37.2% and 35% respectively). Mexican American males and females had the lowest rates of CVD at 31.6% and 34.4% respectively.

The cost of cardiovascular diseases and stroke for 2007 has been estimated at $431.8 billion. This included direct costs such as cost of physicians and other professionals, hospital and other healthcare facility services, medications, home health care, etc., as well as indirect costs such as lost productivity resulting from illness or death [161]. Costs for CHD contribute the highest amount at 151.6 billion, followed by hypertensive disease, stroke, and heart failure [162].

Although rates of death from CVD have declined considerably for the majority of the population in the U.S. [163], mortality rates from CVD for those with diabetes have not decreased to the same extent [164, 165]. Macrovascular disease including myocardial infarction (MI), stroke and peripheral artery disease (PAD) accounts for the major cause of morbidity and

mortality for those with diabetes [90]. Diabetic patients with MI also have a poorer clinical outcome than those without as well as higher rates of re-infarction and heart failure [166]. Research has also shown that individuals with impaired glucose metabolism prior to diagnosis are at risk for CVD problems as well [167, 168], particularly those with impaired glucose tolerance [15, 169, 170]. In addition, there has been some evidence that women with hyperglycemia may have higher risk for CVD than those without [171].

Because T2D and CVD are so intertwined, it will become more and more important that care be directed to both. Recently the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD) recognizing that T2D and CVD are "two sides of a coin", came together to form a task force to publish guidelines for the diagnosis and management of care for the vast number of individuals that have both cardiovascular and metabolic diseases in common [172]. Of late the American Diabetes Association has begun using the term "cardiometabolic risk" to identify those with risk factors for CVD [173]. Recently the American Diabetes Association and the American Heart Association issued a joint statement to attempt to summarize the evidence supporting lifestyle and medical interventions that will prevent the development of CVD in people with diabetes [174]. The report highlighted their similarities and differences in prevention and treatment recommendations, but concluded in jointly supporting the aggressive use of lifestyle modifications to try to reduce or delay the need for medical intervention.

2.3.2 Etiology

Individuals with T2D, as well as those with impaired glycemic function are clearly at increased risk for development of complications related to CVD. There have been several suggestions concerning the mechanisms responsible for the early and aggressive development of atherosclerosis as well as the poor CVD outcomes seen in those with impaired glucose homeostasis including early development of an abnormal endothelial function, platelet hyperactivity, enhanced cellular and matrix proliferation following arterial injury, propensity for adverse arterial remodeling and impaired fibrinolysis with a tendency for thrombosis and inflammation [175].

As described previously, components of the metabolic syndrome using various definitions have been strongly related to the development of CVD [168, 176-179]. Although there has been debate concerning the existence of a metabolic syndrome or other similarly described conditions [25, 180], evidence exists to support the concept of this syndrome as a valid predictor of risk for CVD and that the clustering of these risk factors is more than a coincidence [181-183]. The components of the metabolic syndrome are primarily related to development of CVD in those with glycemic impairment. In a recent study, investigators examined the risk for CVD in the San Antonio Heart Study using National Cholesterol Education Program (NCEP)-Adult Treatment Panel III (ATPIII), International Diabetes Federation, and World Health Organization definitions of the metabolic syndrome and concluded that the metabolic syndrome is associated with a significantly increased risk for CVD, particularly for men age aged ≥45 years of age and women ≥55 years. In addition, all three of the metabolic syndrome definitions demonstrated similar risk for CVD [184].

The two major underlying components of the metabolic syndrome are related to obesity and insulin resistance [185]. Similarly to risk for T2D, increased BMI and weight have been associated with risk for CVD [186-189]. Results from the Nurses Health Study published in 1995 found that even within the "normal" range of weight for women, higher levels of body weight, as well as moderate weight gain after age 18, appeared to increase risk for CHD in middle-aged women [190]. In a further follow-up of the Nurses Health Study, women without CVD at baseline were followed prospectively for 20 years; the study found that overweight and obesity were significantly related to increased risk of coronary heart disease (CHD) [191]. Those with BMI $\geq$ 40.0 kg had 5-fold increased risk of CHD when compared with women with BMI 18.5 and 22.9. Furthermore, similar to the results found for diabetes risk, a modest weight gain during adulthood (4.0-10.0 kg) was associated with increased risk for CHD when compared to women with a stable weight after adjusting for other CVD risk factors and physical activity (RR=1.27; 95% CI, 1.12 to 1.45). For those with 40.0 kg weight gain or more, risk of developing CHD increased considerably (RR=3.86; 95% CI, 3.02 to 4.94). CVD risk has also been examined in overweight and obese children and adolescents with alarming results. Data from the National Heart, Lung and Blood Institute Growth and Health Study (NGHS) found that childhood overweight was significantly associated with increased unhealthful systolic and diastolic blood pressure (defined at or above the sex- and age-specific 95th percentile for systolic and diastolic blood pressure and also considering height), high-density lipoprotein cholesterol, and triglyceride levels in Caucasian and African American girls [122]. Other studies have found increased CVD risk in adulthood to be related to overweight in childhood or adolescence [192, 193].

Insulin resistance, defined as the inability of the body to use insulin efficiently, is comprised of abnormalities in glucose and insulin levels. Insulin resistance is often found in conjunction with obesity; one recent article suggested that varying levels of insulin resistance and sensitivity may be the mechanism responsible for adverse clinical outcomes in those who are obese, rather than obesity in and of itself [194]. Nonetheless, it is known that insulin resistance plays a significant role in the development of type 2 diabetes [195]. As a core component of the metabolic syndrome, recognition that disturbances in glycemic control may also play a significant role in the development of CVD is growing [196]. Research has shown a progressive relationship between non-diabetic glucose levels and CVD risk [167]; this relationship has been shown in various populations. The Study of Health Assessment and Risk in Ethnic groups (SHARE) measured glucose tolerance and risk factors for CVD in 985 individuals of South Asian, Chinese, and European origin living in Canada for greater than 5 years [197]. The results of this large multi-ethnic study found glucose intolerance to be strongly associated with other risk factors for CVD, including age, abdominal obesity, hypertriglyceridemia, high free fatty acids, reduced insulin secretion, and increased insulin resistance. More recently, data from the Heart Outcomes Prevention Evaluation (HOPE) trial, a large international trial which showed that the ACE inhibitor ramipril reduced risk for CV events in diabetic and high-risk non-diabetic subjects, found that glycohemoglobin level was an independent risk factor for a broad range of outcomes, including CV events, heart failure, death and overt nephropathy [198]. A very similar relationship between fasting plasma glucose and outcomes was also noted in the group that included both diabetic and non-diabetic individuals. The relationship between fasting plasma glucose and cardiovascular events was maintained in this group after accounting for the presence or absence of diabetes. Some research has shown

IGT to be a better predictor of CVD and mortality than IFG [199]. Hyperinsulinemia has been found to be an independent predictor of CVD [200-202], however in a recent meta-analysis of studies of circulating levels of three insulin markers (fasting insulin, non-fasting insulin, and pro-insulin) and their relation to CHD risk, the authors concluded that associations between CHD risk and fasting or non-fasting insulin levels may not be as strong as reported previously and that pro-insulin levels may be more strongly associated with CHD risk than are insulin levels [203]. Insulin resistance is also positively correlated with waist circumference and subcutaneous adiposity [204] which are strong predictors of CVD.

Another major component in the development of CVD is dyslipidemia. The INTERHEART study, a case-control study of acute myocardial infarction with 27,098 participants representing several major ethnic groups examined risk factors for CVD in 52 countries and concluded that worldwide, abnormal lipid levels are one of the two most important modifiable risk factors for CVD, with the other being smoking [205]. Total cholesterol, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol have long been associated with the development of coronary heart disease (CHD) [206-209], with serum cholesterol showing a continuously graded effect on risk for CHD [210] as well as CVD and all-cause mortality [211]. Furthermore, lower cholesterol levels have been associated with longevity and decreased risk for CVD [212, 213]. The inverse relationship between HDL levels and development of CHD has also been well documented [20, 214, 215]. Evidence in the past regarding elevated triglycerides, a specific component of the metabolic syndrome, as a predictor of CHD has been somewhat controversial [216, 217], however, considerable data supporting the measure in predicting risk for CHD does exist [218-220]. The level for triglycerides at which risk increases has been examined; one retrospective cohort study that evaluated 740 consecutive

patients subsequently diagnosed with coronary artery disease examined so-called "normal" levels of triglycerides and found that the mean triglyceride level was higher (160 vs. 137 mg/dl; p=0.03) in case patients than in control patients. After adjusting for age, gender and beta-adrenergic blocking agent use, multiple logistic regression analyses revealed triglycerides to be an independent predictor of CAD events with a relative risk of 1.5 (95% CI 1.1%-2.1%). For patients with baseline triglyceride levels $\geq$ to 100 mg/dl, Kaplan-Meier analyses revealed significantly reduced survival from CAD events compared with those with triglyceride levels <100 mg/dl (p=0.008). The authors concluded that triglyceride levels which were previously considered to be in the "normal" range were actually predictive of new CAD events [221]. The NCEP guidelines for the cut-point for determination of risk related to triglycerides were subsequently lowered from 200 mg/dl to 150 mg/dl [20] .

Evidence has shown that dietary fat intake, particularly saturated and trans-fat is associated with the development of dyslipidemia and subsequently CVD [222, 223] . One study conducted in an Italian population looked at consumption of various fats such as butter, olive oil and vegetable oil and risk for CHD in a sample of 4,903 Italian men and women 20 to 59 years of age. The authors found that after adjustment for confounding factors, consumption of olive oil and vegetable oil was inversely associated with serum cholesterol, glucose levels and systolic blood pressure in both sexes leading the authors to conclude that consumption of butter (saturated fat) may detrimentally affect coronary risk factors, while polyunsaturated and monounsaturated fats may be associated with lower coronary risk [224]. A high intake of trans-fat has been implicated as a key component for adverse effects upon lipid profiles [225-228] both increasing LDL and decreasing HDL cholesterol levels; further supporting data has been collected from the Nurses Health Study which has yielded abundant information about diet and

CVD risk. In a study published in 2005 after 20 years of follow-up, intake of trans-fat was related to increased risk for coronary heart disease (RR = 1.33, 95% CI: 1.07, 1.66; p_{trend} = 0.01), while intake of poly-unsaturated fat was inversely related to CHD risk [229].

This relationship was confirmed for men in a cohort of 21,930 men aged 50-69 years who smoked but were free initially of diagnosed cardiovascular disease. The study found after 6.1 years of follow up that men in the top quintile of trans-fatty acid intake had a multivariate relative risk of coronary death of 1.39 (95% CI = 1.09-1.78, p for trend = 0.004) when compared with men in the lowest quintile of trans-fatty intake [230]. Conversely, intake of foods higher in fiber such as whole grains, fruits, and vegetables has been shown to provide a somewhat protective effect upon risk [231, 232]. Other results published regarding the study above found that a diet which included a greater intake of foods rich in fiber was found to greatly reduce the risk for CHD, particularly death [233]. Additional research has supported a high fiber diet as protective against the development of CHD [234-236].

However one large study, the Women's Health Initiative, found that a dietary intervention which reduced total fat intake and increased intake of vegetables, fruits and grains did not significantly reduce the risk of CHD, stroke or CVD in postmenopausal women and achieved only a modest effect for CVD risk factors. The authors concluded that a more specific diet and interventions may be necessary to improve risk factors for, as well as reduce CVD risk [237].

In addition to dietary fat contributing to dyslipidemia, high fat intake is related to one of the most CVD predictive components of the metabolic syndrome, abdominal obesity. Abdominal obesity, particularly waist circumference, has been strongly associated with development of CVD in both men and women [191, 238-240] and some have found WC to be a

better predictor of CVD risk than BMI [241]. Results from the INTERHEART study demonstrated that both waist and hip measures were highly significant after adjustment for BMI [242]. Because abdominal adiposity is such an important risk factor for cardiometabolic risk, it would seem that physicians and the general public should be aware of the use of this primarily simple measure; however, published results from a recent survey indicate quite the opposite. The 'Shape of the Nations' survey was administered to approximately 100 physicians, 400 members of the general population and 100 individuals at risk for CVD in 27 countries. Interestingly, while 58% of physicians recognized abdominal obesity as an important risk factor for CVD, 45% reported never having measured waist circumference and more than half overestimated the waist circumference that puts their patients at risk. Only 42% of the general population were aware of the association between increased waist circumference and increased risk and more than half of the at-risk group had not been told by their PCP about the relationship between abdominal waist circumference and heart disease [243].

Like risk for diabetes, risk for CVD has been associated with lack of physical activity. Risk factors for CVD such as dyslipidemia, hypertension and insulin resistance have been related to lack of physical activity [138, 244, 245], as has the development of CVD [191]. Increased physical activity has been shown to reduce risk for CVD [246-248]. One study prospectively examined the role of walking as compared with vigorous exercise in the prevention of CHD. Total physical activity (walking and vigorous exercise), were examined among 72,488 female nurses who were age 40-65 in 1968. Results showed a strong, graded inverse association between physical activity and the risk for coronary events. Women in increasing quintile groups for energy expenditure had age-adjusted relative risks of 0.77, 0.65, 0.54, and 0.46 for coronary events (P for trend <0.001). This relationship remained strong after adjusting for other risk

factors. Walking was also found to be inversely related with the risk for coronary events, with those in the highest quintile group showing a greater reduction in risk when compared to those who walked infrequently. Regular vigorous exercise was related with similar risk reductions of about 30-40%. The study also found that women who were sedentary and became active in middle adulthood or later had a lower risk of coronary disease than those who remained sedentary [249]. Trends in physical activity are of particular concern in children and adolescents as the latest data from 2005 show that nationwide, only 35.8% of students had been physically active doing any kind of physical activity that increased their heart rate and made them breathe hard some of the time for a total of at least 60 minutes/day on $\geq$ 5 of the 7 days preceding the survey; 43.8% of males and 27.8% of females met current recommendations for physical activity. Furthermore almost 10% had not participated in any vigorous or moderate physical activity during the 7 days preceding the survey [250].

Increased blood pressure, another component of the metabolic syndrome, has also been shown repeatedly to be related to development of CVD including stroke and coronary heart disease in middle-aged as well as younger populations [251, 252]. For those older than 50 year of age, elevated systolic blood pressure is a more significant risk factor for CVD than diastolic [253]. Similar to cholesterol levels, blood pressure has been shown to show a continuous and graded relationship to risk for CVD, with each increment of 20/10 mm Hg doubling the risk of CVD [253]. In 2003 the Joint National Commission on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) released its latest report (JNC 7) with a new category for blood pressure known as "pre-hypertension" with systolic and diastolic ranges of 120-139 mm Hg and 80-89 mm Hg respectively [253]. The JNC7 also described the optimal range for blood pressure to be <120/80 mm Hg. Research has shown that similar to pre-diabetes, blood

pressure in the "high-normal" or prehypertension range is associated with CVD risk [254, 255] and thus is an extremely important modifiable risk factor leading the authors of JNC7 to state "a great potential exists for improved health and increased longevity through control of the blood pressure problem" [253] .

Finally, tobacco use is well-known as one of the strongest modifiable risk factors for CVD [256-259]. In addition, more recent studies have shown a relationship between passive or second hand smoke and development of CVD [260-263]. One recent investigation attempted to assess the risks associated with tobacco use (both smoking and smokeless), as well as second hand smoke, worldwide. Using a standardized case-control study of acute myocardial infarction (AMI) with 27,089 participants in 52 countries (12,461 cases, 14,637 controls), the authors found that when compared with those who never smoked, current smoking was associated with a greater risk for non-fatal AMI (OR= 2.95, 95% CI 2.77-4.14, $p<0.0001$) [264]. Chewing tobacco was also associated with elevated risk, and risk was highest for those who smoked and used chewing tobacco (OR=4.09, 2.98-5.61). Second hand smoke was associated with a graded increase in risk. In 1960, over 40% of the U.S. population smoked [265]; the prevalence rates for adults age 18 and older have declined steadily since 1966 to about 21% [266]. While smoking rates for adults have decreased, for high school students in grades 9-12 in 2005, the prevalence for current smoking was 23%, with white females showing the highest prevalence (27%) and black females showing the lowest (11.9%) [250]. Thus, tobacco use remains an issue of considerable concern demonstrating the importance of continuing efforts to reducing tobacco consumption, both actively and passively in all populations.

2.4 PREVENTION IN PRIMARY CARE

2.4.1 Current Recommendations for Screening

2.4.1.1 Diabetes

At the present time, the American Diabetes Association (ADA) recommends screening to detect pre-diabetes and diabetes for individuals who are 45 years of age and older, particularly in those with a BMI $\geq$ 25 kg/m^2 [87]. The ADA also recommends that screening should be considered for people who are less than 45 years old and who are overweight if they have another risk factor for diabetes. Risk factors include: habitual physical inactivity, having a first degree relative with diabetes, being a member of a high risk ethnic group, having hypertension, low HDL or high triglyceride level, previous diagnosis with IFG or IGT, or having other clinical conditions associated with diabetes. Additional risk factors for women include delivery of a baby weighing more than 9 pounds, diagnosis with gestational diabetes or diagnosis with poly-cystic ovary syndrome. Repeat testing should be completed at 3-year intervals.

For several reasons the ADA recommends that screening should be carried out within the health care setting, using either the fasting glucose test or the two-hour OGTT. The ADA considers that community screening outside of the health care setting may be less effective due to the failure of people with a positive screening test obtaining appropriate follow-up testing and care. There is also the concern that those who screen negative may not receive appropriate repeat testing in the future. The ADA also states that community screening may fail to reach the groups most at risk and inappropriately test those at low risk.

Like the ADA, the International Diabetes Federation (IDF) does not recommend universal screening for those without symptoms, but recommends screening within a health care setting for those determined to have risk factors; for those who screen negative, a repeat assessment should be conducted within 3-5 years [267]. The IDF also recommends the fasting plasma glucose test for screening and cites the low sensitivity but high specificity of using urine glucose for screening, thus indicating that this may be appropriate in very low resource settings where other methods of testing are not available.

The European Association for the Study of Diabetes (EASD) takes a slightly different approach in that it recommends the use of a non-invasive risk score subsequently combined with an OGTT for screening and diagnosis rather than just the fasting plasma glucose alone [268]. This is due to concern regarding the possibility of false negatives occurring with the use of the fasting plasma glucose test only. The EASD acknowledges that the OGTT may not be as feasible or practical at a population level, however maintains that it is essential since this is the only way to diagnose IGT which is more strongly associated with the development of CVD.

The United States Preventive Services Task Force (USPSTF) does not recommend for or against routinely screening asymptomatic adults for type 2 diabetes, impaired glucose tolerance, or impaired fasting glucose, however, it does recommend screening for type 2 diabetes for those individuals with hypertension or hyperlipidemia [269].

2.4.1.2 Hypertension

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) was published in 2003 by the National Institutes of Health National Heart, Lung and Blood Institute [253]. Although screening interval was not mentioned specifically in that report, the Sixth Report (JNC-6)

recommended all adults 18 and older should have a blood pressure assessment: those with blood pressure <130/85 should be checked at least every two years and those with readings at 130/85 and higher should be checked more frequently [270]. Diagnosis should be based on the average of two readings measured on two different occasions. The JNC-7 report classifies normal blood pressure as being < 120 and < 80 mm/Hg and introduces the concept of "pre-hypertension" considered to be in the range of 120-139 mm/Hg for systolic blood pressure and 80-89 mm/Hg for diastolic. JNC-7 further divides blood pressure into two stages: Stage 1 Hypertension (140-159 mm/Hg systolic or 90-99mm/Hg diastolic) and Stage 2 Hypertension (≥ 160 mm/Hg or ≥ 100mm/Hg).

Health-promoting lifestyle measures are the recommended first line of intervention for those diagnosed with pre-hypertension and are subsequently integrated with pharmaceutical therapy throughout the spectrum. Thiazide diuretics are recommended as the first line treatment for those with uncomplicated hypertension and no other compelling indication. JNC-7 also indicates that most individuals with hypertension will require two or more antihypertensive agents to reach a goal of < 140/90 mm/Hg and < 130/80mm/Hg for those with diabetes or chronic kidney disease. This report also presents the methodology for measurement of blood pressure at each physical examination and stresses the importance of controlling systolic hypertension in those over age 50.

The USPSTF recommends that physicians screen adults age 18 and older for high blood pressure, but currently finds insufficient evidence to recommend or not recommend screening for children and adolescents [271]. Like JNC-7 they recommend that diagnosis be made only after completion of two readings on two separate visits.

The American Heart Association/American Stroke Association recommends regular screening for hypertension at least every two years in most adults and more frequently in minority populations and the elderly [272]. The AHA/ASA guidelines further follow those of JNC-7.

The European Society of Hypertension/European Society of Cardiology also have published guidelines concerning hypertension [273]. The guidelines are somewhat similar to the JNC-7 guidelines; however differ on a few key points which are highlighted in an article by Mancia and Grassi published in 2005 [274]. The authors cite general differences including the main focus of the two sets of guidelines, which they feel to be mainly prescriptive in JNC-7 while the ESH/ESC guidelines appear to be more informative and educational. Another difference in the guidelines is the complexity: while the JNC-7 guidelines appear fairly straight forward, the ESH/ESC guidelines are more detailed and somewhat more complicated. Other differences include those in the classification of blood pressure, with the ESH/ESC guidelines suggesting like the JNC-7 that optimal range should be <120mmHg and <80mm/Hg. The ESH/ESC guidelines however do not have a pre-hypertension category, rather include the range of 120-129 mm/Hg and 80-84 mm/Hg as "normal" and 130-139 mm/Hg and 85-89 mm/Hg as "high normal". Hypertension is further categorized as Grade 1 Mild (140-159 mm/Hg or 90-99 mm/Hg), Grade 2 Moderate (160-179 mmHg or 100-109 mm/Hg) and Grade 3 Severe (≥ 180 mmHg or ≥ 110 mm/Hg). ESH/ESC guidelines stress the importance of establishing potential target organ damage in the determination of overall cardiovascular risk and subsequent treatment. Like JNC-7, target blood pressure goals are the same for non-diabetics as well as for those with diabetes and ESH/ESC recommends healthy lifestyle behaviors as the first intervention and that it be subsequently interwoven into pharmaceutical treatment. Mono-

therapy is recommended with subsequent addition of medication as necessary; however, no specific drug per se is recommended.

2.4.1.3 Hyperlipidemia

The National Cholesterol Education Program (NCEP) published it's most recent recommendations and guidelines, Adult Treatment Panel III (ATPIII) in 2001 [20], with updates in 2004 [275]. The NCEP recommends that everyone age 20 and older should have a cholesterol screening completed at least every 5 years, with testing more often as required. Further, the NCEP recommends that testing should include a complete fasting lipid profile (total cholesterol (TC), low density lipoprotein cholesterol (LDLC), high density lipoprotein cholesterol (HDLC) and triglyceride level) completed after a 9-12 hour fast, however, if not possible, then only TC and HDLC cholesterol should be collected. If the TC is $\geq$ 200 mg/dl or the HDLC is < 40mg/dl then a fasting lipid profile should be collected. Treatment is based on the LDL cholesterol level with < 100mg/dl considered to be optimal. The updates in 2004 were related to treatment levels in which those at greatest risk, i.e. individuals with diabetes or existing cardiovascular disease, should have a goal of < 70 mg/dl for LDL treatment. Treatment of elevated triglycerides and low HDL are secondary goals after reaching the desired LDL treatment level.

The USPSTF recommends routine screening for men aged 35 years and older and women aged 45 and older for lipid disorders [276]. Routine screening is recommended for men aged 20-35 and women aged 20-45 if they have other risk factors for coronary heart disease. These risk factors include having diabetes, an immediate family history of CVD in men < 50 years old and women < 60 years old, a family history that is suggestive of familial hyperlipidemia, or multiple coronary heart disease risk factors e.g. tobacco use, hypertension, etc. The USPSTF states that the optimal interval for screening is uncertain, but based on expert opinions mandates every 5

years with shorter intervals for those who have lipid levels close to those warranting therapy. The USPSTF does not recommend an age to stop screening, but recognizes that repeated screening in those who have been screened previously and are older than 65 may not be necessary. Screening should at least include measuring TC and HDLC; the USPSTF does not find evidence to recommend or not recommend routine testing including triglycerides. The USPSTF recommends that counseling concerning the benefits of a diet low in saturated fat and high in fruits and vegetables, regular physical activity, avoiding tobacco use and maintaining a health weight should be provided to all individuals regardless of their lipid levels.

2.4.2 Current Prevention Practices

While the *Healthy People 2010* report emphasizes the importance of improvement in prevention [277], the provision of preventive services continues to be suboptimal. Because primary care physicians' (PCPs') delivery of patient care is more broad-based than other specialties, they are a logical choice for provision of preventive services to patients at risk, however effective prevention programs are lacking. Results from a national survey of U.S. PCPs were published in 1999; the purpose of the data collection was to overcome the shortage of information about prevention practices, as well as to ascertain the relationship between physician demographics and the delivery of preventive care [278]. The Primary Care Providers Survey was created by the Office of Disease Prevention and Health Promotion and 5 primary care professional associations representing family practitioners, pediatricians, internists, OB-GYNs and nurse practitioners. Of the total initial sample of 9,079 physicians, 5400 responded, with 3,881 meeting the study criterion of spending at least 50% of their time in primary care. The survey requested information regarding how often PCPs provided preventive services to their patients, which

included most preventive services that should be given in an office visit such as review of tobacco use, nutrition, exercise and alcohol and drug abuse. The survey also addressed CVD and cancer screening tests, seat belt use, family planning and immunization practices. Adequate provision of services was defined as being delivered >80% of the time. The survey revealed that most PCPs across all disciplines and demographics were not providing adequate preventive services to the patients they serve, with services relevant to this review such as addressing exercise and nutrition found to occur less than 20% and approximately 27% of the time respectively. Only 37.2% of the responding physicians reported acting more than 80% of the time to providing assistance to help their smoking patients stop, while approximately 60% performed a cholesterol test. Blood pressure was the most frequently performed test, with responding physicians indicating that this measure was completed adequately over 87% of the time. Women physicians demonstrated higher rates of provision of prevention services, as did those physicians < age 50, while a progressive decrease was seen in the provision of adequate preventive services corresponding to the change from large metropolitan areas to more rural areas.

Unfortunately, the results of this survey are not unique; there is considerable evidence confirming the lack of provision of preventive services in primary care practice. Data from 2001–2004 National Ambulatory Medical Care Survey, an annual survey of outpatient visits, showed that overall, 32% of patient charts did not include information about tobacco use, 81% of smokers did not receive any assistance with stopping and less than 2% were given a prescription for pharmacotherapy [279]. Another study examined basic preventive care services in elderly patients using the Community Tracking Study Physician Survey which was linked to claims data on Medicare beneficiaries they had treated. Six preventive services were examined: diabetic

monitoring with hemoglobin A1C measurement or eye examinations, screening for colon or breast cancer, and vaccination for influenza or pneumococcus. This study found that overall, the proportion of beneficiaries receiving preventive services was below national standards, leading the authors to conclude that delivery of routine preventive services for Medicare beneficiaries is suboptimal [280]. Other research has confirmed the lack of preventive services available including one study where research nurses directly observed consecutive patient visits in the offices of 138 family physicians to determine rates of provision of preventive service. Medical record review was conducted to determine patient eligibility for services recommended by the U.S. Preventive Services Task Force. The investigators found rates of delivery of prevention services to be low, determining that patients were up to date on only 55% of screening preventive services, 24% of immunizations, and only 9% of health habit counseling services [281].

Patient surveys have also been conducted to determine perception of preventive services being rendered. One such survey sent to 7,997 randomly selected patients from 44 primary care practices (6,830 respondents) found that on average, about two-thirds of the patients in each practice reported that they were up-to-date on preventive services before their clinic visit, however less than 30% of those not up-to-date were offered service if the clinic visit was for a reason other than a checkup or physical examination, with the exception of blood pressure and smoking cessation advice. For those patients who were scheduled to see their physician for a checkup or physical examination, the only prevention service provided more than 50% of the time was Papanicolaou smear [282].

2.4.3 Barriers to Prevention

It is important to recognize the barriers to provision of prevention services. It has been suggested that physicians may not appreciate the value of providing preventive services [278] or that they may have ambivalence regarding their ability to promote adherence and behavior change [283]. PCPs also believe that prevention is important but consider the lack of reimbursement by insurance to be a barrier to provision of services [284]. Competing demands for the PCP during a patient encounter such as acute care, patient requests, chronic illnesses, psychosocial problems, screening for asymptomatic disease, counseling for behavior change, other preventive services, and administration and management of care have all been suggested as major barriers to the provision of specific preventive services to patients [285]. Encouragingly, one survey found that 9 out of 10 primary care physicians felt that it was "definitely" their responsibility to educate patients about health-related risk factors and the majority also felt prepared to provide advice about smoking, alcohol use and exercise, however less than half felt prepared to provide advice on diet, illicit-drug use, depression, or stress [286]. Another barrier to preventive care is related to the provision of services at a “sick” visit versus a visit that has been scheduled specifically for a check-up or physical examination; research has shown that physicians provide more preventive services during a regularly scheduled visit [287]. One direct observational study found that preventive services were delivered in 32% of 3,547 illness visits [288]. The authors suggested that perhaps the “sick” visit should be viewed as an opportunity to provide preventive services, however information delivered during this possibly stressful time may not be well-received.

Time constraints may also present a barrier to prevention; one study examined the factors associated with physician patient volume and looked for differences in selected clinical outcomes

and time use during patient visits in the offices of 108 community family physicians. The rate of preventive services delivery, patient satisfaction, and time used during patient visits was compared between high, medium and low patient volume practices. The study found that physicians in high volume practices had visits that were 30% shorter and scheduled one-third fewer patients for well care. The study also found that patients in high volume practices had lower up-to-date rates of prevention services and also scored lower on patient satisfaction measures. The authors concluded that although the high volume practices were more efficient in time management, this came at the cost of decreased preventive services and lower patient satisfaction [289]. Other barriers to prevention implementation include lack of awareness or familiarity with guidelines and disagreement with guidelines [290] or lack of trust in the guideline source [291]. Finally, one of the most important barriers to sub-optimal provision of prevention is the lack of organized and effective systems for delivery of prevention services [292, 293].

2.4.4 Primary Care Prevention Strategies

It is obvious that much attention has been paid to prevention and the delivery of prevention services, however, even basic prevention services continue to be provided on a less than optimal level. Well-organized office systems are necessary for efficient and effective delivery of prevention services. A survey study was completed to examine the presence and comprehensiveness of organized processes and systems in a sample of primary care clinics which had been shown previously to have a wide variation in rates of providing preventive services [294]. The survey examined the following 10 components: 1) sex-specific guidelines which included minimum age and frequency for specific preventive services to be provided, 2) a

routine screening system for staff to identify which, if any, preventive services are required, 3) a status summary of preventive services on a patient's chart, 4) reminders to bring routine prevention services to the attention of the PCP during a normal visit, 5) resources for patient education, 6) patient follow-up for patient to obtain test results, 7) outreach to include patient relatives to assist in obtaining the preventive service for an identified risk factor, 8) counseling for patients provided by a clinic employee other than the PCP, 9) the scheduling of prevention visits and 10) methods to help patients recognize the need for preventive services and to take action to obtain them. The survey responses documented how infrequently the participating clinics had functioning, organized processes. The three processes that would have most potential to enhance the likelihood of identification of those at risk and providing appropriate counsel (screening systems, status summaries and reminders) were reported to be present in only about one-fourth of the practices. Variation across clinics was seen as well.

The implementation of an organized system need not always be complex; one recent study examined a simple tool, a single checklist reminder form, and the delivery of preventive health services at adult health check-up visits in a family practice setting. The investigators performed a prospective cluster randomized controlled trial at four urban family practice clinics among 38 primary care physicians affiliated with the University of Toronto. The checklist reminder forms (Preventive Care Checklist Forms©) were created to be used by family physicians at adult health check-ups. The forms incorporated sex-specific guidelines for preventive health services as well as a space for documentation of routine procedures such as physical examinations. The study found that the percentage of up-to-date preventive health services delivered per patient at the end of the intervention was 48.9% in the control group and 71.7% in the intervention group, which represented an overall 22.8% absolute increase ($p =$

0.0001) [295]. The authors concluded that the addition of a simple reminder and documentation checklist could be beneficial in improving delivery of prevention services in other practices.

Another attempt at improving provision of preventive services through facilitation intervention specific to individual practices to increase rates of delivery of a broad range of evidence-based preventive services was evaluated. A nurse facilitator met with the participating practices and helped them identify both successes and missed opportunities created by the practice's current approach to prevention. The nurse facilitator helped practices choose from a menu of tools and approaches to help enhance preventive service delivery, as well as to create a plan for change and identify a practice leader for the intervention. The study found a significant increase in global preventive service delivery rates at the 1-year follow-up in the intervention group (31% to 42%) compared to the control group (35% to 37%). An increase in rates specifically for health habit counseling ($p=0.007$) and screening services ($p=0.048$) was seen, but not for immunizations [296]. The authors concluded that a prevention approach which is designed to meet particular practice needs may increase the delivery of global prevention.

In conjunction with provision of preventive services is the action required to achieve risk reduction, in other words a "prescription" for prevention, i.e. provision of preventive intervention for risk reduction. Again, primary care practices are well positioned to provide this care for their patients, however while advice regarding prevention and risk reduction may be provided, assistance and follow-up may be lacking. In a cross-sectional direct observation study of 300 family medicine outpatient visits, the content of each discussion of exercise, diet, and weight loss was documented by an observer. The investigators found that in 56% of observed visits discussion of exercise, diet, or weight loss occurred, however, advice rarely included the offer of assistance or any type of plan for follow-up. The authors concluded that while physicians

provide exercise, diet, and weight loss advice to obese patients and those with chronic conditions, the content of the advice rarely included specific components that could increase healthy behavior change [295].

Although there are not many examples of intervention provision in primary care practice, some research has been done. One study assessed the provision of counseling for overweight and obese patients in a primary care practice setting and found that those who received counseling from the PCP had significantly higher weight loss and more favorable behavior to control weight than those who received no counseling [297]. While it may be effective for PCPs to provide counseling, due to some of the barriers mentioned above, particularly time constraints, additional strategies for intervention should be employed. In a study examining nutritional counseling in primary health care for patients at high risk of ischemic heart disease, two strategies of nutritional counseling were evaluated [298]. Sixty general practitioners (GPs) were cluster randomized to either provide nutrition education themselves, or to refer to a dietician. The study found that while weight loss was larger in the dietician group, increase of HDL-cholesterol was larger in the GP group and the reduction of the cardiovascular risk score was significantly larger in the GP group ($p<0.001$). The authors concluded that while the nutritional education provided by the GP was significantly important in reducing risk, a long-term lifestyle intervention delivered by even these highly motivated GPs was difficult to implement in a practice setting. Another randomized study examined a year long lifestyle intervention for reduction of CVD risk in Sweden for efficacy and feasibility. A physiotherapist, a dietician, a physician were responsible for the intervention; other members of the team were additional physiotherapists, a laboratory nurse and two assistants. The intervention consisted of supervised physical activity, counseling for diet and follow-up meetings. The authors found that the

intervention significantly reduced some parameters of risk for CVD and was feasible to provide in a primary health care setting using existing staff members [299].

2.4.5 Summary of Prevention in Primary Care Practice

The USPSTF was reconvened in 1998 by the Agency for Healthcare Research and Quality (AHRQ) to update the guidelines for preventive services. At that time the importance of prevention of chronic diseases such as diabetes and CVD was emphasized. Since then, despite an abundance of published research documenting the efficacy and cost-effectiveness of diabetes prevention and CVD risk reduction, progress regarding these issues has been limited. For many reasons, the primary care practice setting provides a unique opportunity for prevention. Data from the U.S. Center for National Statistics published in 1998 showed that on average, patients of all ages attended a physician visit 2.8 times per year; for those over age 25, visit rates varied between 2.2 and 6.3 times per year [300]; thus patient visits occur frequently in this setting, and individuals may often interact with the same healthcare staff. In general, patients expect to receive advice and guidance from their health care providers [301] and as mentioned above, health care providers also perceive this to be a part of their role [286]. The primary care practice setting is an integral component of the entire medical system and thus could become the basis for prevention screening as well as provision of behavioral change interventions for risk reduction in the U.S.

While it is apparent that there are obviously many barriers to providing prevention services in a primary care practice setting, as discussed earlier, research has suggested that it is feasible. The challenge thus becomes to determine the most effective and efficient methods for identifying those at risk and delivering preventive interventions in the primary care practice

setting. It is also important to begin to understand certain factors, e.g. a patient's perception for disease risk that may influence potential for patient success in such prevention intervention programs. The utilization of combined, organized systematic approaches, which include available staff members as well as the PCP, may be an effective method for delivery of preventive risk identification screening services as well as prevention intervention for diabetes and CVD risk reduction.

2.5 CONCLUSION

While the literature supports the rationale for diabetes prevention from both a scientific and cost-effective perspective, implementation of diabetes prevention in a 'real-world' setting is challenging and certainly many barriers exist. Translational research to examine these issues, as well as the effectiveness and feasibility of "real-world" diabetes prevention is lacking. For many reasons the primary care practice venue provides an ideal environment for prevention management on a permanent basis. This project will address these prevention translation issues through 1) assessment of a screening program for identification of those at risk, 2) evaluation of a modified DPP lifestyle intervention delivered in a primary care practice setting for individuals identified to be at risk and 3) evaluation of a potential motivator for lifestyle change, risk perception and performance in a lifestyle change program. Due to the lack of translational research related to diabetes prevention and CVD risk reduction, it is anticipated that this project will make a significant contribution to the existing literature.

3.0 METHODS

3.1 BRIEF OVERVIEW OF THE STEP UP PROJECT

STEP UP was a one-group, prospective study which examined a structured screening program for identification of those at risk for T2D and CVD and also evaluated the delivery of a modified DPP lifestyle intervention in four primary care practices in Western Pennsylvania. Patients who were registered with the four practices and who were between the ages of 25-74 were invited for prevention screening using a computer driven recruitment and screening program. Individuals without previously reported diagnosis of diabetes, with BMI $\geq$ 25kg/m^2 and at least three of the five components of the metabolic syndrome (based on National Cholesterol Education Program Adult Treatment Panel III) [20] were eligible for the Group Lifestyle Balance (GLB) program, an adaptation of the individual lifestyle intervention utilized in the DPP. A total of 2,786 prevention screening letters were sent with 350 individuals attending screening and 97 determined to be eligible for the intervention; subsequently 51 subjects were enrolled in the intervention component of the project. Outcome measures included the collection of blood for the pre and post lipid profile and glucose (at least 2 hour fast requested), resting blood pressure, waist circumference and BMI; global risk was also assessed pre and post intervention. In addition, two surveys were administered before and after the intervention: the mRPS-DD and the CDC's 14-Item Health Related Quality of Life [68]. A third component of the project was the

completion of a chart review of those subjects in the targeted screening group as well as another group who were not targeted for comparison to determine whether identification of risk states had improved as a result of the screening.

3.2 PROJECT DEVELOPMENT

3.2.1 Primary Care Practice and Preventionist Selection

Four primary care practices, two urban and two rural, were identified in the Western Pennsylvania area. The practices were approached initially about participation and agreed to implement the screening and lifestyle intervention in their practices. Meetings were held with the medical directors of each practice as well as other available physicians and staff members to review the plan for translation and to elicit their input into how the study protocol would best work in their setting.

Each practice was asked to identify a "preventionist" to oversee the prevention screening program, including screening, recruitment and delivery of a lifestyle change intervention program. The preventionists were required to have a healthcare background; four were nurses and two were health educators (in one practice the position was split and in one practice the preventionist was replaced when she left the position). In two practices, the preventionists were identified from within the practice; in the other two practices the preventionists were brought in specifically for the position. The preventionists completed clinical measurement certification through the project STEP UP Coordinating Center for the measures that were collected including

blood pressure, height, weight, and waist circumference, as well as training regarding prevention screening and use of the computer driven program.

3.2.2 Group Lifestyle Balance Program

The original DPP Individual Intensive Lifestyle Intervention was developed at the University of Pittsburgh by the DPP Lifestyle Resource Core; the details of the intervention have been documented previously [302]. Members of the original DPP lifestyle team collaborated to adapt the individual intervention to a group-based program and to condense the program from 16 individual sessions delivered over 24 weeks to 12 group sessions delivered over 12-14 weeks. Other modifications included concentrating on healthy food choices rather than specifically the food pyramid, a focus on calorie as well as fat intake from the beginning of the intervention and more emphasis on the pedometer. As in the original DPP lifestyle program, the goals of the GLB intervention were to achieve and maintain a 7% weight loss, and to safely and progressively increase physical activity to 150 minutes per week of moderately intense physical activity similar to a brisk walk.

The GLB curriculum was administered by the trained preventionist(s) in each practice at the primary care practice locations. Initially, training guidelines for delivery of the GLB program were developed and a training workshop was held for the preventionists involved in this project, as well as approximately 40 other healthcare professionals from the local area. Each participant received a copy of the GLB participant handouts, Fat and Calorie Counter, self-monitoring books for keeping track of food and physical activity, a pedometer with instructions, a set of measuring cups and spoons, and a chart for self-monitoring weekly weights over the course of the program. Participants who did not own a scale were given one. All subjects were

asked to self-monitor weight, food intake and physical activity and were given feedback concerning progress.

3.2.3 Screening Guidelines

Because the guidelines for prevention screening often come from different sources and can be confusing and disjointed at times, a concise, "user-friendly" document summarizing current prevention screening guidelines for diabetes and cardiovascular disease was compiled based on the recommendations for prevention screening regarding diabetes, hypertension, dyslipidemia, and obesity [20, 253, 275, 303, 304]. The goal was to organize the current guidelines for ease of use, including recommended tests and time schedules to eliminate these barriers in providing prevention services in primary care practices.

3.2.4 Computer Driven Screening Program and Database Development

The members of this project contracted with Flipside Media, Inc. to work with them to create a questionnaire and data collection system to be used in the identified primary care practices. Laptops running the custom software application were used to track, screen and report on targeted patients within the practices. Additionally this system included a study recruitment tool that integrated with the office's existing patient database. The program allowed the preventionist to send invitation letters to eligible patients and then track their progress through the program. The system was designed to assess and evaluate all of the data collected at the screening, as well as to create a patient-specific report. The data were stored locally on the laptops and once a week were synchronized with a central server. This sync process transferred

the collected data to the central database, generated and emailed status reports to the researchers, and updated the software on the laptop to any newer versions.

The system is based on Flipside's ScoreMD screening and data collection platform. Embracing open source tools due to their standardization and interoperability, the ScoreMD is built upon a Unix-based operating system, Apache web server, MySQL database, the PHP scripting language, PDF-based reporting, secure web services for data transfer, and is usable through standard web browsers (like Internet Explorer, Firefox/Mozilla, Safari, and Opera).

Initially, each practice was assisted in preparing a data set that included all practice patients age 25-74 in 2005 that had been seen by a practice physician within the past three years. In planning for this project and from discussions with the practices, it was assumed by all involved that existing patient data sets could be utilized for this project. However, while two of the practices had an existing database that was converted relatively easily to the platform required by the computer program, the others needed more extensive assistance. The two that had existing databases were actually part of a patient billing system already in place that included all of the information required for recruitment for the screening. In the other two practices, the outside company that handled billing had to be contracted to provide the patient data in a usable format. Even with the data supplied, in one practice there were still several patients that had to be entered by hand. The entire dataset development was very time consuming and created an unforeseen delay in beginning the project. Once all of the datasets were in place, all patients were assigned a random 8-digit ID number with the link to the patient's identifying information kept in a secure location on site.

3.3 ELIGIBILITY AND RECRUITMENT

3.3.1 Screening

Within each practice, one quarter of the year (a consecutive 13-week period of time) was identified; all patients age 25-74 who were registered as patients at the participating primary care practices and had birthdates within the 13-week window were eligible for a prevention screening invitation. Using the computer program, invitations were sent near the time of the patient's birthday. The invitations, which encouraged the recipient to call the preventionist to set up an appointment were generated automatically by the program and sent out weekly by the preventionists. A subsequent follow-up telephone call was made if no response was received within one month. Preventionists were asked to make three such attempts at reaching the patient, calling at different times and days of the week, including weekends and evenings. De-identified information concerning invitation mailing and subsequent contact was tracked by the Coordinating Center, with appropriate reminders for follow up contact sent to the preventionists as necessary.

This prevention screening and chart review project received approval by the University of Pittsburgh Medical Center Quality Assurance Council.

3.3.2 Group Lifestyle Balance Intervention

All participants in the GLB program were patients of the participating practices who had attended screening or had been referred by one of the participating physicians. Inclusion criteria consisted of males and females without previously reported diagnosis of diabetes, age 25-74

years in 2005 with BMI $\geq$ 25kg/m^2 and at least three of five components of the metabolic syndrome (based on National Cholesterol Education Program Adult Treatment Panel III) [20] identified at screening. At the time of study, the NCEP had not yet changed its glucose criterion, although the American Diabetes Association had lowered its criterion for pre-diabetes from a fasting glucose of 110 mg/dl to 100 mg/dl [305]. Therefore patients who met the above criteria with only 2 components of the metabolic syndrome with a fasting glucose between 100 mg/dl and 109 mg/dl were also included at their primary care physician's discretion. Exclusion criteria included previously reported diabetes, pregnancy, lack of physician approval and inability to sign informed consent. Participants meeting eligibility criteria were invited to take part in the intervention program. A total of 51 individuals enrolled in the intervention component of the study; 43 were enrolled from the screening and 8 were enrolled via direct physician referral. This research project was approved by the University of Pittsburgh Institutional Review Board and the University of Pittsburgh Medical Center Quality Assurance Council, as well as the Surgeon General's Office of Review. Eligible and interested patients signed informed consent prior to beginning the study.

3.4 OUTCOME MEASURES

3.4.1 Screening

Patients attended a brief 30 minute screening visit which was conducted at the primary care practice, completing a short interview that included questions about medical, social and family history. The preventionist reviewed the chart for pre-existing blood glucose and lipid profiles

and other clinical measures, i.e., blood pressure, height, weight, and waist circumference. This information was subsequently entered into the computer program which determined if and when screening measures were necessary according to the guidelines. After completion of the required testing the program determined the prevention follow up schedule and provided a written summary for the patient, preventionist and physician. All measures were completed by the certified preventionists from the practices.

3.4.2 Group Lifestyle Balance Intervention

Enrolled participants were asked to attend an assessment to obtain clinical measures prior to beginning and again at the conclusion of the intervention. All clinical measures were obtained by a certified preventionist and/or certified STEP UP Center staff member. Blood pressure was measured in a sitting position in the right arm after resting for five minutes. First appearance and last heard (phase V) Korotkoff's sounds were used to define the pressure readings; the measures were repeated three times with a thirty second wait between each reading [306]. An average of the 2nd and 3rd readings was computed. Height and weight were measured twice without shoes with the average computed; BMI was calculated as average weight divided by average height squared (kg/m^2). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest; the measurement was repeated twice and the average computed.

Total cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol and glucose were measured after at least a two-hour fast using the Cholestech LDX System by a certified laboratory assistant. Global CVD risk assessment [307] was estimated and medication use was assessed via participant interview. In addition, weight was recorded weekly at each session.

Two surveys were collected at the pre and post intervention assessment visits; the mRPS-DD and CDC's 14-Item Health Related Quality of Life survey. The mRPS-DD responses were evaluated for the third part of this project and the survey is discussed further below.

3.4.3 Modified Risk Perception Survey for Developing Diabetes

The Risk Perception Survey for Developing Diabetes (RPS-DD) developed by Walker, et al., is designed for assessment of multiple dimensions of perceived risk for developing diabetes [308]. During the initial survey development, all items of the survey were reviewed for content and face validity by a panel of clinical diabetes experts, risk perception experts, and health psychologists. A pilot study was conducted with 74 nondiabetic, overweight, middle-aged individuals [309], after which the survey was revised slightly to enhance validity, reliability and ease of use. The original RPS-DD included 53 items and four subscales as well as other individual items to assess various aspects of risk perception. Internal consistency reliability for the four subscales was assessed using Cronbach α coefficients, both in a physician population as well as in an ancillary study population in the DPP [310, 311].

The survey was modified by the authors for this study; specifically it was shortened to include only the 32 items pertaining to the subscales, as well as the 3 items regarding lifestyle behavior. In addition, 5 questions pertaining to risk for diabetes development in relation to lifestyle changes were added, for a total of 40 items. The self-administered mRPS-DD was completed by enrolled participants at the baseline and post-intervention assessments. The Personal Control subscale (4 items [alpha] = 0.67, physician population, 0.68, DPP population) reflects perceived control over developing diabetes with a higher score indicating greater perceived control. The Comparative Disease Risk subscale assesses perceived risk for

development of 15 diseases and conditions on a scale ranging from 1 ("almost no risk") to 4 ("high risk") with a higher score indicating a greater perceived risk ([alpha] = 0.86 physician population, 0.83 DPP population). The Comparative Environmental Risk subscale uses the same scale and measures 9 perceived environmental risks, such as driving accidents, air pollution and extreme weather ([alpha] = 0.83 physician population, 0.81 DPP population). Finally, the Optimistic Bias subscale (2 items [alpha] = 0.64 physician population, 0.71 DPP population) reflects an individual's perception for risk for developing diabetes as compared to others of the same gender and age, with a lower score indicating less perceived risk and more optimistic bias. The survey also includes 2 items which assess worry about developing diabetes (Worry Sum) and a Composite Risk Score which includes all 32 items; a higher score indicates higher overall perceived risk.

3.5 CHART REVIEW

In addition to the collection of patient screening data, a chart review was conducted to examine the efficacy of the prevention screening. The computer driven chart review program was developed with Flipside Media and incorporated all aspects of the screening measures. Similar to the prevention screening program, the chart review program was designed to automatically perform calculations such as BMI and determination of diabetes and CVD risk based on the information entered, as well as appropriate follow up for identified risk states. Development of the chart review program took several months, with ongoing internal testing of individual questions and calculations conducted throughout the process. The completed chart review system was subsequently tested using "dummy" charts which were reviewed by the principal

investigator and program coordinator for this project to determine reliability and accuracy. Correct responses were corroborated for training for the chart reviewers.

Chart reviews were conducted by trained staff members that were independent of the research component of the project. All of the chart reviewers were healthcare professionals (2 registered nurses and 1 health educator) with prior experience conducting chart reviews. The chart reviewer training was conducted by the program coordinator again using "dummy" charts; comparisons were made between the previously determined correct responses and the chart reviewers' responses. All discrepancies were addressed and corrected. Ongoing quality assurance was completed by the chart reviewers; 5% of the charts were randomly assigned to be repeated for review by a different chart reviewer and were completed on an on-going basis throughout the project to determine and resolve any potential problems.

A 'pre' screening (primary) chart review which covered the 13 months immediately prior to the 13-week screening period was conducted for those who had the prevention invitation letters sent. Similarly a 'post' invitation (secondary) chart review was conducted for the 13 month period forward from the date of the invitation letter. A comparison group consisting of those with birthdates in another quarter of the year and not invited for screening was similarly examined by chart review. All data collected was de-identified by the chart reviewers and uploaded to the STEP UP Coordinating Center.

4.0 PAPER 1: A COMPREHENSIVE PREVENTION SCREENING PROGRAM FOR PRIMARY CARE PRACTICE

For Future Publication

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4.1 ABSTRACT

OBJECTIVE: To evaluate a structured prevention screening program incorporating national guidelines for type 2 diabetes (T2D) and cardiovascular disease (CVD) risk identification and management in primary care practice. **METHODS**: The program was implemented in 4 primary care practices in Western Pennsylvania; screening invitations were sent to patients aged 25-74 whose birthdates feel within a selected quarter of the year. Chart review was conducted for two 13-month periods preceding and following the screening invitation for those invited for screening (n=3,610). A comparison group consisting of those with birthdates in another quarter of the year and therefore not invited for screening was similarly examined (n=3,506). Measures assessed included the prevalence of elevated LDL cholesterol, fasting blood glucose, blood pressure and BMI. **RESULTS**: Of the 1,963 eligible patients, 350 (17.8%) attended screening, 776 (39.5%) were unable to be reached and 837 (42.6%) refused. A total of 224 patients (64%) had at least one risk factor meriting further medical evaluation; after chart review, 142 patients (41% of those screened) were confirmed to have a potentially new risk state found at screening. The target group demonstrated a significantly greater increase from the pre to the post-screening review in prevalence of diagnosed hyperlipidemia (4.1% vs. 2.1%, $p<0.001$), pre-diabetes (1.7% vs. 0.7%, $p<0,007$) and obesity (3.8% vs. 1.4%, $p<0.001$) than the comparison group. **CONCLUSION:** Although response to the screening invitation was modest, these results support the importance of prevention screening in identifying those at risk.

4.2 INTRODUCTION

Often referred to as a "touch of sugar" and frequently perceived by the general population as nothing more than a nuisance requiring a pill, type 2 diabetes has continued to hide behind a wall of ignorance and denial, with the truth often revealed only after an individual is diagnosed with the disease. Currently over 20 million people or about 7% of the US population are estimated to have diabetes, with one-third unaware (1). With rates increasing steadily around the world (2), diabetes is clearly one of the most important public health concerns of our time.

A major complication of diabetes, cardiovascular disease (CVD) is the leading cause of death for those with diabetes in the U.S. Individuals with diabetes are 2-4 times more likely to have heart disease or suffer a stroke than those without diabetes (3). CVD is the most costly complication of diabetes, accounting for more than $17 billion of the $91.8 billion in annual direct medical costs for diabetes in 2002 in the U.S. (4).

CVD risk factors are often present in the interim stages prior to diagnosis with T2D and predict its development (5-14). The clustering of these conditions of risk including insulin resistance, dyslipidemia, obesity and hypertension has been referred to as syndrome X, insulin resistance syndrome and more recently the metabolic syndrome. While definitions of and criteria for inclusion in this disorder have varied (15-20) and even its very existence as a syndrome has been debated (21; 22), research has supported the conclusion that the grouping of these risk factors generally places an individual at increased risk for both type 2 diabetes and CVD (23-28). It seems appropriate therefore, that prevention be directed toward both type 2 diabetes and CVD, a position consistent with the recent American Diabetes Association cardiometabolic initiative and joint statements form both the U.S. and European diabetes and cardiology associations (21).

Current estimates from the Center for Disease Control indicate that over 54 million people in the US have pre-diabetes (1). In addition, using NCEP ATP III diagnostic criteria, the estimated unadjusted prevalence of the metabolic syndrome in the U.S. was approximately 23% based on NHANES data from 1988-1994 (29), while data from NHANES 1999-2000 showed a significant increase in prevalence to 26.7% (30). The current target group for joint diabetes/CVD prevention thus likely exceeds a quarter of the adult population.

Fortunately proven strategies exist for the prevention or delay of type 2 diabetes and for the reduction of CVD risk (31-35) in those at risk for diabetes by virtue of impaired glucose tolerance. While most physicians practice some form of prevention screening, many are falling short of recommended prevention guidelines (36-38). When prevention screening does occur it may often be combined with a "sick" visit where other acute medical conditions require attention or the patient may be ill thus rendering risk assessment and counseling difficult. Other reasons for lack of routine prevention assessment may be attributable to multiple and confusing prevention guidelines (39), physician and patient time constraints, patient ignorance concerning screening requirements, cost of testing and both physician and patient attitude and personal characteristics (40).

For these reasons, a systematic birthday-based prevention screening program incorporating national guidelines designed for type 2 diabetes and CVD risk assessment for patients in a primary care practice setting was developed and evaluated. The screening program was devised to address some of the above barriers to prevention screening and risk identification, specifically a lack of organized prevention screening for risk identification, as well as simplification of prevention guidelines for easier implementation, provision of patient education information regarding individual risk and alleviating time constraints.

4.3 METHODS

Initially, a concise, "user-friendly" document summarizing current guidelines was compiled based on the recommendations for prevention screening regarding diabetes, hypertension, dyslipidemia, and obesity (41-45). In addition, a computer driven screening program was developed to facilitate the collection of screening information and to provide immediate feedback regarding risk and necessary follow-up.

4.3.1 Practice and Preventionist Identification

Four primary care practices, two urban and two rural, were identified in the Western Pennsylvania area. Each practice was asked to identify a "preventionist" to oversee the prevention screening program, including screening, recruitment and delivery of a lifestyle change intervention program. The preventionists were required to have a healthcare background; four were nurses and two were health educators (in one practice the position was split and in one practice the preventionist was replaced when she left the position). In two practices, the preventionists were identified from within the practice; in the other two practices the preventionists were brought in specifically for the position. The preventionists completed clinical measurement certification through the Diabetes Prevention Support Center (DPSC) for the measures that were collected including blood pressure, height, weight, and waist circumference, as well as training regarding prevention screening and use of the computer program.

4.3.2 Computer Driven Screening Program

In collaboration with Flipside Media, Inc. a lap top driven questionnaire and data collection system was developed to track, screen and report on targeted patients within the practices. The system included a study recruitment tool, integrated with the office's existing patient database, which facilitated sending invitation letters to eligible patients and tracking their progress. The system also generated a patient-specific report. The data were synchronized weekly with a central server, through which progress reports (indicating who needed to be contacted) were generated and emailed to the researchers weekly. The system is based on Flipside's "ScoreMD" screening and data collection platform which is built upon a Unix-based operating system, Apache web server, MySQL database, the PHP scripting language, PDF-based reporting, secure web services for data transfer, and is usable through standard web browsers (like Internet Explorer, Firefox/Mozilla, Safari, and Opera).

4.3.3 Eligibility and Recruitment

Initially, each practice was assisted in preparing a data set which included all practice patients age 25-74 in 2005 that had been seen by a practice physician within the past three years. All patients were assigned a random 8-digit ID number with the link to the patient's identifying information kept in a secure location on site. Within each practice, all patients with birthdates within one quarter of the year (a consecutive 13-week period of time) were identified as eligible for a prevention screening invitation and were sent computer generated invitation letters near their specific birthday. The invitations, which encouraged the recipient to call the preventionist to set up an appointment, were sent out weekly by the preventionists. Up to three subsequent

follow-up telephone calls at different time and days of the week were made if no response was received within one month. This prevention screening and chart review project received approval by the University of Pittsburgh Medical Center Quality Assurance Council.

4.3.4 Screening and Data Collection

Patients attended a brief 30 minute screening visit which was conducted at the primary care practice, completing a short interview concerning medical, social and family history. The preventionist reviewed the chart for pre-existing blood glucose and lipid profiles, blood pressure, height, weight, and waist circumference. This information was subsequently entered into the computer program which determined if and when screening measures needed to be performed according to the guidelines. After completion of the required testing the program also determined the prevention follow up schedule and provided a written summary for the patient, preventionist and physician. The prevention screening was provided at no cost to the patients, however any follow-up lab tests or care that was required as a result of the screening were billed for in the usual manner.

4.3.5 Chart Review

In addition to the collection of patient screening data, a chart review was conducted to examine the efficacy of the prevention screening. Chart reviews were conducted by trained staff members that were independent of the research component of the project. A 'pre' screening (primary) chart review which covered the 13 months immediately prior to the 13-week screening period was conducted for those who had the prevention invitation letters sent. Similarly a 'post'

invitation (secondary) chart review was conducted for the 13 month period forward from the date of the invitation letter. A comparison group consisting of those with birthdates in another quarter of the year and not invited for screening was similarly examined by chart review. All data collected was de-identified by the chart reviewers and uploaded to the STEP UP Coordinating Center.

4.3.6 Outcome Measures

All clinical measures were obtained by a certified preventionist. Blood pressure was measured in a sitting position in the right arm after resting for five minutes. First appearance and last heard (phase V) Korotkoff's sounds were used to define the pressure readings; the measures were repeated twice with a thirty second wait between each reading. An average of the 2nd and 3rd readings was computed. Height and weight were measured twice without shoes with the average computed; BMI was calculated as average weight divided by average height squared (kg/m^2). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest; the measurement was repeated twice and the average computed.

Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and glucose were recorded from the patient chart or when necessary, were completed by the practice or referred lab. Type 2 diabetes and global CVD risk assessment (46) was completed automatically by the program, as well as determination of follow-up scheduling.

4.3.7 Statistical Analysis

The efficacy of the computer-assisted screening program was evaluated by documenting the proportion of individuals responding to screening invitation by age and gender, the reasons for declining the screening invitation and the proportion of cases identified that were contacted after a reminder from the central DPSC, using the chi-square test as appropriate.

The proportion of patients within the selected quarter that were 1) evaluated for diabetes/CVD risk according to national guidelines, 2) newly identified to be at risk and 3) newly identified to be at risk and received appropriate action were also documented from the chart review. For the purposes of this evaluation, appropriate action was defined as the reasonable response that would be expected to occur upon the identification and documentation of a risk factor state, i.e., scheduling a repeat test or follow-up visit, beginning a new treatment or changing treatment type or dose, or referral to a specialist. Situations where the time interval following detection of a new risk factor was not sufficient for action within the chart review period were not counted as lack of action. Patient attendance or compliance with recommendations was not required for the action to be considered appropriate; for example if it was documented that a repeat visit was to occur but the patient did not attend, the clinic action in attempting to schedule the appointment was still considered to be appropriate. The chi-square test was utilized to examine appropriate action for those who attended screening versus those who did not.

In addition, the change in prevalence of diagnosed risk conditions including diabetes, pre-diabetes, hypercholesterolemia, hypertension and obesity between primary and secondary reviews was examined in both the target and comparison groups using the non-parametric McNemar's test for related categorical data. The target and comparison group's change in

prevalence was subsequently compared using the chi-square test. The study sample size was based on the ability to detect with 80% power, a 20% increase in the prevalence of known hyperlipidemia and hypertension between pre and post. One of the rural practices was sold prior to the secondary chart review phase for the target group and thus could not provide complete reviews. The chart review data from this practice was excluded from the analysis of prevalence of diagnosed conditions.

4.4 RESULTS

4.4.1 Recruitment

Three of the primary care practices reported a similar number of registered patients (range 2,150-2,659); however the fourth, urban, center was a larger practice with 5,539 patients. Figure 1 shows the planning and recruitment scheme for this project. A total of 2,786 letters were sent out across all practices; those found to have moved away from the area permanently, to have a different primary care physician outside the practice, or found to be deceased were subsequently excluded (n=823). Of the remaining 1,963 patients, 776 (39.5%) were not able to be reached with three phone calls and 837 (42.6%) refused screening. Among refusals, most common known reasons were illness/medical condition (23.1%), scheduling issues (lack of time or out of area-21.9%), felt screening was not necessary (18.8%) and lack of insurance (11.6%). A significantly higher proportion of males than females refused the screening invitation (69.1% vs.

58.1%, p<0.01). Three hundred and fifty (17.8%) of those invited attended a screening assessment.

Of the 350 individuals that attended a screening visit, 216 (61.7%) self-responded after receiving the invitation. Of the remaining group, 45 individuals (12.9%) required one follow-up telephone call to schedule a visit, 49 (14%) and 40 (11.4%) scheduled a visit on the second and third follow-up calls respectively. A significantly higher proportion of those who attended the screening and self-responded to the invitation were male (69.7% vs. 58.6%, p=0.05). There were no differences noted for age and self-response.

Screening attendance rates varied by clinic with a high of 34.2% and a low of 7.0% (p<0.01). The two rural clinics, both of whom used internally assigned preventionists had significantly higher rates of screening attendance than the urban clinics with externally identified preventionists (27.9% vs. 10.9%, p<0.01).

4.4.2 Screening Results

The median age of those screened was 49 years old; 26.3% were less than age 40, 60% were age 40-64, 13.7% were 65 and older (Figure 2). Seventy-two percent of those screened were women. A total of 68 patients (19.4%) were from minority ethnic groups (African American (17.2%) and other (2.2%)). The two urban practices were significantly more ethnically diverse with 51.2% non-white participants compared to 1.4% non-white participants in the rural practices (p<0.01); these racial proportions reflect the local community structure.

Of the 350 individuals that attended screening, 277 (79.1%) were found to have a body mass index (BMI) $\geq$ 25kg/m^2, of whom 97 (27.7% of those screened) had no reported history of

diabetes and met criteria for the metabolic syndrome (based on National Cholesterol Education Program Adult Treatment Panel III) (42), thus were eligible to participate in a lifestyle change program. A total of 43 patients (45.3%) enrolled in the prevention program, representing a yield of 2.2% from the attempted invitation of 1,963 patients.

4.4.3 Identification of Risk Factors at Screening

Overall, regardless of previous diagnosis, 224 patients (64% of those screened) had at least one risk factor meriting further medical evaluation (405 total risk factor states noted) (Table 1). New potential risk factor states were identified by examining elevated levels and assessing patient report of previous diagnosis at screening; 21 patients (6%) attending screening were found to have elevated blood pressure (SBP $\geq$ 140 and/or DBP $\geq$ 90) without reporting a previous diagnosis, while elevations in glucose at the diabetes and pre-diabetes levels were seen in 9 (2.6%) and 56 (16%) respectively. Elevated total cholesterol ($\geq$ 200mg/dl) was identified in 78 (22.3%) and elevated triglycerides ($\geq$150 mg/dl) in 72 (20.6%) individuals without previously reported dyslipidemia. Thus a total of 236 potentially new risk states were identified at screening. Furthermore, almost one-half (n=66, 44.9%) of 147 patients who reported no previous diagnosis with any of the above conditions had at least one risk factor which warranted further follow-up.

4.4.4 Chart Review for Potential New Risk Factors

Results of the chart review are further shown in Table 1 and revealed that of the 21 individuals with new potential hypertension, 2 (9.5%) had a previous diagnosis of hypertension recorded on

the patient chart (2 did not have a chart review completed). Similarly, of the 56 with glucose in the pre-diabetes range, 3 (5.4%) had a diagnosis noted in the chart (2 had not had a chart review completed), while for the 72 with elevated triglycerides, 7 (9.7%) had this noted previously in the chart. No previous diagnoses of diabetes was noted for 8 of those with glucose levels in the diabetes range; however one did not have a chart review completed. Of the 78 with cholesterol levels greater than or equal to 200mg/dl, 7 (9%) had a diagnosis noted on the chart (6 had no chart review completed). Thus excluding those without chart review, 206 potential cases of new hypertension, diabetes, pre-diabetes or hypercholesterolemia were identified at screening, with only 19 (9.2%) of those conditions being already noted in the chart. This translates to 142 patients (41% of those screened) being identified through screening to have one or more potentially new risk states.

4.4.5 Chart Review

A total of 7,116 chart reviews were completed with 3,765 (2,011 target and 1,754 comparison) completed prior to the screening period (primary review) and 3,351 (1,599 target and 1,752 comparison) completed post-screening (secondary review). The results of the chart review for diagnosis detection are presented in Table 2. Changes in the prevalence of diagnosed conditions in the target group increased significantly from the primary review to the secondary review for hyperlipidemia (20.1% vs. 23.1%, $p<0.01$), for pre-diabetes (2.0% vs. 3.2%, $p=0.005$), for diabetes (10.1% vs. 10.8%, $p=0.004$), for obesity (15.5% vs. 16.9%, $p=0.03$), and for hypertension (30.4% vs. 31.5%, $p<0.05$). Similar results were found for each condition within the comparison group, with the exception of pre-diabetes which showed only a marginal increase in diagnosis (3.7% vs. 4.3%, $p=0.06$). Rates of diagnosis detection from the primary to

the secondary review were compared between the target and comparison groups. The target group demonstrated a significantly greater increase from the primary to the secondary review in prevalence of diagnosed hyperlipidemia (4.1% vs. 2.1%, $p<0.001$), pre-diabetes (1.7% vs. 0.7%, $p=0.007$) and obesity (3.8% vs. 1.4%, $p<0.001$) than the comparison group; a greater increase in prevalence of both diagnosed hypertension and diabetes was also noted but was not significant.

Overall appropriate follow-up action was examined for each risk factor identified in all charts included in the chart review with primary and secondary reviews (Table 3). A risk factor was counted if it was recorded at least once during the chart review period; patients were assumed to be fasting when not specifically noted in the chart as non-fasting. Including the target and comparison groups for both primary and secondary review, a total of 189 charts were noted to have glucose levels above 125 mg/dl and 682 within the pre-diabetes range of 100mg/dl-125mg/dl (those with previous diagnosis of diabetes were excluded for both groups); appropriate follow-up action was noted for 95 (50.3%) and 151 (22.1%) charts respectively. A total of 1,823 charts were noted to have an elevated blood pressure recorded ($\geq$140 and/or $\geq$ 90 mmHG); appropriate action was noted for 620 (34%), while 728 were noted to have elevated LDL cholesterol (based on risk), with appropriate action noted for 330 (45.3%). Elevated triglycerides were noted on 901 charts with appropriate action noted for 479 (53%). Obesity (BMI >30kg/$m^{2)}$ was also examined; 1,816 charts were noted to have obesity with appropriate follow-up noted for 541(29.9%). Overall appropriate action for abnormal risk factors noted in the chart was 36%.

The same risk factors and appropriate action were examined for charts of individuals who attended screening and had a post-screening (secondary) review completed (n=185 individuals) as well as for those with a secondary chart review who were not screened (n=3,065). These

results are shown in Table 4. A significant difference was noted between those who completed the screening versus those who did not for appropriate action for pre-diabetes (39% vs. 15.1%, $p<0.01$) and obesity (41% vs. 30.9%, $p=0.03$); no significant differences were noted for appropriate action for diabetes, hypertension, elevated LDL or triglycerides. Overall results for appropriate action were higher in the screened versus non-screened group (41% vs. 36%); however, this difference was not significant.

4.5 DISCUSSION

The results of this evaluation demonstrate that prevention screening for risk identification for type 2 diabetes and cardiovascular disease is feasible in a primary care practice setting and can be successful in identifying many at risk so that appropriate action and follow up may occur. It is interesting to note that over 60% of the individuals that attended a screening visit responded to the invitation letter and scheduled a visit without further recruitment contact. This suggests that letter mailing may be a reasonable method to contact patients for prevention screening as well as being time-saving and fairly inexpensive. Although no formal cost-effectiveness evaluation was performed, based on feedback from the preventionists, the authors estimate that on average approximately 5 minutes per individual was spent during the recruitment process. For this project this would translate to about to about 164 hours of time per clinic or about 32% of a full-time employee's annual hours. Much of the time initially was spent in the identification of patients that were actually eligible to be contacted, i.e., alive, still living in the area and listing that primary care physician as their provider. Once a practice has developed and subsequently maintains a database, future time spent on contacting patients would be minimized.

As noted, recruitment rates varied significantly across the clinics (34.2% versus 7%) , with the two rural clinics who used internally assigned preventionists demonstrating significantly higher recruitment rates than the two urban clinics with preventionists brought in specifically for the position. These results suggest that recruitment for screening may be higher when done by someone the patients already are familiar with and trust, i.e. the internally assigned preventionist. However, other reasons for this discrepancy could certainly exist, for example, both of the externally assigned preventionist clinics were in an urban area with a significantly higher non-white population attending screening. Because these proportions reflect the racial makeup of the communities it is conceivable that certain racial barriers related to screening may exist. There may also be some inherent differences between urban and rural responses to health care. It will be important to further evaluate these issues in order to develop appropriate recruitment methods for different settings.

Several key themes emerged from the data concerning refusal of prevention screening: medical illness/health condition, lack of time/out of the area, felt screening was not necessary and lack of insurance were the top rated known reasons for refusal. Medical problems (47) and lack of time/inconvenience are reasons that are often cited for non-participation (48; 49). Further investigation revealed that of those who felt that prevention screening was not necessary, over half (57%) were missing at least one risk assessment measure including weight, glucose, blood pressure or LDL measure within the 13 month primary review period prior to screening. It is interesting to note that lack of insurance was a common reason for refusal even though there was no charge for the screening visit. There were also a fair number of individuals that cited "other" unknown reasons for non-participation. Research has suggested that those who do not participate in health-related research may be at higher risk than those who do (50). Similarly

individuals who do not take part in preventive practices may also be at higher risk; thus it is important to further evaluate reasons for refusal in order to reach out to patients that may not initiate a "healthy" visit with their physician.

Of the 350 individuals that attended a screening assessment visit, 224 (64%) had at least one risk factor warranting further medical follow-up (405 elevated risk factors), with 206 risk factors subsequently determined to not have been previously diagnosed through patient self-report at screening and chart review. This translates to 142 patients (41% of those screened) with potentially new risk states. Thus the importance of screening is once again substantiated, and may be a consideration when planning for financial support for a prevention screening program as all of the risk factors identified are potentially billable in the future as follow up services provided by the practices. The authors estimate based on preventionist feedback that each screening visit took about 30 minutes to complete; when considering a preventionist salary of approximately $50,000, each visit cost approximately $12 in staff time (excluding fringe). It is anticipated that the screening program and process could be streamlined in the future to permit the patient to complete a large portion of the information prior to or at the visit, which would allow for a significant reduction in staff time. It is also conceivable that using a program such as this could actually save cost by decreasing physician time spent in reviewing old results, determining risk manually and evaluating the prevention schedule as all of these components would be completed prior to the actual encounter with the patient.

While more than half of those screened were identified as having at least one elevated risk state warranting further follow-up, it is somewhat disturbing to note that overall, for the entire group with chart reviews completed, only 36% of elevated risk factors noted in the charts received appropriate follow-up. The screened group exhibited slightly better follow-up with

41% of elevated risk factors receiving appropriate action in the chart review conducted post-screening. Appropriate action for pre-diabetes and obesity was significantly higher in the screened group when compared to the non-screened group. Overall , elevated LDL-C, glucose in the diabetes range (>125mg/dl), and triglycerides seemed to receive appropriate action most often, while blood pressure received appropriate action in one-third or less of both the screened and non-screened groups. While the lack of appropriate follow up for blood pressure is surprising, it is possible that the focus on diabetes prevention for this project influenced the significant increase in appropriate action for pre-diabetes and obesity. When performing the chart review, along with other actions considered appropriate, a follow-up visit scheduled for a patient was counted even if the patient did not actually attend. Because patient non-compliance with return visits is a well-known problem, the actual number receiving appropriate follow-up action may thus be even lower than these results indicate.

A greater increase in the prevalence of all diagnosed conditions was found from the primary to the secondary review for the target group versus the comparison group, with significantly greater increases noted in prevalence of diagnosed hyperlipidemia, pre-diabetes, and obesity. These results mirror those found concerning appropriate action above and again support the effectiveness of prevention screening.

Although widely recognized as being essential for prevention of many chronic diseases, organized screening programs for risk factors leading to these conditions are lacking; little progress has been made toward making prevention part of our health care system (51). While other stimuli for preventive services have been examined such as patient satisfaction as a mechanism to prompt physicians to refer for prevention (52) it is generally agreed that in order for preventive service use to increase, prevention must become an integral part of the health care

system (40). The results of this project validate the need for prevention screening and describe a means for implementation in a health care system. A computer driven prevention screening program such as described could certainly be integrated into the usual routine of a primary care practice. The program has several advantages: 1) reminder invitation letters may be set up to be sent out on a regular schedule automatically with little time and effort on the part of the primary care staff; 2) the program provides a print-out of the screening information for the patient and physician thus providing an excellent opportunity for patient education about risk, 3) the results, risk assessment and time schedule for prevention measures are completed and available to the physician at the time of visit, thus potentially facilitating better time management for the physician and 4) ongoing screening would be provided on a regular basis with built-in follow-up guidelines, thus making the entire process somewhat less daunting but more effective for practices.

There are some limitations to this project including 1) a smaller than desired sample size responding to and attending screening, thus possibly limiting the observed results and 2) a lack of a formal cost analysis which would be very beneficial in further understanding financial implementation of prevention screening in the health care system.

There will certainly be challenges to implementing a program such as this including a general lack of the existence of patient databases within primary care practices, thus necessitating that this step be completed first, as well as getting physicians and staff "on-board" with the idea of prevention screening. Ensuring that follow-up action after risk states are identified is completed is another challenge, although this seems to be better when risk factors are discovered as part of a structured program as shown here.

Future areas of study should include examination of potential barriers to recruitment for preventive services, including racial, cultural and financial concerns, research to continue to follow post-screening action taken for risk states that are identified and comprehensive cost analysis to help clinicians determine how best to make prevention work in their setting.

While prevention has become the "buzz" word of this century, very few concrete measures have been taken toward one of the most key components of prevention: identification of those at risk. The information provided here offers an overview of the importance of prevention screening as well as present a roadmap for prevention screening implementation which is rooted in the health care system.

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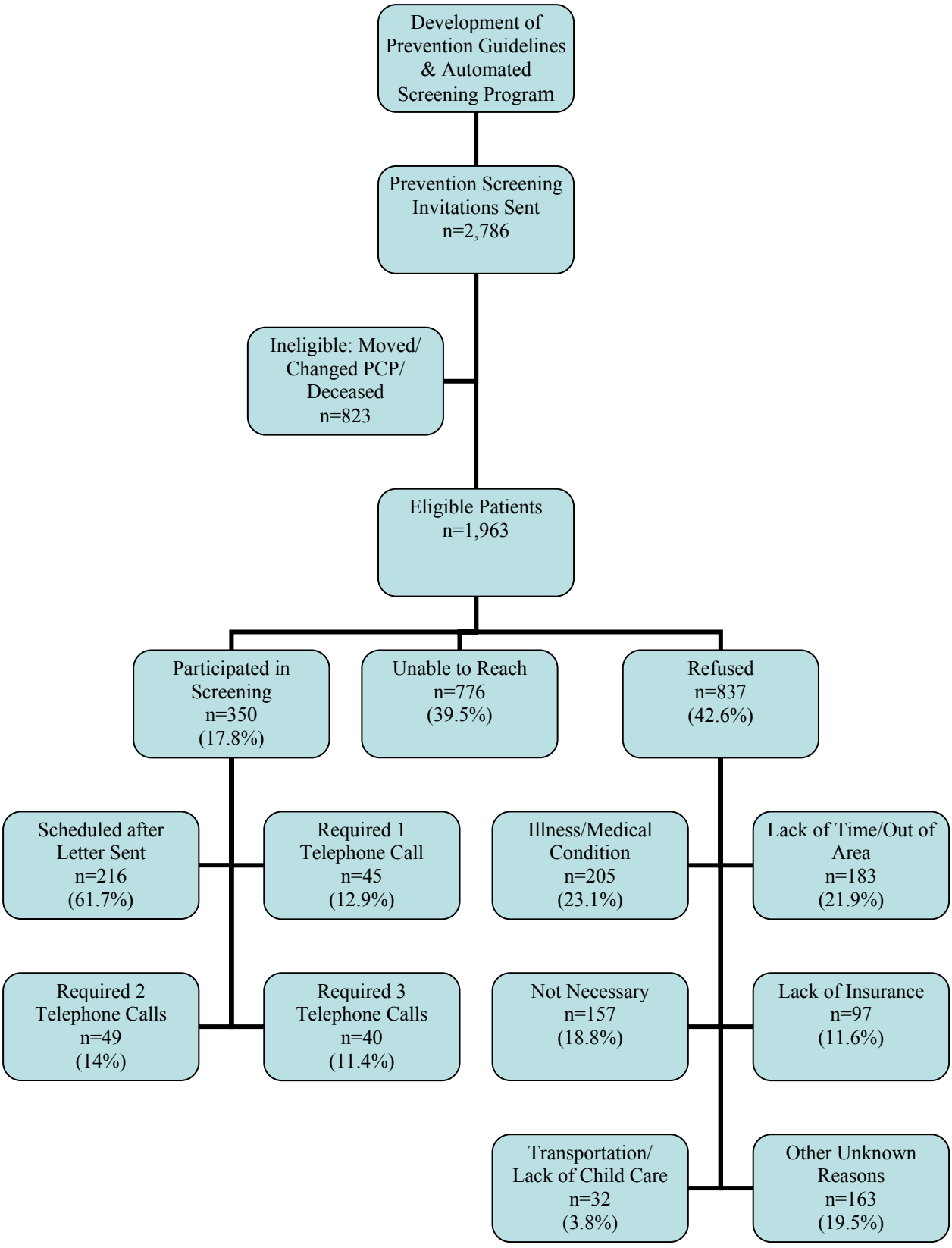

Figure 4-1 Screening Program Development and Recruitment

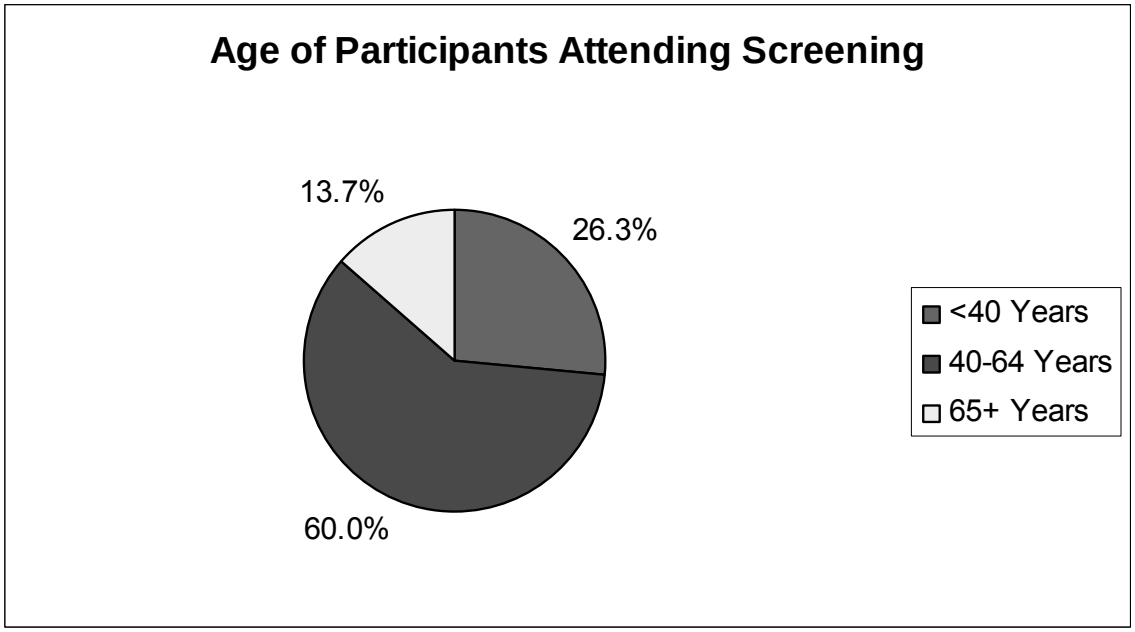

Figure 4-2 Age of Participants Attending Screening

Table 4-1 Potential New Risk Factors Identified at Screening

n=350

	Elevated Risk Factors Identified at Screening **n=224 patients (64% of those screened)**	**Potential New Risk States at Screening** (Excluding those w/previously reported diagnosis)	**Potential New Risk States Based on Chart Review** (Excluding those w/previous diagnosis on chart review) **n=142 patients (41% of those screened)**	
TC ≥ 200mg/dl	139	78	5	7 w/previous diagnosis 6 w/o chart review
Trig ≥ 150mg/dl	114	72	5	7 w/previous diagnosis
SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg	66	21	7	2 w/previous diagnosis 2 w/o chart review
FBG ≥ 126 mg/dl	23	9	8	1 w/o chart review
FBG ≥ 100 mg/dl & ≤ 126 mg/dl	63*	56	1	3 w/previous diagnosis 2 w/o chart review
Total Risk Factors	405	236	206	

* Those with previously reported diabetes excluded

Table 4-2 Prevalence of Diagnosed Conditions between Primary and Secondary Review

	Hyperlipidemia		**Hypertension**		**Diabetes**		**Pre-diabetes**		**Obesity**	
	Primary Review	Second Review	Primary Review	Second Review	Primary Review	Second Review	Primary Review	Second Review	Primary Review	Second Review
Target n=1,600	321 (20.1%)	370 (23.1%) p<0.01	487 (30.4%)	504 (31.5%) p=0.05	162 (10.1%)	179 (10.8%) p=0.004	33 (2.0%)	51 (3.2%) p=0.005	248 (15.5%)	271 (16.9%) p=0.03
Comparison n=1,650	345 (20.9%)	377 (22.8%) p<0.01	491 (30.0%)	524 (31.8%) p<0.01	162 (9.8%)	173 (10.5%) p=0.007	61 (3.7%)	71 (4.3%) p=0.06	271 (16.4%)	289 (17.5%) p<0.01

Table 4-3 Elevated Risk Factors and Appropriate Action for Whole Group

	Whole Group Primary and Secondary Chart Review (n=7,116)	
	Elevated Result	Appropriate Action
Glucose > 125mg/dl	189	95 (50.3%)
Glucose 100-125 mg/dl	682	151 (22.2%)
BP >=140 or 90 mm/Hg	1,823	620 (34.0%)
LDL (based on risk)	728	330 (45.3%)
Triglycerides >= 150 mg/dl	901	479 (53.2%)
Obesity BMI >30 kg/m^2	1,816	541 (29.8%)
Total	6,139	2,216 (36.1%)

Table 4-4 Secondary Chart Review for Screened vs. Non-Screened

	Screened Group Secondary Chart Review (n=185)		**Non-Screened Group Secondary Chart Review (n=3,065)**	
	Elevated Result	Appropriate Action	Elevated Result	Appropriate Action
Glucose > 125mg/dl	11	6 (55.5%)	67	30 (44.8%)
Glucose 100-125 mg/dl	41	16 (39.0%)	245	37 (15.1%)*
BP >=140 or 90 mm/Hg	73	20 (27.4%)	636	214 (33.6%)
LDL (based on risk)	49	23 (46.9%)	247	117 (47.3%)
Triglycerides >= 150 mg/dl	46	24 (52.2%)	300	179 (59.7%)
Obesity BMI >=30 kg/m^2	117	48 (41.0%)	625	193 (30.9%)**
	337	137 (41%)	2,120	770 (36%)

*p<0.01 **p=0.03

5.0 PAPER 2: DPP AND THE REAL WORLD: TRANSLATING THE DIABETES PREVENTION PROGRAM LIFESTYLE INTERVENTION TO PRIMARY CARE PRACTICE

For Future Publication

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5.1 ABSTRACT

Objective: To assess the effectiveness and feasibility of a modified version of a proven lifestyle intervention program delivered in a primary care practice setting. **Research Design and Methods:** Four primary care practices were invited to participate in a lifestyle intervention effort; 51 participants (42 female) without prior history of diabetes with a body mass index (BMI) $\geq$25kg/m2 and metabolic syndrome (NCEP ATPIII definition) were enrolled in the 12-session Group Lifestyle Balance (GLB) program which was adapted from the intensive lifestyle intervention utilized in the Diabetes Prevention Program. The GLB program closely followed the DPP protocol with minor adaptations; weight loss and physical activity goals remained at 7% and 150 min/week respectively. Anthropometric measures were collected before and after the intervention. **Results:** Using last observation carried forward methodology for participants who did not complete the intervention, average weight loss, comparing the pre and post-intervention assessments, was 4.6 lbs. (2.2% relative loss, $p<0.001$). An average 0.5 pound weight loss per week was estimated ($p<0.001$) after adjusting for starting weight and clinic. Waist circumference, BMI and fasting blood glucose decreased an average of 0.69 in. (1.6%, $p=0.003$), 0.82 kg/m^2 (2.3%, $p<0.001$) and 4.63mg/dl (3.7%, $p=0.02$) respectively. A positive correlation was noted between total activity minutes and total pounds lost (Spearman's $r=0.36$, $p=0.01$). **Conclusion:** The results of this translational research suggest that the GLB program was successful in reducing some parameters of risk for diabetes and cardiovascular disease in this group of individuals with metabolic syndrome. The DPP lifestyle intervention can be adapted for use in the "real-world" and is feasible to conduct in a primary care practice setting.

5.2 INTRODUCTION

In 2001, the Diabetes Prevention Program (DPP) ended prematurely due to significant results indicating that the intensive lifestyle intervention utilized in the program was highly successful in reducing risk for type 2 diabetes in all groups regardless of ethnicity, age or gender (1). Other studies have also demonstrated the efficacy of lifestyle intervention and reduction in risk for type 2 diabetes (2-5). In addition, the DPP lifestyle intervention was found to be effective in reducing risk factors for cardiovascular disease (CVD) (6) and components of the metabolic syndrome (7). While it is apparent that type 2 diabetes and CVD risk can be lowered with lifestyle intervention, the translation of these intervention programs in a real-world setting presents a number of challenges.

Some of these challenges include lack of trained personnel, patient recruitment and retention, coordination of care, and availability of quality programs (8). Primary care practices provide an ideal venue for institutional delivery and reinforcement of prevention intervention, long-term, for several reasons. They employ individuals who have the knowledge and background to be trained to deliver a lifestyle intervention. Patients are familiar with their primary care practice staff, routine, and location, which could facilitate participation and retention. Finally, since one of the most important aspects of prevention intervention is continued monitoring regarding lifestyle change, primary care practices are well placed to provide ongoing follow-up care. For these reasons, translation of a modified DPP Group Lifestyle Balance (GLB) intervention for patients with the metabolic syndrome was assessed for effectiveness and feasibility in a variety of moderately low income and ethnically diverse primary care settings.

5.3 RESEARCH DESIGN AND METHODS

This prospective study used a one-group design to deliver intervention, incorporating pre and post intervention testing of subjects in four diverse primary care practices in the Western Pennsylvania area (two urban and two rural practices). The two rural practices were approximately 1-2 hours from Pittsburgh, while the urban practices were within close proximity to the city. Each of the participating practices was asked to identify a "preventionist" to be responsible for implementation of the GLB program. The identified preventionists included nurses, a health educator and an exercise physiologist. One practice shared the responsibilities between two nurses. Preventionists were required to attend a two-day training workshop which addressed all aspects of the intervention and was conducted by faculty at the study STEP UP Coordinating Center. Additionally, preventionists took part in a pilot GLB intervention themselves where they completed all of the components of the program as well as clinical outcomes measurement certification through the Coordinating Center.

5.3.1 Participant Inclusion and Exclusion Criteria

Inclusion criteria consisted of males and females without previously reported diagnosis of diabetes, age 25-74 years in 2005 with body mass index (BMI) $\geq$ 25kg/m^2 and at least three of five components of the metabolic syndrome (based on National Cholesterol Education Program Adult Treatment Panel III) (9) identified at screening. At the time of study, the NCEP had not yet changed its glucose criterion, although the American Diabetes Association had lowered its criterion for pre-diabetes from a fasting glucose of 110 mg/dl to 100 mg/dl (10). Therefore patients who met the above criteria with only 2 components of the metabolic syndrome with a

fasting glucose between 100 mg/dl and 109 mg/dl were also included at their primary care physician's discretion. Exclusion criteria included previously reported diabetes, pregnancy, lack of physician approval and inability to sign informed consent.

5.3.2 Recruitment and Study Population

In order to facilitate screening for diabetes and CVD risk, a computer driven screening program was developed which provided immediate feedback regarding the patient's risk and determined eligibility for the GLB program. Invitations for prevention screening were sent to all practice patients age 25-74 with birthdays within a specific quarter of the year. The screening assessment included collection of medical and family history, fasting lipid and glucose and clinical measures consisting of blood pressure, height, weight, and waist circumference. A total of 350 patients attended the screenings, with 97 (27.7%) found to meet eligibility criteria for the intervention.

Eligible patients were invited to take part in the study which included attendance at the 12-session GLB program, as well as pre and post intervention assessments. Of the 97 eligible individuals, 54 declined participation, yielding a study population of 43. Specific reasons for non-participation are not available as the screening component was not part of the research evaluation. An additional 8 participants who met the eligibility criteria were directly referred by the practice physicians to the program. This research project was approved by the University of Pittsburgh Institutional Review Board and the University of Pittsburgh Medical Center Quality Assurance Council, as well as the Surgeon General's Office of Review. Eligible and interested patients signed informed consent prior to beginning the study.

5.3.3 Procedures and Outcome Measures

Enrolled participants were asked to attend an assessment to obtain clinical measures prior to beginning and again at the conclusion of the intervention. All clinical measures were obtained by a certified preventionist and/or certified STEP UP staff member. Blood pressure was measured in a sitting position in the right arm after resting for five minutes. First appearance and last heard (phase V) Korotkoff's sounds were used to define the pressure readings; the measures were repeated three times with a thirty second wait between each reading (11). An average of the 2nd and 3rd readings was computed. Height and weight were measured twice without shoes with the average computed; BMI was calculated as average weight divided by average height squared (kg/m^2). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest; the measurement was repeated twice and the average computed.

Total cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol (total cholesterol - HDL cholesterol) and glucose were measured after at least a two-hour fast using the Cholestech LDX System by a certified laboratory assistant. Global CVD risk assessment (12) was estimated and medication use was assessed via participant interview. In addition, weight was recorded weekly at each session.

5.3.4 Intervention

The original DPP Individual Intensive Lifestyle Intervention was developed at the University of Pittsburgh by the DPP Lifestyle Resource Core and has been described in detail elsewhere (13). Members of the original DPP lifestyle team collaborated to adapt the individual intervention to a group-based program and to condense the program from 16 individual sessions delivered over 24

weeks to 12 group sessions delivered over 12-14 weeks. Other modifications included concentrating on healthy food choices rather than specifically the food pyramid, a focus on calorie as well as fat intake from the beginning of the intervention and more emphasis on the pedometer. As in the original DPP lifestyle program, the goals of the GLB intervention were to achieve and maintain a 7% weight loss, and to safely and progressively increase physical activity to 150 minutes per week of moderately intense physical activity similar to a brisk walk.

The GLB curriculum was administered by the trained preventionist(s) in each practice at the primary care practice location. Groups were conducted during the daytime as well as in the evening with the participants selecting the time that best fit their schedule. Each participant received a copy of the GLB participant handouts, Fat and Calorie Counter, self-monitoring books for keeping track of food and physical activity, a pedometer with instructions, a set of measuring cups and spoons, and a chart for self-monitoring weekly weights over the course of the program. Participants who did not own a scale were given one. All subjects were asked to self-monitor their daily weight, food intake and physical activity and were given feedback concerning progress.

5.3.5 Sample Size Estimation and Statistical Analysis

Based on the local DPP weight loss experience and using this variance estimate, we estimated that 21 subjects were needed to detect a 7% weight loss (as per the DPP goal) with α=0.05 and 90% power. The DPP achieved a 7% mean weight loss in the intensive lifestyle (ILS) group after 6 months. In translation to a real-world setting, we assumed the new intervention might achieve only half the DPP goal by 3 months, i.e. a 3.5% mean weight loss, requiring 78 subjects.

Analyses were carried out using the SAS statistical package (version 9.1, SAS Institute, Cary North Carolina, USA). The mean change between pre and post intervention measures was analyzed using the Paired Student's *t*-test when change data was normally distributed (weight, waist circumference and BMI); however, for most measures the non-parametric Wilcoxon Matched-Pairs Signed Rank test was used. Mixed models were used to examine weight change over time (repeated measures per participant) adjusting for weight at study entry and clustering of participants within clinical site; individual participant and clinical sites were random effects in this model. Correlations were calculated using Pearson's or Spearman's correlation coefficient r. Primary analyses were conducted on an intention to treat basis; to handle missing data we used last observation carried forward methodology for participants who did not attend the post assessment visit (n=51). Subjects with changes in medication during the course of the intervention for the condition being evaluated were excluded from the analyses (4 were excluded from lipid analysis and 6 were excluded from hypertension analysis); in addition 8 participants whose glucose results were affected by a laboratory error were excluded from glucose analysis. Secondary (per protocol) analyses were also performed for the group (completers) that attended at least 50% of the intervention sessions and the pre and post intervention assessments (n=28).

5.4 RESULTS

The mean age of the participants in this study was 52.9 years; the majority (82%) of participants were female (n=42/51) and approximately 25% of the participants were non-white. Baseline clinical measures for the total group are shown in Table 1. There were no notable differences in baseline measures between gender with the expected exception of a higher HDL cholesterol for

females (43.8 mg/dL v. 31.4 mg/dL, $p<0.05$). Average BMI for the group was greater than 30kg/m^2.

A total of 31 participants (61%) attended 6 or more of the 12 intervention sessions, with 81% of those (25 participants) attending 8 or more sessions. Retention (defined as attending at least half of the sessions) varied between the clinics with a range of 38.5% - 81.8% ($p<0.05$) (Figure 1). Attendance at fifty percent or more of the sessions was associated with achieving 3.5% weight loss ($p=0.002$) and reaching the 150 minutes/ week physical activity goal ($p=0.003$).

Table 2 shows the results of the pre and post intervention measure comparisons for the total group (n=51) and those who completed the intervention and the post assessment visit (n=28). Overall weight loss for the total group was significant with an average weight loss of 4.6 pounds (2.2%, $p<0.001$). Using mixed models, participant weight loss was estimated as an average of 0.5 pound per week ($p<0.001$) after adjusting for starting weight and clinic. A significant decrease from pre to post intervention was also found for waist circumference (-0.69 inches, 1.6%, $p=0.003$), BMI (-0.82 kg/m^2, 2.3%, $p<0.001$) and glucose (-4.63 mg/dl, 3.7%, $p=0.02$). No significant changes were noted for systolic or diastolic blood pressure or total, non-HDL or HDL cholesterol. There is no suggestion of heterogeneity between the clinics for any of the measures with the exception of waist circumference, where one center had an increase in contrast to all other centers.

A sub-analysis of "completers" (those who attended at least 50% of the intervention sessions as well as the pre and post assessments, n=28) was also conducted. Significant results were seen in the same variables as for the total population, although mean weight loss was greater in this group (7.22 pounds, 3.5%, $p<0.001$), and a marginally significant decrease in

diastolic blood pressure (-2.55 mm/Hg, 2.5%, p=0.09) was noted. The change results comparing pre and post intervention measurements were not impacted by age or by gender.

Attainment of the program goals was examined for both the total and "completer" groups (Figure 2). In the total group of 51 participants, four participants reached the weight loss goal of 7% (7.8%), while 11 (21.6%) reached 5% or greater and 17 participants (33.3%) had 3.5% or more weight loss. Of those participants who recorded physical activity minutes (n=21), 12 (57.1%) were successful in reaching the physical activity goal (average of $\geq$ 150 minutes/week) with an overall mean of 242.5 (sd=398.6, range=0-1,914) activity minutes per week observed. For those who recorded both initial and later activity (n=16), a non-significant mean increase of 46.1 (sd=139.6, 28.3%, p=0.11) in activity minutes was noted.

Within the "completers" group, 4 of 28 participants reached the 7% weight loss goal (14.3%), while 10 (35.7%) and 15 (53.6%) achieved weight loss of at least 5% and 3.5% respectively. Of the 18 "completers" who recorded physical activity minutes, 12 (66.7%) met the physical activity goal, with an overall mean of 274.88 (sd=423.0) activity minutes per week. Of those completers who recorded activity level for both initial and later weeks (n=15), a significant increase in mean physical activity minutes of 51.13 (sd=142.99, 31.8%, p=0.04) was noted.

Overall, a positive correlation was observed between total activity minutes and total pounds lost (Spearman's r=0.36, p=0.01). Furthermore, a significant association between attainment of the activity and weight loss goals was noted; 25% of those who attained activity goal (n=12) vs. 2.5% of those who did not (n=39) were successful in reaching the weight loss goal (p=0.03).

5.5 DISCUSSION

The current project is one of the first attempts to take the successful intervention utilized in the DPP, modify it for real-world implementation and evaluate its effectiveness in a primary care setting. The results suggest that the current GLB adaptation of the DPP lifestyle intervention can be successfully delivered by trained healthcare providers in diverse primary care practices, with comparable weight loss to that achieved in DPP itself. As is well known, translation from research to the "real-world" presents a number of challenges, which make the current findings particularly encouraging.

One notable difference between research studies such as the DPP and the real world is the population being examined. Unlike volunteer research, the current program targeted all primary care practice patients found to be at risk, rather than the more selective recruitment of volunteers already willing to participate in a clinical treatment trial. In a recent analysis of the physical activity component of the DPP intervention, investigators found that the level of reported physical inactivity in the DPP cohort was less than that reported in the NHANES III subgroup with impaired glucose tolerance (14) suggesting that the DPP volunteers were probably healthier and more motivated. Thus it is likely that the participants enrolled in this translation project were less likely to be as motivated to be successful in the program both from a recruitment and retention perspective.

Retention of enrollees in an intervention program can be difficult in a research environment, however, may be even more challenging in real-world settings operating with limited funds and devoid of monetary rewards or incentives. In the current study, about 60% of participants attended at least half of the sessions. Interestingly, there was a significant difference between retention rates in two clinics (81.8% vs. 38.5%, $p<0.05$) although there were no

significant differences in age, gender or ethnic distributions in these clinics and both clinics were located in an urban setting. This finding warrants further investigation to determine what factors may contribute to program retention.

Comparisons for retention to similar translational programs are limited; however, one such translational study in a workplace setting exhibited about 95% retention. Participants were encouraged to attend during work hours without loss of pay or personal time and received other small incentives (15). Another lifestyle translation study involving a partnership between a university and a local HMO noted a 92% retention rate; patients were charged an initial commitment fee which was returned in its entirety if the subject met certain attendance requirements (16). These translation attempts suggest that allowing patients to attend sessions during work without loss of pay and offering some incentive and/or reimbursement for attendance may be beneficial in improving retention. Since the current project's evaluation indicated a correlation between attendance and weight loss as well as physical activity, attention to provision of motivational items for attendance should be an important consideration for future translational efforts.

Likewise, levels of interest for primary care staff working in the real world may be dissimilar to those involved in traditional research, with different goals and role expectations. One study examining health care provider attitudes toward the detection and management of those at risk for diabetes found that many have concerns including lack of resources and questionable patient motivation for making lifestyle change (17). It is important to note that the preventionists who were trained to deliver the GLB had no prior experience in behavioral modification, or specialist diabetes interest and had varied backgrounds. One important lesson learned from this project concerns the importance of offering prevention education not only for

the preventionist involved in delivering prevention, but for other staff members and physicians as well. Staff input and "buy-in" appear to be important components in facilitating success with a lifestyle change program in a primary care practice setting.

The GLB was successful in reducing certain risk factors for diabetes and CVD including weight, BMI, waist circumference and glucose. Weight loss data from the DPP is only available for the 6 month follow up visit forward, so we are unable to directly compare weight loss in the DPP at 3 months to the GLB weight loss; however, review of the trend in the DPP at 3 months shows a mean weight loss of 3.5%, similar to that achieved by over half of the "completer" group. As it is expected that the effectiveness of an intervention may be reduced when being translated from research to clinical practice (18), thus these findings are encouraging.

Strengths of this study include a prospective follow-up design in one of the first efforts to translate the DPP lifestyle intervention to a real-world health care setting. In addition, we were able to collect measures of change in risk parameters for subjects in both rural and urban primary care settings. Data were analyzed according to the principle "intention to treat" as well as for those that actually completed the program and follow-up assessment.

Limitations of this study include: 1) a lower number of participants enrolled than originally anticipated, thus not permitting practice specific comparison analyses, 2) the number of men enrolled in the program limited gender comparisons for success in the program, however, that less men than women took part in the program is not an unusual finding, 3) the attrition of participants and subsequent lack of evaluation of those who did not complete the intervention, and 4) the limited period of study (3 months) due to funding considerations

We have successfully adapted the individual lifestyle intervention utilized in the DPP for group implementation in a "real-world" setting while maintaining the fundamental aspects of the

original intervention. The current project is an important step in moving from efficacy to effectiveness in diabetes prevention translation. The results suggest that the GLB program, delivered by trained health professionals, was feasible and effective in reducing some parameters of risk for type 2 diabetes and CVD in this group of individuals with the metabolic syndrome. It will be important to evaluate the GLB program in larger populations and other venues over time. Additional future areas of study should address methods of delivery of GLB versus standard care, as well as in-depth cost analysis. It will also be important for future evaluations to consider longer follow-up.

In the "real-world", patients with risk factors for diabetes and CVD are often told to "lose weight and increase activity". It is hoped that this, and similar programs will enable physicians to write a "prescription" for lifestyle change (and insurers to cover the costs) with the assurance that tangible health benefits will ensue.

Acknowledgements

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Table 5-1 Baseline Characteristics of Study Population

	Female (n=42) Mean (sd)	Male (n=9) Mean (sd)	Overall (n=51) Mean (sd)
Weight (pounds)	212.8 (44.7)	231.0 (24.8)	216.0 (42.3)
Total Cholesterol (mg/dL)	194.5 (31.3)	176.2 (28.7)	191.3 (31.4)
HDL Cholesterol* (mg/dL)	43.8 (11.1)	31.4 (5.7)	41.6 (11.4)
Non-HDLC (mg/dL)	150.7 (32.1)	144.8 (28.2)	149.7 (31.2)
Blood Glucose (mg/dL)	98.4 (18.4)	100.6 (17.6)	98.8 (17.9)
Systolic Blood Pressure (mm Hg)	122.9 (19.1)	130.1 (19.3)	124.2 (19.1)
Diastolic Blood Pressure (mm Hg)	77.8 (12.6)	80.4 (8.3)	78.3 (11.9)
Waist (inches)	42.8 (5.9)	44.8 (3.9)	43.2 (5.6)
Body Mass Index[1]	36.9 (7.9)	35.2 (3.9)	36.6 (7.4)

Data are means (standard deviation)

*$p<0.05$, statistically significant difference between genders

[1]n=50, height missing for 1 participant

Table 5-2 Pre and Post Intervention Comparisons

	Total Group n=51						Completers n=28					
Variable	n	Pre-Mean (sd)	Post-Mean (sd)	Mean Change (sd)	Mean % Change	p-value		Pre-Mean (sd)	Post-Mean (sd)	Mean Change (sd)	Mean % Change	p-value
Weight (pounds)	51	216.0 (42.3)	211.4 (43.0)	-4.60 (7.2)	-2.2%	<0.001	8	213.98 (46.9)	206.76 (47.8)	-7.22 (8.1)	-3.5%	<0.001
Total Cholesterol* (mg/dL)	47	190.57 (31.4)	190.74 (32.4)	0.17 (23.9)	0.8%	0.92	5	194.0 (30.2)	195.52 (33.1)	1.52 (32.0)	1.96%	0.69
HDL* (mg/dL)	47	42.11 (11.5)	42.77 (11.7)	0.66 (7.1)	2.2%	0.32	5	44.56 (13.1)	45.48 (13.2)	0.92 (9.63)	3.45%	0.41
Non-HDL* (mg/dL)	47	148.47 (31.2)	147.98 (32.8)	-0.49 (22.6)	-0.51%	0.84	5	149.44 (29.9)	150.04 (33.7)	0.6 (30.0)	1.8%	0.92
Glucose** (mg/dL)	43	99.09 (15.7)	94.46 (15.5)	-4.63 (16.7)	-3.7%	0.02	1	102.28 (16.1)	95.28 (18.9)	-7.0 (19.4)	-5.9%	0.03
SBP* (mm Hg)	45	122.41 (17.9)	124.23 (19.9)	1.82 (9.31)	1.6%	0.29	2	124.73 (16.2)	126.50 (20.2)	1.77 (12.0)	1.5%	0.71
DBP* (mm Hg)	45	77.59 (11.8)	76.58 (10.9)	-1.00 (5.39)	-0.08%	0.22	2	79.09 (8.3)	76.55 (5.9)	-2.55 (7.0)	-2.5%	0.09
Waist (inches)	51	43.16 (5.58)	42.46 (5.67)	-0.69 (1.61)	-1.6%	0.003	8	42.85 (5.3)	41.63 (5.5)	-1.21 (2.0)	-2.8%	0.003
BMI (kg/m^2)	50	36.55 (7.35)	35.74 (7.45)	-0.82 (1.18)	-2.3%	<0.001	8	36.85 (8.8)	35.62 (9.0)	-1.23 (1.3)	-3.53%	<0.001

*Patients with med changes excluded

**n=43 due to lab error

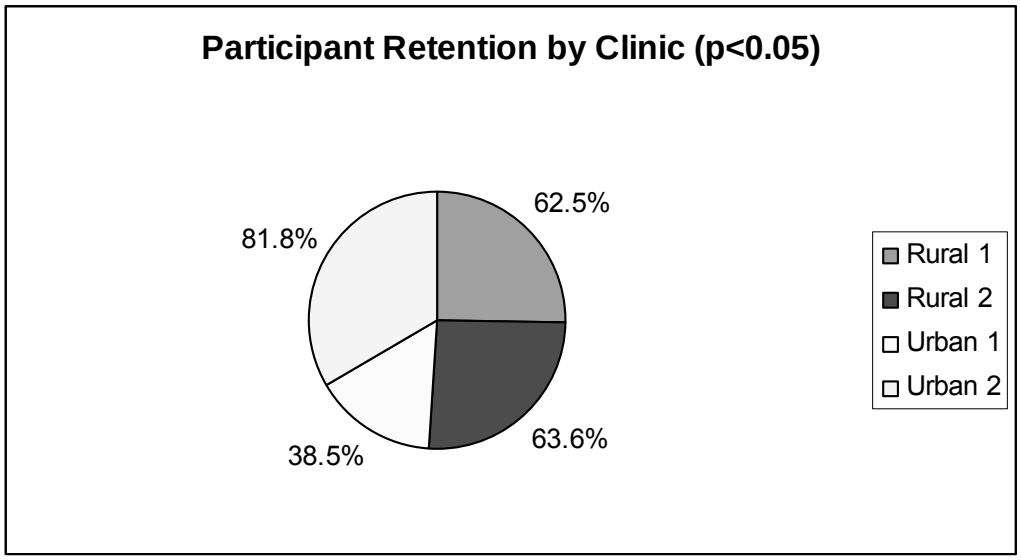

Figure 5-1 Participant Retention by Clinic

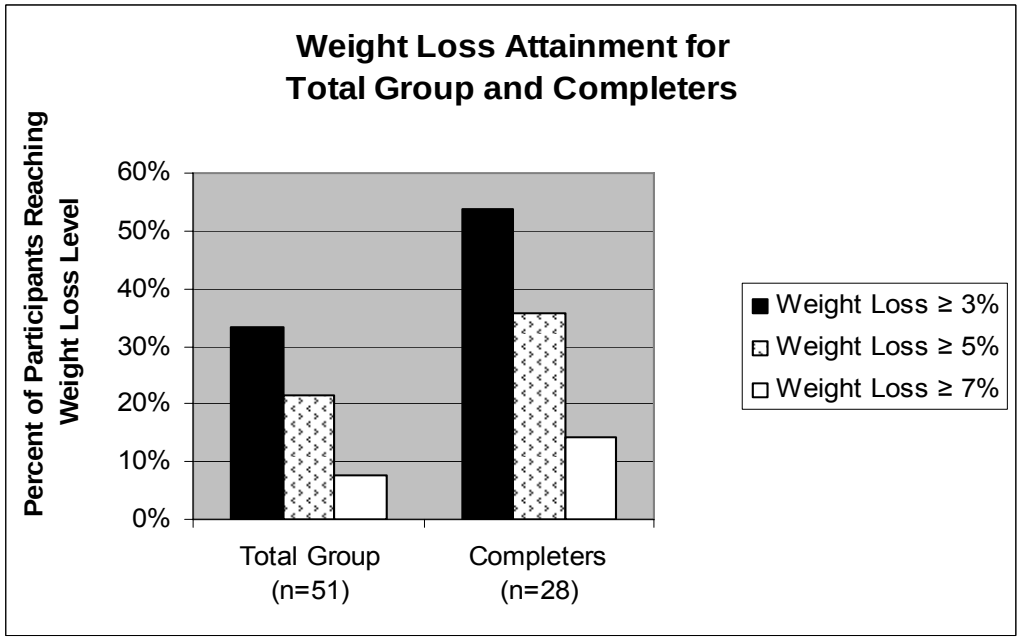

Figure 5-2 Weight Loss Attainment for Total Group and Completers

6.0 PAPER 3: RISK PERCEPTION FOR DIABETES AND PERFORMANCE IN A MODIFIED DPP PROGRAM

For Future Publication

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6.1 ABSTRACT

Objective: Individuals with the metabolic syndrome (MS) are at risk for development of type 2 diabetes and cardiovascular disease. Prospective data relating perception of health risk and achievement of lifestyle changes are lacking. **Methods:** Fifty-one patients with the MS who participated in the Group Lifestyle Balance (GLB) program completed a modified Risk Perception Survey for Developing Diabetes (mRPS-DD). The GLB, adapted from the Diabetes Prevention Program (DPP) included the same intervention goals with minor modifications. Participants had no prior history of diabetes, BMI $\geq$25 and at least 3 components of MS (NCEP ATPIII definition). The mRPS-DD included questions concerning attitude about lifestyle behaviors, health, environmental and individual risk. **Results:** Over one-third (37.3%) of this high risk group perceived their health risk to be almost none/slight. A greater proportion of those who completed the program believed prior to starting that their risk for development of diabetes within the next 10 years was moderate/high (64.3% v. 25%, p=0.05). Risk perception for diabetes development decreased significantly between pre and post assessments (p=0.03); no difference in clinical outcome was observed between those who perceived a decrease in risk and those who did not. **Conclusion:** Over one-third of this high risk group did not correctly perceive their risk. Risk perception for diabetes decreased after participation in the GLB; however, no differences in clinical outcomes were noted between those who perceived a risk reduction and those who did not. Results of this evaluation underscore the importance of incorporating diabetes risk communications into lifestyle change programs.

6.2 INTRODUCTION

Diabetes, specifically type 2 diabetes which accounts for 90-95% of all diabetes cases [1], has become one of the largest public health challenges of our time. In the US, over 12 million people have diabetes and an additional 8 million are undiagnosed [2]. The seriousness of the disease is well-known as it is the sixth leading cause of death in the United States [3]. Diabetes is strongly related to cardiovascular disease [4] and is the leading cause of new blindness and kidney failure in those age 20-74 years old and a major cause of lower limb amputation [2]. Diabetes costs in the US in 2002 exceeded $132 billion and are expected to worsen over time [5]. Even more frightening is the fact that an estimated 54 million Americans have pre-diabetes, thus are at increased risk for developing type 2 diabetes, as well as heart disease and stroke [6].

The metabolic syndrome, a clustering of risk factors including insulin resistance, dyslipidemia, obesity and hypertension has also been associated with increased risk for both type 2 diabetes and cardiovascular disease [7-11]. In 2002, the overall prevalence of the metabolic syndrome in adults in the US over age 20 years was 24%, with a considerable increase with age: the prevalence in 50-year-old subjects was >30%, while over 40% of subjects age 60 years had the metabolic syndrome [12].

Recent results from prevention studies demonstrated that type 2 diabetes can be successfully prevented or delayed through lifestyle intervention [13-15]. Furthermore, the Diabetes Prevention Program (DPP) also demonstrated the efficacy of an intensive lifestyle intervention for diabetes prevention [16], as well as effectiveness in reducing risk for metabolic syndrome [17] and cardiovascular risk factors [18]. With the advent of these important results, understanding the factors that contribute to an individual's performance in programs which

facilitate the lifestyle changes necessary for beneficial health outcomes becomes of primary concern.

One component of many theories of health behavior is that an individual with a high perceived risk of harm would be motivated to take action to reduce his or her risk ([19-21]. While some research supports the relationship between perceived risk and protective action [21-24], studies that prospectively examine risk perception for diabetes development and reduction of risk through lifestyle change are lacking. Several studies, however, have examined cross-sectional data for perceived risk of developing diabetes; Walker et al., collected data on physician's personal risk perception for developing diabetes [25] as well as perception of risk for developing diabetes in participants in the DPP, who were at high risk with impaired glucose tolerance [26]. The first study found that physicians who were at higher risk (based on self-reported risk factor categories) had significantly greater comparative risk perception scores and greater perception of diabetes risk than those with lower risk. Similarly, nearly 80% of the participants in the DPP sub-study examining personal risk for diabetes development ranked diabetes as a moderate/high risk. In another study, the predictive effects of health beliefs on weight loss in subjects at high risk for type 2 diabetes who were participating in a weight loss intervention were examined. No relationship was found between health beliefs and subsequent behavior including attendance, weight loss, dietary intake or fasting glucose [27]. Although this was a prospective study, results were reported for the baseline risk survey responses only and did not address results post-intervention. In addition, single items of belief were measured rather than the use of a survey with composite scores. We are not aware of any other prospective studies examining risk perception for development of diabetes and performance in a lifestyle change program.

Lifestyle change has been shown to be effective in reducing risk for development of type 2 diabetes; however, prospective data concerning risk perception and performance in a lifestyle change program are lacking. Thus, the current project investigated prospectively patient perception of risk for developing diabetes and performance outcomes in Group Lifestyle Balance (GLB) program, a lifestyle change program adapted from the Diabetes Prevention Program's highly successful intensive individual lifestyle intervention. Specifically, baseline mRPS-DD responses were examined, as well as the correlation with clinical outcomes and measures of success in the program. In addition, changes in response after completion of the program were assessed.

6.3 RESEARCH DESIGN AND METHODS

6.3.1 Subjects

The study participants were identified through screenings held in four primary care practices in the Western Pennsylvania area; two were urban practices and two were rural. The Diabetes Prevention Support Center of the University of Pittsburgh (DPSC), was responsible for oversight of the program in these four primary care practices. Participants aged 25-74 years with BMI $\geq$ 25 kg/m^2 and no previous history of diagnosed diabetes were eligible for the GLB program if they had at least three of the components of the metabolic syndrome as per the NCEP ATP III guidelines [28]. A total of 51 participants were enrolled in the program. Exclusion criteria included: self-report of previously diagnosed diabetes, pregnancy, lack of physician approval and inability to sign informed consent.

6.3.2 Intervention

The original DPP Individual Intensive Lifestyle Intervention was developed at the University of Pittsburgh by the DPP Lifestyle Resource Core and has been described in detail elsewhere [29]. Members of the original DPP lifestyle team collaborated to adapt the individual intervention to a group-based program and to condense the program from 16 individual sessions delivered over 24 weeks to 12 group sessions delivered over 12-14 weeks. Other modifications included concentrating on healthy food choices rather than specifically the food pyramid, a focus on calorie as well as fat intake from the beginning of the intervention and more emphasis on the pedometer. As in the original DPP lifestyle program, the goals of the GLB intervention were to achieve and maintain a 7% weight loss, and to safely and progressively increase physical activity to 150 minutes per week of moderately intense physical activity similar to a brisk walk.

6.3.3 Procedures and Outcomes Measures

This prospective study used a one-group design incorporating pre and post intervention testing of subjects. Enrolled participants were asked to attend an assessment to obtain clinical measures prior to beginning and again at the conclusion of the intervention. All clinical measures were obtained by a certified preventionist and/or certified DPSC staff member. Blood pressure was measured in a sitting position in the right arm after resting for five minutes. First appearance and last heard (phase V) Korotkoff's sounds were used to define the pressure readings; the measures were repeated three times with a thirty second wait between each reading [30]. An average of the 2nd and 3rd readings was computed. Height and weight were measured twice without shoes with the average computed; BMI was calculated as average weight divided by average height

squared (kg/m^2). Waist circumference was measured at the midpoint between the lower rib margin and the iliac crest; the measurement was repeated twice and the average computed.

Total cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol and glucose were measured after at least a two-hour fast using the Cholestech LDX System by a certified laboratory assistant. Global CVD risk assessment [31] was estimated and medication use was assessed via participant interview. In addition, weight and physical activity minutes were recorded weekly at each session.

6.3.4 Modified Risk Perception Survey for Developing Diabetes

The Risk Perception Survey for Developing Diabetes (RPS-DD) developed by Walker, et al., is designed for assessment of multiple dimensions of perceived risk for developing diabetes [32]. During the initial survey development, all items of the survey were reviewed for content and face validity by a panel of clinical diabetes experts, risk perception experts, and health psychologists. A pilot study was conducted with 74 nondiabetic, overweight, middle-aged community individuals, after which the survey was revised slightly to enhance validity, reliability and ease of use. The original RPS-DD included 53 items and four subscales as well as other individual items to assess various aspects of risk perception. Internal consistency reliability for the four subscales was found to be acceptable using Cronbach α coefficients.

The survey was modified by the authors for this study; specifically it was shortened to include only the 32 items pertaining to the subscales, as well as the 3 items regarding lifestyle behavior. In addition, 5 questions pertaining to risk for diabetes development in relation to lifestyle changes were added, for a total of 40 items. The self-administered mRPS-DD was completed by enrolled participants at the baseline and post-intervention assessments. The

Personal Control subscale (4 items) reflects perceived control over developing diabetes with a higher score indicating greater perceived control. The Comparative Disease Risk subscale assesses perceived risk for development of 15 diseases and conditions on a scale ranging from 1 ("almost no risk") to 4 ("high risk") with a higher score indicating a greater perceived risk. The Comparative Environmental Risk subscale uses the same scale and measures 9 perceived environmental risks, such as driving accidents, air pollution and extreme weather. Finally, the Optimistic Bias subscale reflects an individual's perception for risk for developing diabetes as compared to others of the same gender and age, with a lower score indicating less perceived risk and more optimistic bias. The survey also includes 2 items which assess worry about developing diabetes (Worry Sum) and a Composite Risk Score which includes all 32 items; a higher score indicates higher overall perceived risk.

6.3.5 Statistical Analysis

Analyses were carried out using the SPSS Statistical package (Version 15.0). The first set of analyses examined cross-sectional data for baseline measures; differences between gender, age and race for all 51 participants were examined using t-tests for equality of means or the non-parametric equivalent Mann-Whitney for Independent Samples and Pearson chi-square. Correlations between the subscales and measures of success in the program including weight loss, total activity minutes and attendance were evaluated using Spearman's correlation coefficient r. Pearson chi-square test was used to explore associations among perceived risk for diabetes and performance in the GLB program. Performance measures included achievement of program goals and adherence (attendance at 50% or more of the sessions and the last assessment visit). The mean change between pre and post survey responses was analyzed for those who

completed both a baseline and post-intervention survey (n=34) using the non-parametric Wilcoxon Matched-Pairs Signed Rank test. The Mann-Whitney test for Independent Samples was utilized to examine differences in changes in risk between groups. Significance for all results was set at 0.05. This study was approved by the University of Pittsburgh Institutional Review Board.

6.4 RESULTS

All 51 participants completed baseline mRPS-DD surveys, while 34 (27 female, 7 male, 26 Caucasian, 7 African American, 1 Hispanic, age range 30-74) provided post intervention surveys. There were no significant differences in age or pre-intervention weight between those who completed both the pre and post mRPS-DD surveys and those who did not.

6.4.1 Baseline Results

Mean baseline values for the subscales were evaluated by gender, race and age for differences (Table 1). Women showed a higher mean Personal Control subscale value (3.1 vs. 2.6, $p<0.01$) indicating greater feelings of personal control over health. A borderline higher mean Worry Sum score was also noted for men (3.1 vs. 2.6, $p=0.08$) indicating greater worry about diabetes. No significant differences were noted between Caucasian and African American baseline responses for the subscales. Both Comparative and Personal Disease risk sores ($p=0.04$ and 0.02 respectively) were higher in those 50 years and older demonstrating higher perceived risk for

disease. A borderline higher mean Composite Risk score was also noted in those over age 50 (2.3 vs. 2.1, p=0.08).

Table 2 shows the 15 diseases or conditions which comprise the Comparative Disease Risk score ranked by mean score; those who indicated they already have the disease or condition were removed from the analysis. Risk for high blood pressure had the highest mean score, with diabetes ranked second; diabetes demonstrated the greatest proportion of high perceived risk (29.4%) and moderate/high risk (62.7%) responses when compared to the other diseases/conditions. When individuals were asked about their risk perception for diabetes development, if they did not make any changes in their current lifestyle, the number believing they were at high risk remained essentially the same for risk of developing diabetes in 10 years at 33% but for risk of diabetes in 1 year, risk decreased to only 16%.

6.4.2 Correlation of mRPS-DD and Outcomes

The next part of the analyses examined whether there was any relationship between risk perception and several quantitative measures of behavioral success in the program including 1) weight loss, 2) total number of activity minutes achieved, and 3) number of sessions attended. The mean weight loss in the program was 4.6 pounds (sd=7.1); total mean activity minutes for all participants achieved over the course of the program was 665.6 (sd=2,209) and the mean number of sessions attended was 6.6 (sd=4.2), with 31 (61%) attending at least half of the sessions. Correlations are shown in Table 3 and generally show little association between the subscales and any of the three outcomes; the only one approaching significance was that between Comparative Disease Risk and physical activity minutes (Spearman's r=0.28, p=0.05).

Achievement of the program goals was also examined categorically in respect to baseline survey responses. In terms of weight loss, when collapsing the responses strongly disagree/disagree and strongly agree/agree, a marginally significant higher proportion of those who achieved a 3% or higher weight loss disagreed/strongly disagreed with the statement "If I am going to get diabetes, there is not much I can do about it" (42.9% v.11.1%, p=0.07, Figure 1). There were no differences noted for achieving weight loss in overall perception of risk for diabetes, or belief that risk was high for developing diabetes in the next one or ten years if no changes to lifestyle behaviors were made.

Attainment of the physical activity goal was also assessed; a marginally higher proportion of those who reached the activity goal believed they were at moderate/high risk of developing diabetes than those who did not meet the activity goal (91% versus 57.5%, p=0.07). A higher proportion of those who achieved the activity goal also noted a belief at baseline that their risk was high for developing diabetes in the next one (64% vs. 35%, ns) or ten years (82% vs. 50%, p=0.08) if no changes to lifestyle behaviors were made.

Another measure of success in the program is adherence, defined as attending at least half of the sessions and the final assessment visit for this project. A total of 28 participants attended at least 50% of the sessions and the final assessment visit. A marginally greater proportion of those who completed the program believed prior to starting that their risk for development of diabetes within the next 10 years was moderate/high (64.3% v. 25%, p=0.06, Figure 2). There were no significant differences in the adherent versus non-adherent group regarding overall perception of risk for diabetes or risk of developing diabetes within one year if they did not make any lifestyle changes.

6.4.3 Changes in mRPS-DD post assessment

Responses regarding general attitudes about diabetes development were assessed for the 34 subjects who completed both a pre and post intervention survey. A significant increase in the perceived Personal Control subscale score was noted (p=0.02), while single item questions designed to assess belief in personal control over health risks and feelings that personal effort may control diabetes risk showed marginally significant increases (p=0.06, 0.07 respectively). The only other subscale to demonstrate any change was the Composite Risk score which showed a significant decrease (p=0.03) indicating a reduced perception of risk overall. While neither the Personal nor Comparative Disease Risk subscales demonstrated differences between baseline and post-intervention, when examined specifically by individual diseases/conditions, the only item that showed a significant change in reported risk perception was diabetes, which demonstrated a significant decrease in risk perception from the pre assessment survey to the post (p=0.03) with the proportion believing they were at moderate/high risk at baseline decreasing from 62.7% to 35.3% post-intervention. Baseline measures for both groups were examined and no significant differences were noted. In addition, each group was stratified by decrease in risk perception for diabetes and composite score changes; all groups demonstrated a significant decrease in BMI, but the group whose risk perception stayed the same or increased also showed significant decreases in glucose and diastolic blood pressure. Furthermore, there were no differences between the groups regarding attainment of weight loss goals.

6.5 DISCUSSION

The results of this study indicate that less than two-thirds of this study population was concerned about developing diabetes at baseline with 62.7% rating risk for development of diabetes as moderate/high risk. At post-intervention, there was a significant reduction in perception of risk for diabetes with only 35.3% believing themselves to be at moderate/high risk. These results are lower than the responses from the participants in the DPP, where nearly 80% of the sample believed themselves to be at moderate/high risk. These results may reflect their participation in a lifestyle program which they may believe decreases their risk.

That over one-third believed themselves to be at only slight/almost no risk for developing diabetes clearly represents a problem in education as subjects were told of their risk before starting the GLB program. Similar findings however have been noted previously with perception of risk for developing diabetes [33, 34], as well as for other conditions such as hypertension [35], heart attack [36], stroke [37] and AIDS [38]. Thus, education concerning risk may be the first step toward diabetes prevention and risk reduction. This is an important point for educators to consider as they approach patients to begin discussions regarding diabetes prevention.

Measuring the link between the success of a lifestyle change program and perception of risk is difficult. In this analysis we have examined behavioral successes such as weight loss, physical activity minutes achieved and number of sessions attended. For all three of these quantitative measures, little association was noted with any of the subscales with the exception of Comparative Disease Risk and total physical activity minutes. Although this relationship was not shown to be strongly correlated, it may suggest that concern about developing diseases or conditions provided some motivation for physical activity in this group.

Regarding attainment of the program goals for weight loss and physical activity, it is interesting to note that those who were successful in achieving at least 3% weight loss did not feel hopeless about their situation prior to beginning the intervention which was demonstrated by their greater disagreement with the statement "if I am going to get diabetes there is not much I can do about it". Such fatalistic attitudes are common in the "real-world" of diabetes education and prevention. One study that looked at risk perception for developing diabetes through a telephone survey found that those with multiple risk factors were less likely than those with fewer risk factors to believe that anything could be done to change the course of diabetes development [39]. In addition, the same study also found that those with certain risk factors including family history, high blood pressure and high cholesterol were less likely to believe that they could do anything about developing diabetes. This relationship was not confirmed in the current project.

It is not clear whether this attitude is due to a lack of knowledge regarding research supporting success in the prevention or delay of diabetes, or if in spite of having knowledge, these individuals choose to ignore it. Regardless, ascertainment of an individual's perception of control regarding the development of diabetes, as well as determination of whether a fatalistic attitude exists may be important concepts to consider when enrolling a patient in a lifestyle change program so that appropriate education can be provided.

When looking at baseline versus the post-intervention responses for the individuals that completed both, two of the risk perception subscales showed significant changes. The Personal Control subscale showed a significant increase indicating an overall feeling of having more control over health. In addition, the Composite Risk score showed a significant decrease representing a reduced perception of overall risk. These results suggest that participation in a

lifestyle change program may increase feelings of personal control and responsibility for health risk, as well as decreasing feelings of overall risk. For the individual components of the Personal and Comparative Risk scores, it is interesting to note that only risk perception of diabetes decreased significantly in the pre and post analysis.

It is of some concern that although a decrease in perceived risk for both diabetes and the overall Composite Risk subscale score was noted, evaluation of clinical outcomes measures when stratified by risk perception belief did not show any differences between the groups. This could indicate that the individuals taking part in this program may have had a "false sense of security" due to their participation alone, rather than due to any actual reduction in risk. Thus, it may be important in future planning for lifestyle change programs to consider including materials that continually address and redirect the focus of the program back to diabetes prevention and individual risk.

Strengths of this study include a prospective study design that allowed for assessment of relationships between attitude and subsequent performance in the Group Lifestyle Balance program. This evaluation is one of the first using the mRPS-DD prospectively to evaluate risk perception performance. Other strengths include a fairly diverse study population with 27% being non-white.

The main limitation to this evaluation is the small sample size which limits the power to find significant changes where in some cases only trends are noted. In a post hoc power analysis, given the observed weight loss and sample sizes in those perceiving themselves at high risk for diabetes versus those who did not, we had 80% power to detect a difference in weight loss of 7.4 lbs more than what was observed. However, this evaluation was primarily a feasibility study; because the survey has not been utilized on a large scale, this information will

be helpful to others in planning for research studies examining risk and using this survey. Another limitation was the fact that there was no control group, thus comparisons between post-intervention responses were not permitted. In addition, these results were obtained in a small group of individuals in Western Pennsylvania and so may not be generalizable to other populations.

Because concern regarding individual misconception of personal risk has been shown in this and other investigations, in moving forward, it will be important to evaluate methods of conveying risk effectively both prior to initiation, as well as during the provision of a lifestyle change program. The concept of risk perception for disease and subsequent preventive behavior change is still widely unknown, thus future studies should continue to utilize and evaluate the survey prospectively in larger groups as intervention programs continue to grow. As the results of this investigation indicated that success in the program, as measured by achieving some weight loss, was associated with belief that something can be done to prevent diabetes, other areas of study should include examining the fatalistic attitude often observed that nothing can be done to prevent diabetes to determine possible interventions to negate this.

In this small investigation of individuals at high risk for developing diabetes, perception of risk subscales were generally not significantly related to performance in the GLB program, however, trends observed support the concept of risk perception acting as a motivator for lifestyle change. In addition, the results suggest that success in the program is related not only to completion of the program and making lifestyle changes, but also to a positive (or less negative) attitude toward the possibility of diabetes prevention. Due to the increasing diabetes crisis, it will become ever more essential to understand what education/ information is helpful for increasing an individual's chances of success in making lifestyle changes; risk perception for

diabetes development remains an unstudied concept, thus larger investigations are needed to examine this concept further.

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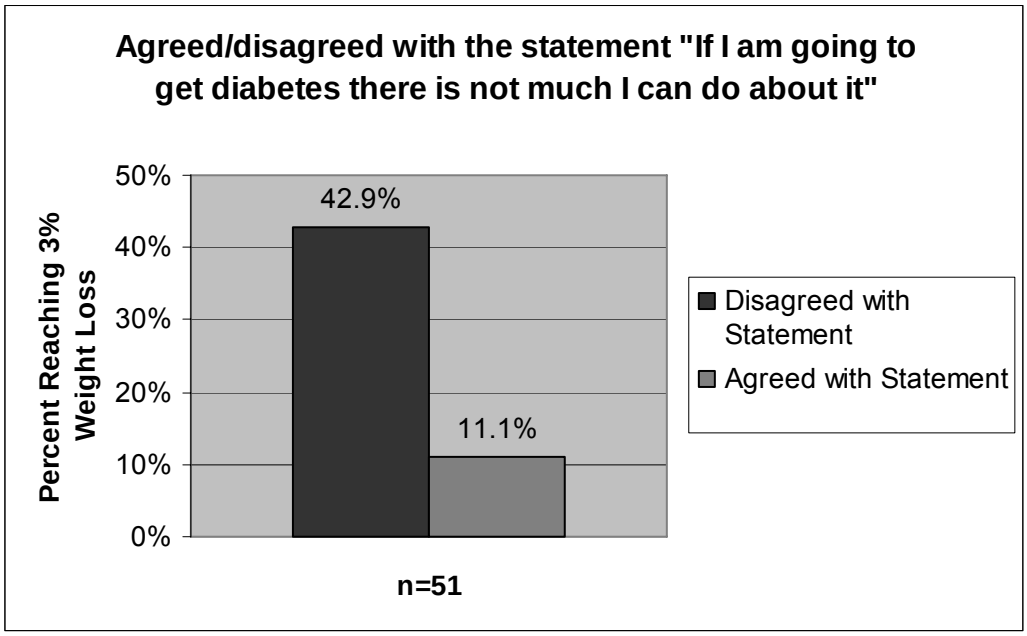


Figure 6-1 Baseline Perception Regarding Diabetes Prevention by 3% Weight Loss

p=0.07

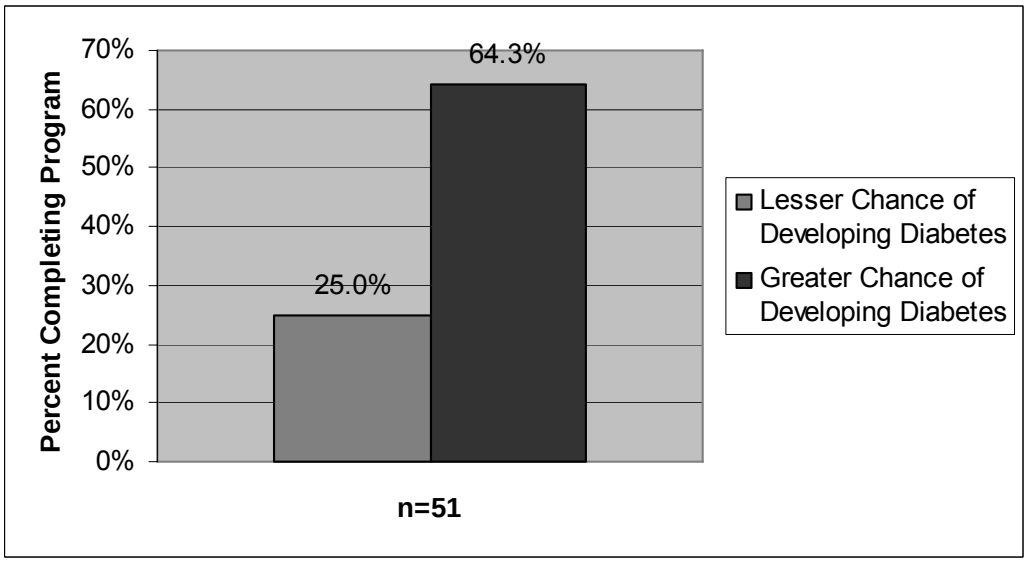


Figure 6-2 Pre-Intervention Perceived Risk of Diabetes by Completion of GLB

p=0.06

Table 6-1 Baseline Mean Subscale Results

(n=51)

	Gender			Race			Age		
	Male (n=9)	Female (n=42)	p	Caucasian (n=37)	Non-white (n=14)	p	25-49 years (n=20)	50-74 years (n=31)	p
Personal Control	2.6	3.1	<0.01	3.0	3.0	ns	3.0	3.0	ns
Optimistic Bias	2.3	2.0	ns	2.0	2.3	ns	2.1	2.1	ns
Worry Sum Score	3.1	2.6	0.08	2.7	2.6	ns	2.8	2.6	ns
Comparative Disease Risk	2.1	2.1	ns	2.2	1.9	ns	1.9	2.2	0.04
Personal Disease Risk	2.3	2.4	ns	2.5	2.2	ns	2.1	2.5	0.02
Environmental Risk	1.8	1.6	ns	1.7	1.7	ns	1.6	1.7	ns
Composite Risk	2.3	2.2	ns	2.2	2.1	ns	2.1	2.3	0.08

Table 6-2 Baseline Perceived Risk of Diseases/Conditions*

(n=51)

Comparative Disease or Condition Risks	**n**	**Mean Scores**	**Percent Responding "High Risk"**	**Percent Responding "Moderate" or "High Risk"**
High Blood Pressure	25	3.0	40.0	64.0
Diabetes	51	2.8	29.4	62.7
Heart Disease	45	2.7	28.9	62.2
Cancer	46	2.5	17.4	54.4
Stroke	48	2.4	16.7	43.8
Arthritis	29	2.4	13.8	51.7
Impotence (men only)	8	2.0	-	37.5
Osteoporosis	48	2.0	10.4	27.1
Hearing Loss	46	1.7	4.3	19.5
Asthma	48	1.6	4.2	12.5
Blindness	51	1.6	3.9	15.7
Infections	47	1.6	2.1	14.9
Kidney Failure	49	1.5	2.0	16.3
Foot Amputation	51	1.4	3.9	7.8
AIDS	51	1.0	-	-

*Those already diagnosed with the disease/condition are excluded

Table 6-3 Baseline Subscale Scores and Quantitative Measures of GLB Success

(n=51)

	Weight Difference	**Physical Activity Minutes**	**Number of Sessions Attended**
	Spearman's rho	Spearman's Rho	Spearman's Rho
Personal Control	0.00	0.06	-0.11
Optimistic Bias	-0.03	-0.05	-0.13
Worry Sum Score	-0.02	-0.04	-0.09
Comparative Disease Risk	0.16	0.28*	0.17
Personal Disease Risk	0.17	0.24	0.15
Environmental Risk	-0.03	0.06	-0.05
Composite Risk	0.12	0.19	0.09

* p=0.05

7.0 DISCUSSION

The gap between research and practice has been well documented; it has in fact been suggested that it may take one or two decades for original research to be translated to clinical practice [312]. The Diabetes Prevention Program announced that intensive lifestyle intervention was efficacious in reducing risk for type 2 diabetes by 58% in 2002, thus at the present time, five years have already passed. As noted, there was considerable evidence to support an intervention for prevention of diabetes prior to the DPP, and during the five years since publication of the DPP results there have been additional supporting results published. Thus, it seems clear that the time has come to begin translating diabetes prevention research to practice. Because lifestyle intervention has been shown to be one of the most efficacious interventions for risk reduction for diabetes, with the added bonus of minimal or no side effects, it would appear that translation attempts should focus on adapting the lifestyle intervention for real-world application.

The findings of this project, not only an attempt at translating a modified DPP lifestyle intervention but also the development of a screening program to identify those at risk, support the concept that a prevention screening and intervention program can be effectively implemented in a primary care practice setting. The primary focus of the prevention screening project was to evaluate the effectiveness and achievability of an organized program for prevention screening and risk identification. The recruitment results showed that the majority (61.7%) of individuals who attended screening initially responded to a letter sent to explain the importance of

prevention and to offer them an opportunity to be screened. These results suggest that mailing an invitation for screening may be a fairly efficient and cost-effective method of recruiting for prevention screening. Another finding regarding recruitment for prevention screening was the difference noted between the urban/outside preventionist and rural/internal preventionist screening rates (27.9% vs. 10.9%, $p<0.01$). Although the difference in screening rates may be related to the preventionist specifically, it is important to consider that the clinics with lower screening rates also had a higher minority population than the clinics with higher screening response, thus there may be contributing racial or other socioeconomic barriers. Barriers to health care and preventive services related to racial and socioeconomic reasons have been well-documented [313-316] and have also been previously noted to be related to attitudes about testing, lack of knowledge and environmental factors such as lack of transportation or lack of time [317]. It is also possible that there are inherent differences in people living in rural versus urban communities that may contribute to these differences. While it has been documented that rural populations often are actually less likely to receive health screenings, this may due primarily to a lack of services being available [318]. Another finding of note is that a significantly higher proportion of men refused screening than women, with 71.7% of those attending screening being female. It will be important to examine reasons for the noted discrepancies in screening invitation response, as well as participation in future prevention screening projects as they may impact how prevention screening is presented in different community settings and to a variety of individuals.

Prevention screening was successful in identifying 206 potentially new risk states which translates to 142 patients (41% of those screened) with potentially new conditions of risk identified through screening. Of those screened, 97 individuals without diabetes met the criteria

for metabolic syndrome and were eligible for prevention intervention, with 43 taking part in the Group Lifestyle Balance program offered at each practice. Furthermore, regardless of whether they were previously diagnosed or not, 224 patients (64%) were found at screening to have at least one risk factor meriting further medical evaluation.

These results strongly support the concept of prevention screening for several reasons. First, the identification of over 40% of those screened with newly found risk states could indicate previously undetected chronic conditions contributing to increased risk for diabetes and CVD. The identification of these conditions should theoretically lead to reduced risk for these individuals in the future. Second, following the previous line of reasoning, when individuals are identified as being at risk, in order to reduce that risk, it is imperative that a prevention intervention program is readily available and accessible. This project demonstrated the feasibility of identification of those at risk and subsequent enrollment in a prevention program offered in the primary care practice setting; however, as the number enrolled were only about half of those found to be eligible, it will be important to try to understand the barriers to participation in lifestyle change programs when considering future lifestyle program implementation. Finally, as 82 individuals (23.4% of those screened) with at least one elevated risk factor warranting further follow up had been previously diagnosed, this project also demonstrates the importance of regular, systematic follow up for those already diagnosed with chronic diseases/conditions such as the ones discussed here in order to assure that risk states are controlled.

The results of the subsequent chart review again support the concept of prevention screening to identify risk; a greater increase in the prevalence of all diagnosed conditions was found from the primary to the secondary review for the target group versus the comparison

group, with significantly greater increases noted in prevalence of diagnosed hyperlipidemia, pre-diabetes, and obesity.

The chart review also revealed that only 36% of elevated risk parameters noted in the chart review for those who did not attend screening and 41% of those who attended screening and had a post-intervention review completed received appropriate follow-up. These are important findings showing that in general, not only are screening guidelines not being met, but that even when patients are identified as being at risk only a small proportion of them are receiving appropriate follow-up. This underscores the importance of providing easy to use guidelines and education for those in practice, as well as the availability of appropriate interventions for risk reduction.

For those identified as being at risk, the Group Lifestyle Balance program proved to be effective in reducing some parameters of risk for diabetes including weight, waist measurement and glucose. The program was successfully implemented in each of the four practices by health care professionals who were trained to deliver the intervention, as well as to conduct the prevention screening. It is important to note that the preventionists had no prior experience in behavioral modification or any specialist diabetes interest and had varied backgrounds. Thus, a large pool of health professionals is potentially eligible to deliver the GLB with appropriate training. This suggests that the provision of trained healthcare professionals delivering group lifestyle intervention in primary care practice is feasible and could be a potential sustainable model for the "real world".

As is well known, translation from research to the "real-world" presents a number of challenges, thus it was anticipated that results from the current translation project would be somewhat reduced from those seen in the DPP. As noted, the Group Lifestyle Balance program

was successful in significantly reducing some parameters of risk including weight, waist circumference, BMI and glucose. Unfortunately no changes were noted for blood pressure, total cholesterol, non-HDL cholesterol, or HDL cholesterol; however one of the limitations of this project was the lack of a long-term follow-up period, thus there may have been changes over time that were not observed.

The number of sessions attended was positively correlated with weight loss ($p=0.002$) and physical activity minutes ($p=0.003$). Attainment of the program goals was examined for both the total and "completer" groups. In the total group of 51 participants, 7.8% reached the weight loss goal of 7%, while 21.6% and 33.3% had weight loss of at least 5% and 3.5% respectively. Within the "completers" group, 4 of 28 participants reached the 7% weight loss goal (14.3%), while 35.7% and 53.6% achieved weight loss of at least 5% and 3.5% respectively. In the DPP, 49% of lifestyle participants reached the 7% goal by the completion of the core intervention at the end of six months [319]; in the current project, 33.3% and 53.6% in the total and completer groups respectively met a weight loss goal of 3.5% at 3 months, similar to the trend for weight loss in the DPP at 3 months. The Finnish Diabetes Prevention Study (FDPS) found that after one year, 43% in the lifestyle intervention group had reached the study goal of 5% weight loss [320]. Recent results of the Good Ageing in Lahti Region (GOAL) Lifestyle Implementation Trial, an effectiveness study examining a program based on the FDPS in a "real-world" health care setting, demonstrated 12% reaching the goal at the end of one year [321]. It will be important to continue to study the implications of these translation efforts over a longer period of time.

The importance of physical activity in reaching weight loss goals for lifestyle change is underscored by the results of the intervention. Overall, a positive correlation was observed

between total activity minutes and total pounds lost (Spearman's r=0.36, p=0.01) and a significant association between attainment of the activity and weight loss goals was noted; 25% (n=12) of those who attained the activity goal vs. 2.5% (n=39) of those who did not were successful in reaching the weight loss goal (p=0.03).

Because the process of making lifestyle changes is so complex, it is important to consider other factors related to success, in particular understanding motivation for change. The primary goal of the third component of this project was to investigate the relationship between perceived risk and performance in the GLB program. The Risk Perception Survey for Developing Diabetes (RPS-DD) was modified for use in this population. Baseline results for the mRPS-DD, predictive responses for performance in the GLB program and comparisons between responses at baseline and again after intervention for those who completed both assessments were examined.

In general, it would seem logical that individuals who perceive their risk for diabetes development to be high would also be highly motivated to make changes to reduce that risk. For the high-risk individuals participating in this project, risk perception for diabetes development was ranked second on the list for mean scores (high blood pressure was ranked first) and represented the greatest proportion of high risk (29.4%) and moderate/high risk (62.7%) responses when compared to the other diseases/conditions. However, this represents less than two-thirds of the individuals in this high risk group accurately identifying themselves to be at risk.

When examined specifically by individual diseases/conditions, the only item which showed a significant change in reported risk perception was diabetes, which demonstrated a significant decrease in risk perception from the pre assessment survey to the post (p=0.03) with the proportion believing they were at moderate/high risk at baseline decreasing from 64.7% to

35.3% post-intervention. When examining those with a decrease in perceived risk for diabetes versus those whose perception of risk did not change or increased, there were no significant differences noted between the groups for change in any of the clinical outcomes measures including weight, BMI, glucose, systolic or diastolic blood pressure, total cholesterol, LDL cholesterol, non-LDL cholesterol or waist circumference. Because perception of risk decreased, but actual observed changes in risk were not different in those who perceived a decrease and those who did not, these results suggest that it is important to consider including materials which reinforce the concept of diabetes risk throughout a lifestyle change program, in order to keep the individual focused on their actual risk for diabetes development.

7.1 FUTURE PUBLIC HEALTH IMPLICATIONS

Quite obviously, prevention and risk reduction cannot occur if those at risk are not identified in some manner. While prevention screening and risk assessment do occur, assessments are often haphazard and not rooted in the healthcare system. Some of the barriers to risk identification which have been presented in the introduction include lack of structured screening over time resulting in testing being overlooked or repeated unnecessarily, confusing screening guidelines, lack of time on the part of the physician and primary care staff, and poor patient understanding of risk. The current project presents a systematic and organized model for prevention screening which could be implemented throughout the healthcare system, as well as an effective and feasible lifestyle intervention for those identified as being at risk.

One of the major barriers to prevention screening is the lack of an organized system in which individuals can be screened and subsequently followed over time. The advantage of an

automated program is that once a patient is entered into the system, the follow-up schedule is set for the patient based on current recommendations, with little effort or configuring on the part of physicians or primary care staff. The results of the current project which indicated that only a small proportion of identified risk states receive appropriate follow-up underscore the importance of incorporating a structured follow-up plan, with reminders for the patient as well as the physician and primary care staff.

Another potential advantage to a computer driven system is that the information required to obtain a risk assessment is entered in the program prior to the actual visit with the physician, thus potentially saving time by avoiding manual risk assessment. The components of the computer program would appear to save time for physicians and staff for whom currently all such determination must be done manually, however it will be important to study the implications of such a program from a cost and time saving perspective. Because many of the guidelines for prevention are somewhat confusing, another advantage to a structured program is that the guidelines have been put together in an easy to use format and in this system are actually built into the program. Physicians can enter specific information about the patient and the risk assessment is performed automatically.

The results of the prevention screening component of this project demonstrate that prevention screening for risk identification for type 2 diabetes and cardiovascular disease is feasible in a primary care practice setting and can be successful in identifying those at risk so that appropriate action and follow up may occur. Prevention screening was effective in identifying potentially new risk states that had not been previously noted or diagnosed and also demonstrated a significant increase in the prevalence of clinically diagnosed hyperlipidemia and pre-diabetes.

Mailing of invitation letters for prevention screening was effective in recruiting those patients who actually attended screening. The implications of these findings from a public health perspective are important in that a prevention screening program in primary care practice using an automated patient recruitment and screening tool could be a model for application on a large scale for identifying those at risk within the existing health care system. It is apparent that more work is needed on reaching the large proportion of individuals who decline; for those who do respond and are identified with potential risk states, mechanisms for facilitating appropriate follow up will be needed.

While identification of those at risk for diabetes and CVD development is the first step in reducing risk, risk identification cannot stand alone. Comprehensive lifestyle change programs delivered in practical and easily accessible settings are an essential partner in disease prevention. The current project is one of the first attempts to take the successful intervention utilized in the DPP, modify it for real-world implementation and evaluate its effectiveness in a primary care setting. A major component of this project is the development and evaluation of the Group Lifestyle Balance program as well as the development of the training guidelines and workshop for the program. All of the preventionists involved were healthcare professionals without special backgrounds in diabetes who were able to successfully deliver the intervention in their settings. Thus this work has clearly demonstrated the feasibility of training health care professionals within primary care practices to deliver lifestyle intervention on a broad scale. The combination of the availability of a group lifestyle change program and established training guidelines represent a key implication for public health in providing a model for lifestyle intervention translation. As has been discussed, lifestyle change programs for those at risk are lacking, thus even when identifying a patient as being at risk a physician is limited in what he

can “prescribe”; generally patients are told to “lose weight and exercise”. With the availability of a successful group intervention for lifestyle change, as well as a mechanism for training appropriate individuals in the delivery of the intervention, this project provides an outline for delivering intervention for those determined to be at risk on a wide-scale basis.

With the advent of evidence that type 2 diabetes can be prevented or delayed, as well as the increasing availability of evidence-based lifestyle interventions, understanding the behavioral factors that may be related to success in lifestyle change programs becomes of primary importance. The current project is one of the first to examine perception of risk for developing diabetes using a modified Risk Perception Survey for Developing Diabetes prospectively to investigate the relationship between performance in a lifestyle change program and perception of risk prospectively.

The results of this study of a group of individuals with metabolic syndrome participating in the Group Lifestyle Balance program indicate that over half of this study population was concerned about developing diabetes at baseline. It is of concern that although the majority of this high risk group correctly perceived their risk at baseline, almost 40% perceived their risk to be slight or none at all. These results could have implications for public health in that they reflect other studies of perceived risk for various other chronic diseases as well as diabetes [322-327] in which individuals who are at risk for a disease or condition do not perceive their risk accurately. As we move forward with diabetes prevention efforts, an important initial step will be to determine ways to best translate the correct perception of risk to those who are identified as being at risk.

Another important point to consider is that at post-intervention, there was a significant reduction in perception of risk for diabetes with only 35.3% believing themselves to be at

moderate/high risk. It is of concern that an actual difference in risk reduction between those who perceived a decrease in risk and those who did not was not observed. Therefore, it may be important for those planning lifestyle change programs in the future to consider including materials that continue to address and redirect the focus of the program back to the primary reason for the program: diabetes prevention and risk reduction.

No relationship was noted between any of the risk perception subscales and weight loss in the GLB program; however, this may likely be due to a lack of power for this component of the project (see limitations). While none of the risk perception subscales were related to weight loss in the GLB program, it is interesting to note that those who were successful in achieving at least 3% weight loss did not feel hopeless about their situation prior to beginning the intervention which was demonstrated by their disagreement with the statement "if I am going to get diabetes there is not much I can do about it". From a public health perspective, this suggests that it may be important to assess an individual's perception regarding their attitude toward development of diabetes prior to entering a lifestyle change program. It may also be important to determine the basis for their attitude and to provide education where needed, as having a negative attitude about one's ability to change the course of diabetes development could potentially prohibit a positive outcome.

Due to the increasing diabetes crisis, it will become ever more essential for those involved in translating diabetes prevention to the public on a large scale to understand what education/information is helpful for increasing an individual's chances of success in making lifestyle changes. For the most part, perception of risk for developing diabetes remains an unstudied area in which larger studies are needed to evaluate its relationship with success in making healthy lifestyle choices.

7.2 LIMITATIONS

While the STEP UP project provided an excellent opportunity to evaluate a prevention screening program as well as a first attempt at translating the successful lifestyle intervention utilized in the DPP to a "real-world" situation, there are a few limitations that are applicable to all three papers and should be noted.

Study Design The STEP UP project did not include a control group (due to the non-research priorities of the funding source), thus results for comparison to standard care are not available. Furthermore, the project did not include long-term follow-up of participants, thus only pre and post intervention results are available. This may limit the prognosis for this prevention program over time, although long-term maintenance will be a focus of subsequent research.

Study Population The participants in the STEP UP program were from four primary care practices in Western Pennsylvania. While an effort was made to select both rural and urban practices, the results of this project may not be generalizable to individuals in other areas.

Sample Size The actual number of patients at the participating practices was smaller than what was anticipated by the practices, thus yielding a smaller number of individuals screened and subsequently lower enrollment in the GLB program and mRPS-DD evaluation. A larger sample size would have provided better power for detecting differences in outcomes measures.

The following include the limitations specific to each paper.

7.2.1 Paper 1

The lack of a formal cost analysis, which would be very beneficial in further understanding financial implementation of prevention screening in the health care system, is a limitation of this

component of the project. A cost analysis of the recruitment procedures for prevention screening would provide an assessment of the time and cost involved in recruiting patients to come in for screening. Furthermore, information about the actual cost of the screening itself would be helpful for planning purposes. Finally an in-depth evaluation of the potential revenues to be generated for practices in the identification and follow-up of those at risk would be helpful in determining how such a program could become self-sustaining.

7.2.2 Paper 2

In addition to the small sample size, attrition of participants and subsequent lack of evaluation of those who did not complete the intervention was a considerable limitation of the analysis of this component of the project. Number of sessions attended was positively correlated with weight loss, thus the importance of engaging and retaining participants cannot be stressed enough. It should be noted that some of the attrition in one of the clinics may be related to the fact that the fate of one of the clinics was unclear and patients were uncertain as to whether they would need to find another primary care practice. Another potential limitation was requiring only at least a 2-hour fast for the blood sample; however, it was felt that because this was not a clinical trial, but a translational effort to a real-world situation, it was important to try to make participation as "user-friendly" as possible by accommodating subjects' busy and varied schedules, thus encouraging maximum attendance. These are issues that certainly arise when dealing with "real-world" situations. In addition, as mentioned above, the limited period of study (3 months) due to funding considerations was also a considerable limitation to this component of the project, in that a long-term follow-up for continued change in outcomes measures was not feasible.

7.2.3 Paper 3

In addition to the limitations described that affect all three papers, the main limitation to this component of the project was the original small sample size. Because this survey was not the primary focus of this project, it was anticipated that this component of the project was likely considerably underpowered to find differences if they did in fact exist. In a post hoc power analysis, given the observed weight loss and sample sizes in those perceiving themselves at high risk for diabetes versus those who did not, we had 80% power to detect a difference in weight loss of 7.4 lbs more than what was actually seen in the study. Attrition from the program was also limiting as the additional post-survey responses from those who did not complete the program may have provided some insight into changes in perception of risk that may influence decisions to discontinue lifestyle changes.

7.3 FUTURE RESEARCH

There are several areas for future research regarding prevention of diabetes and reduction in cardiovascular risk to be noted. Regarding screening for prevention, in order to improve screening attendance and subsequently risk identification, it will be important to further evaluate reasons for refusal and the barriers that exist concerning recruitment for prevention screening. While mailing an invitation to attend prevention screening was an effective method for recruiting those that actually attended screening in this project, other methods, such as offering incentives or performing screenings within a less clinical environment to engage those who did not attend screening should be evaluated in order to increase the overall yield and reach those who may not

normally have contact with their primary care practice. Other areas of future research regarding prevention screening include examining ways to improve appropriate follow-up on risk states identified through prevention screening. These could include the evaluation of automated programs such the one described in this project specifically directed toward appropriate follow up post screening, educational programs regarding guidelines for follow up for physicians and staff, or a combination of both. Finally, one of the most important areas of future research concerning prevention screening, will be cost-analysis of 1) recruitment of patients to attend screening, 2) the cost of the actual prevention screening visit, 3) the potential revenue brought into a practice through identification of billable conditions requiring follow up and 4) an overall, long-term evaluation of the cost-effectiveness of identification of risk assuming that appropriate action occurs and outcomes are reduced.

Future research regarding translation of a lifestyle change intervention should include longer observation of the intervention to establish if lifestyle changes can be expanded upon and/or maintained over time. This will be important in determining the best ways to provide lifestyle intervention and in developing materials to help individuals continue a healthy lifestyle over a lifetime. Other areas of study should address delivery of the lifestyle program in other settings such as in a community or worksite setting. As there is a large potential pool of heath care professionals to be trained to become preventionists, investigating other areas for delivery will increase the dissemination of information on a wider scale. Another important area for future research should address attrition from the program to determine if this was unique to these sites or if this will be a common problem that will occur in the real world of translation. It will be important to try to develop strategies to promote retention, possibly including incentives which may be monetary in nature, for example, rebates on costs for health care, reimbursement

for attendance, or time off from work to attend sessions. Finally, other delivery modes of the intervention should be explored in the future, for example using multi-media tools such as DVD's or CD's to deliver the intervention, or via the Internet, television broadcast or long-distance learning for rural areas.

Risk perception for developing diabetes is a relatively new concept and could take on an important role in the future as prevention becomes more mainstreamed. It will be important to understand what motivates individuals to take part in lifestyle change programs and what makes them continue and succeed in living more healthfully. Future areas of research regarding risk perception should examine risk perception in a larger group over a longer period of time. It is possible that some of the individuals who initially did not perform well, could become engaged in the future, thus it will be important to asses their risk perceptions over time.

7.4 CONCLUSION

The need for diabetes prevention in general has been well established; the difficulty now lies in trying to translate what is known from research to application in the real world. This project is an important first step in the war on diabetes; however there is still much to be done on many levels. The findings of the current project support the concept of prevention screening as an integral part of a comprehensive preventive service; however, controversy regarding screening on a broad scale continues. While the International Diabetes Federation's recent consensus statement on diabetes prevention recommended prevention based on controlling modifiable risk factors through screening [328], others have debated the merit of screening, and believe that there is still uncertainty over the extent to which the benefits of prevention screening justify the

costs and outweigh the potential harms [329]. It has also been suggested that because the main population burden of CVD related to hyperglycemia does not generally come from a small number of individuals with high levels of glucose, but rather from a large number of people with moderately elevated glucose levels, it would be most logical to focus prevention on attempting to lower mean glucose levels overall by reducing obesity and increasing physical activity in the general population [330]. Others have recommended screening for those with other high risk states such as hypertension or dyslipidemia [331] or in noting the significant relationship between diabetes and CVD have suggested incorporating diabetes risk assessment with existing vascular risk assessments [332].

It would seem that these ideas do not need to be mutually exclusive; an infrastructure for prevention screening could be developed by implementing screening in larger systematic controlled environments such as hospitals or health plans, and could continue to be monitored and evaluated for effectiveness and cost while moving forward. Because of the closely interwoven relationship between diabetes and CVD, it seems reasonable to asses risk for both simultaneously as was the concept in this project in the assessment of the metabolic syndrome. Furthermore, those found to be at risk should be provided an evidence-based risk reduction program such as the Group Lifestyle Balance program described here. At the same time, global efforts toward reducing obesity and increasing physical activity in the population at large should be of primary importance. Officials and policy makers will need to come on board in order to initiate meaningful policy changes at top levels to make prevention a national priority.

Screening and subsequent risk identification in and of itself may be related to some risk factor modification for CVD [333, 334]; however, evidence exists to the contrary. In one study which reported significant changes in behavior after risk screening for cholesterol, the results

were based on self-reported lifestyle behavior changes; actual objective measures did not show any significant changes [335]. Another recent study examined the impact of conducting a targeted stepwise diabetes screening program on health-related lifestyle behaviors (physical activity, dietary habits, alcohol use or smoking) in a Danish population aged 40–69 years. The results of this investigation indicated that there were no clinically significant lifestyle changes which occurred as a result of being screened [336]. Other research has demonstrated that the addition of counseling to screening is more effective than screening alone [337, 338] Thus, the concept of pairing evidence-based intervention with screening appears to be an appropriate model for comprehensive prevention.

The current project found that a modified DPP intervention, the Group Lifestyle Balance program, was successful in significantly reducing weight, BMI, waist circumference and glucose levels in this group of individuals at high risk for diabetes with metabolic syndrome. The intervention was delivered by health care professionals with no special background in diabetes who were trained in the provision of the intervention, thus demonstrating that there is a large pool of potential individuals who can be trained to provide prevention intervention. In order to have the largest impact possible, third party reimbursement for intervention delivered by trained health care professionals will be necessary, perhaps in conjunction with a nominal fee that patients will be reimbursed for when meeting certain goals such as attendance or adherence.

Medicare would be an obvious place to begin implementing primary prevention of diabetes as costs for the population in that age group are considerable and will continue to increase as the baby-boomers reach Medicare age. As Ackerman et al. reported, when compared with placebo, providing the lifestyle intervention at age 50 years could prevent 37% of new cases of diabetes before age 65 [64]. The authors also noted that offering the DPP lifestyle

intervention for eligible people between the ages of 50 and 64 could provide financial return on investment for private payers and long-term benefits for Medicare. In a review examining prevention of diabetes in a clinical setting, Burnet, et al. concluded that the cost-effectiveness analysis of the DPP provided "a compelling case for increased insurance coverage of nutrition and physical activity interventions in persons at high risk for diabetes" [339]. Prevention intervention programs could be initiated through system-based referrals based on prevention screening results with ongoing efficacy and cost evaluation.

In summary, the STEP UP project demonstrated the feasibility of a comprehensive program for the prevention of diabetes and CVD risk reduction. The project included 1) a set of easy to use guidelines for prevention, 2) a computer driven prevention recruitment tool and screening program, 3) a modified DPP lifestyle change intervention, and 4) an established training program for instruction in delivery of the intervention. The results of this project suggest that prevention is feasible and effective and can be carried out in a primary care practice setting. Although there will continue to be many barriers to implementation of prevention within our health care system, the described project provides a framework for a model that could potentially be implemented throughout the country as well as setting the stage for the development of a national prevention service.

APPENDIX A: STEP UP PREVENTION SCREENING GUIDELINES

STEP UP General Follow-up Guidelines*

1. All patients with "normal" results should receive general information regarding prevention of diabetes, CVD, healthy lifestyle, weight control and regular exercise, as well as their future prevention screening schedule.

2. Primary care practices should feel free to supplement the health pamphlets and brochures provided by STEP UP.

3. In terms of action based on a screening value, STEP UP generally suggests an abnormal value be repeated within three months before initiating therapy, particularly drug therapy.

4. Using the patient tracking system on the laptop, preventionists should review patients result forms annually to assess the need for scheduling of a prevention screening appointment. In the case where an office visit is not required, the patient should be sent a letter informing them that all is well and that they will be due for a visit the following year.

5. Other sources for information:

    a. American Diabetes Association:
        i. www.diabetes.org or 1-800-DIABETES
    b. American Heart Association
        i. www.americanheart.org or 1-800-AHA-USA
    c. Centers for Disease Control
        i. www.cdc.gov or 1-800-311-3435
    d. National Cholesterol Education Program
        i. www.nhlbi.nih.gov/about/ncep or 301 592 8573
    e. National Diabetes Education Program
        i. http://www.ndep.nih.gov/ or 301-496-3583
    f. National High Blood Pressure Education Program
        i. www.nhlbi.gov/guidelines/hypertension
    g. United States Preventive Services Task Force
        i. http://www.ahcpr.gov/clinic/uspstfix.htm

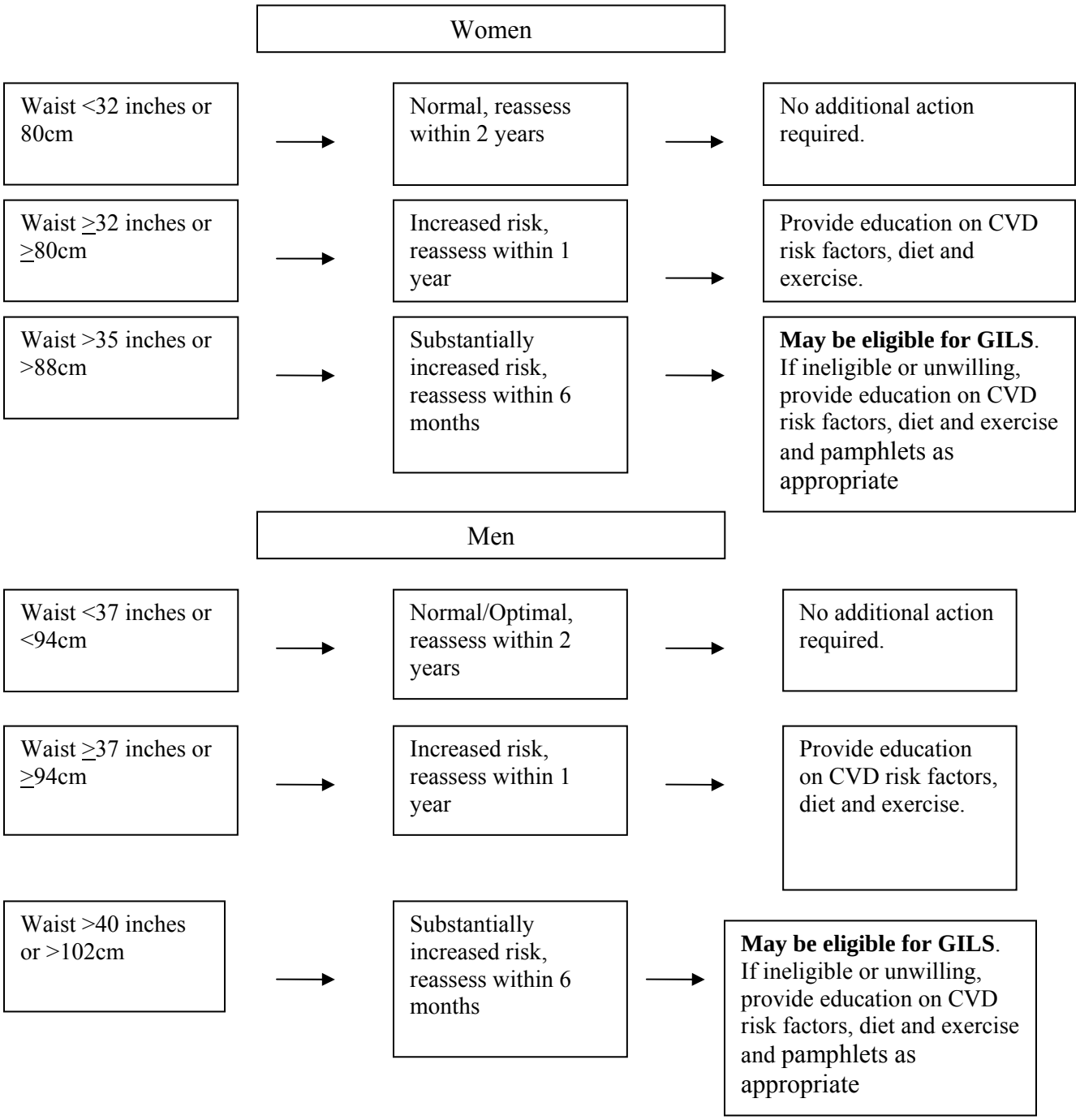
*NOTE: Group Lifestyle Balance (GLB) was originally called Group Intensive Lifestyle (GILS) and is referred to as GILS in this document.

STEP UP **BMI** SCREENING GUIDELINES

1. Overweight and obesity should be assessed in all individuals every two years for those who have not been overweight (≥25kg/m2) in the past.
2. Overweight and obesity should be assessed more frequently for those who have been or are overweight or obese.

BMI < 18.5kg/m2	Underweight	Assess weight loss, determine if recent, e.g. within 3-6 mos. If weight loss is ≥5% and unintentional, recommend PCP follow-up.
BMI = 18.5-24.9	Normal/ Optimal: Recheck within 2 years	No additional action required.
BMI = 25.0-29.9	Overweight: Recheck within 1 year	Recommend healthy lifestyle changes and reinforce appropriate weight goals. Provide weight loss counseling and pamphlets as appropriate.
BMI ≥ 30kg/m2	Obese: Evaluate and refer as soon as possible	If ineligible or unwilling, provide counseling as necessary. Initiate weight management program through caloric restriction and increased caloric expenditure as appropriate. Goal: Reduce body weight by 10% in first year of therapy.

STEP UP **WAIST CIRCUMFERENCE** SCREENING GUIDELINES



****** If Waist Circumference > 40 inches for MEN or >35 inches for WOMEN may be eligible for GILS.**

STEP UP **BLOOD GLUCOSE** SCREENING GUIDELINES

1. General guidelines:

    - All patients should have a diabetes risk assessment every three years (see risk factors listed below).
        i. Diabetes Risk Factors:
        - Age ≥45 yrs,
        - BMI ≥ 25 kg/m2.
        - Family History of diabetes (parents, siblings, children),
        - Race/ ethnicity (African-American, Asian-American, Hispanic-American, Native-American & Pacific Islanders),
        - IFG or IGT,
        - History of GDM or baby >9lbs.,
        - Hypertension (>140/90 or previous diagnosis)
        - HDL cholesterol <35mg/dl or triglycerides ≥250 mg/dl,
        - Polycystic ovary syndrome,
        - History of vascular disease

    - FPG should be performed every 3 years for those age ≥ 45 years
    - FPG should be performed every 3 years for those age <45 years and at least two other diabetes risk factors (see above risk factors)
    - Diabetes risk should be assessed for all others (<45 and 0-1 diabetes risk factors) every three years

2. Patients should fast for at least 2-4 hours but not longer than 14 hours before blood glucose test; patients who have fasted less than 2 hours should be scheduled for an appointment for a fasting glucose whenever possible. If it is not possible for the patient to return for a fasting glucose, a random glucose should be collected. Any person with a random glucose of ≥ 200mg/dl should be strongly encouraged to schedule an appointment for a fasting glucose or see their PCP.

3. Clinics may perform a finger stick blood glucose screening check if they prefer. The finger stick should be used as a SCREENING rather than as a diagnostic tool. It is important for clinics to know how their glucose monitoring meter is calibrated (this information should be included with the meter information). For those that are whole blood-calibrated, results will be 10-15% lower than a venous plasma sample result. For those meters that are plasma-calibrated, results may be compared directly with a laboratory plasma sample. Cut-point criteria for finger stick blood glucose are as follow:

Whole Blood-calibrated Sample

Fasting	≥90
Non-fasting	≥120

Plasma-calibrated Sample

Fasting	≥100
Non-fasting	≥140

Any finger stick sample meeting the above criteria indicates that an appointment should be scheduled for a fasting blood glucose. Finger stick results will not be acceptable for inclusion in GILS.

STEP UP **BLOOD GLUCOSE** SCREENING GUIDELINES-continued

Fasting glucose <100	Normal/Optimal 1. Reassess diabetes risk within 3 years. 2. If age ≥45 OR age <45 and at least two diabetes risk factors repeat FPG within 3 years	Provide information regarding risk factors for diabetes, identify and discuss any risk factors present. For those with at least one risk factor provide diabetes prevention pamphlet.
Fasting glucose = 100-109	Meets ADA criteria for IFG/Pre-diabetes • If patient has 2 other components of MS, physician may offer OGTT, repeat FBS or HbA1c within 6 wks if being considered for GILS. • If patient does not have at least 2 other risk factors, confirm FBG within 6 weeks.	Based on 2 hr OGTT, repeat FBS or HbA1c results (with 2 other components of MS) it will be up to the physician to determine eligibility for GILS. If ineligible and/or unwilling, review FBG to confirm or refute IFG diagnosis. 1. IFG confirmed-Provide counseling and pamphlet regarding pre-diabetes 2. Not confirmed-reassess within one year with counseling and pamphlet
Fasting glucose ≥ 110 AND <126	Meets ADA criteria for IFG/Pre-diabetes • Repeat fasting glucose within 6 weeks to confirm.	IFG confirmed: Determine eligibility for GILS and enroll if eligible. If ineligible and/or unwilling: Provide counseling and pamphlet regarding pre-diabetes If IFG NOT confirmed: Reassess within one year, provide counseling and pamphlet regarding pre-diabetes
Fasting glucose ≥ 126	Meets ADA criteria for diabetes • Repeat fasting glucose within 6 weeks to confirm.	Diabetes confirmed: Institute diabetes education following ADA guidelines of care. Diabetes NOT confirmed: May consider for GILS. May consider repeating FBG within 6 weeks.

****** If FBG ≥ 100 and <126 may be eligible for GILS.**

STEP UP **PULSE** SCREENING GUIDELINES

1. PULSE: Monitor pulse for at least 30 seconds to one minute to assess rate and rhythm after five-minute rest:

Pulse Rate $\geq$ 50 and $\leq$100, and regular rhythm	→	Optimal; reassess within two years.
Pulse Rate <50 OR >100 OR irregular rhythm	→	Abnormal, ECG may be considered to assist in treatment considerations for blood pressure and/or lipids.

STEP UP **SMOKING** SCREENING GUIDELINES

1. SMOKING (cigarette, cigar and/or pipe) should be assessed at every clinic visit.

Non-smoker	→	Optimal; reassess at next visit.
Smoker	→	Risk factor for CVD. Assess patient's interest in smoking cessation. Provide information regarding CVD risk and smoking. Provide smoking cessation handout and local smoking cessation information when available. Reassess within one year.

STEP UP **BLOOD PRESSURE** SCREENING GUIDELINES

1. Blood pressure should be measured at least every two years.
2. Blood pressure should be measured after 5 minute rest period sitting in a chair.
3. Two blood pressure readings should be measured at least one minute apart. (see Manual of Operations for complete assessment procedures)

Blood Pressure <120 and <80	Normal/Optimal: Blood pressure should be re-assessed within 2 years.	No additional action required.
Blood Pressure = 120-39 OR 80-89	Pre-hypertensive: Recheck within one year[1]	May be eligible for GILS. Provide education on CVD risk factors, diet and exercise and blood pressure pamphlet as appropriate Consider drug therapy for *"compelling" indication
Blood Pressure = 140-159 OR 90-99	Stage 1: Confirm within 2 months; if not confirmed (<140/90) recheck within one year[1]	May be eligible for GILS. Provide education on CVD risk factors, diet and exercise and blood pressure pamphlet as appropriate Mono-drug therapy indicated. Consider addition of additional drug for *"compelling" indication
Blood Pressure = 160-179 OR 100-109	Stage 2: Confirm within one week and evaluate or refer within 1 month[1]	May be eligible for GILS. Provide education on CVD risk factors, diet and exercise and blood pressure pamphlet as appropriate Mono-drug therapy indicated. Consider addition of additional drug for *"compelling" indication
Blood Pressure >180 OR >110	Stage 2 Elevated: Evaluate or refer immediately or within 1 wk[1]	May be eligible for GILS. Provide education on CVD risk factors, diet and exercise and blood pressure pamphlet as appropriate Two drug combination for most. Consider addition of additional drug for *"compelling" indication
SBP≥140 AND DBP <90	Isolated Systolic Hypertension: Confirm following above using systolic reading[1]	May be eligible for GILS. Treatment recommendations for older people with HBP, including those who have isolated systolic hypertension should follow the same principles outlined for the general care of hypertension. In many individuals, lower initial drug doses may be indicated to avoid symptoms.

* Compelling indications: Include heart failure, post MI, high coronary disease risk, diabetes, chronic kidney disease, recurrent stroke prevention

[1] **Blood pressure ≥ 130 or ≥85 may be eligible for GILS**

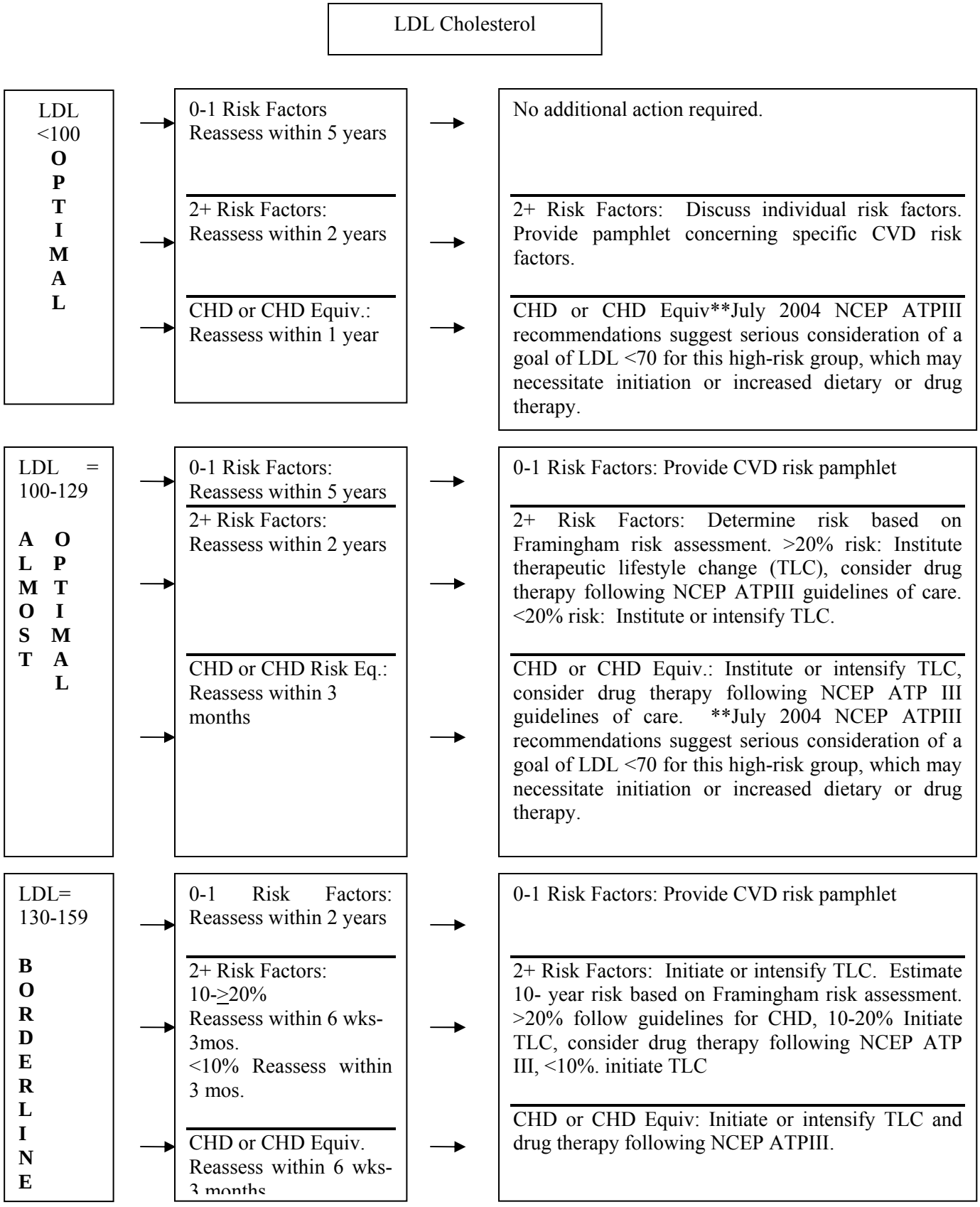
STEP UP **LIPID** SCREENING GUIDELINES

1. A complete lipid profile should be measured every five years for adults ≥20 years of age.
2. Patients with at least two risk factors for CVD should be checked every 2 years.
3. Lipid profile should be completed after a 9-12 hour fast.
4. If not fasting, collect only total cholesterol and non-HDL cholesterol. If total cholesterol is ≥ 200mg/dl or HDL cholesterol is <40mg/dl, fasting lipid profile should be scheduled.
5. If lipid lowering treatment is started a 30-60% reduction in LDL-C should be achieved

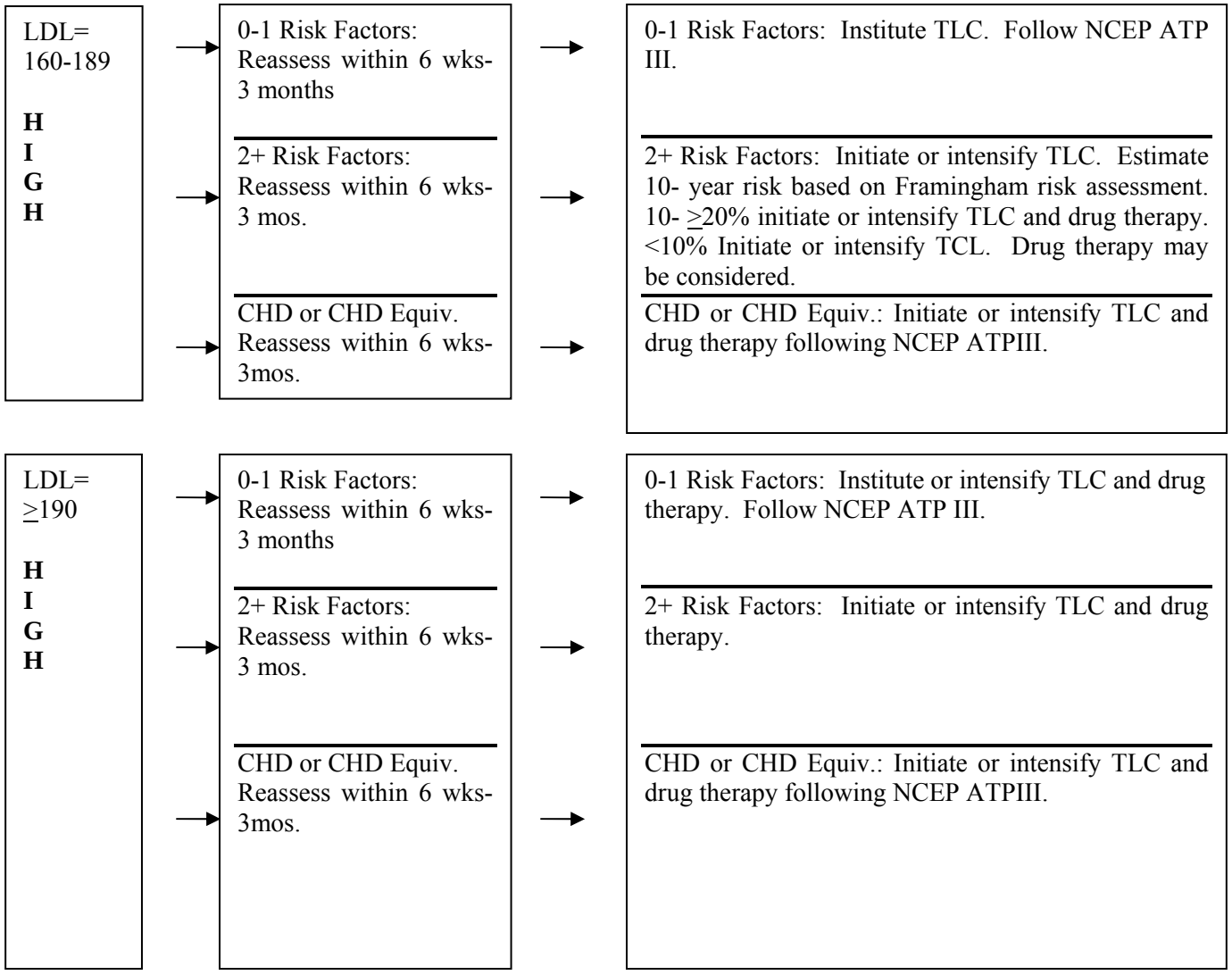
CVD Risk Factors: Assess and determine CVD risk factors:

1. Cigarette Smoking
2. Hypertension (blood pressure >140 or >90) or on antihypertensive medication
3. Low HDL cholesterol (<40mg/dl)
4. Family history of premature CHD (CHD in male first-degree relative <55 yrs. or CHD in female first-degree relative <65 yrs.)
5. Age:
   Men: ≥45 years of age
   Women: ≥55 years of age

   Negative Risk Factor: HDL ≥ 60mg/dl (removes one risk factor)


LDL Cholesterol
LDL <100 OPTIMAL
0-1 Risk Factors Reassess within 5 years
2+ Risk Factors: Reassess within 2 years
CHD or CHD Equiv.: Reassess within 1 year
No additional action required.
2+ Risk Factors: Discuss individual risk factors. Provide pamphlet concerning specific CVD risk factors.
CHD or CHD Equiv**July 2004 NCEP ATPIII recommendations suggest serious consideration of a goal of LDL <70 for this high-risk group, which may necessitate initiation or increased dietary or drug therapy.
LDL = 100-129 ALMOST OPTIMAL
0-1 Risk Factors: Reassess within 5 years
2+ Risk Factors: Reassess within 2 years
CHD or CHD Risk Eq.: Reassess within 3 months
0-1 Risk Factors: Provide CVD risk pamphlet
2+ Risk Factors: Determine risk based on Framingham risk assessment. >20% risk: Institute therapeutic lifestyle change (TLC), consider drug therapy following NCEP ATPIII guidelines of care. <20% risk: Institute or intensify TLC.
CHD or CHD Equiv.: Institute or intensify TLC, consider drug therapy following NCEP ATP III guidelines of care. **July 2004 NCEP ATPIII recommendations suggest serious consideration of a goal of LDL <70 for this high-risk group, which may necessitate initiation or increased dietary or drug therapy.
LDL= 130-159 BORDERLINE
0-1 Risk Factors: Reassess within 2 years
2+ Risk Factors: 10-≥20% Reassess within 6 wks-3mos. <10% Reassess within 3 mos.
CHD or CHD Equiv. Reassess within 6 wks-3 months
0-1 Risk Factors: Provide CVD risk pamphlet
2+ Risk Factors: Initiate or intensify TLC. Estimate 10- year risk based on Framingham risk assessment. >20% follow guidelines for CHD, 10-20% Initiate TLC, consider drug therapy following NCEP ATP III, <10%. initiate TLC
CHD or CHD Equiv: Initiate or intensify TLC and drug therapy following NCEP ATPIII.

LDL Cholesterol-continued



Triglycerides and HDL Cholesterol

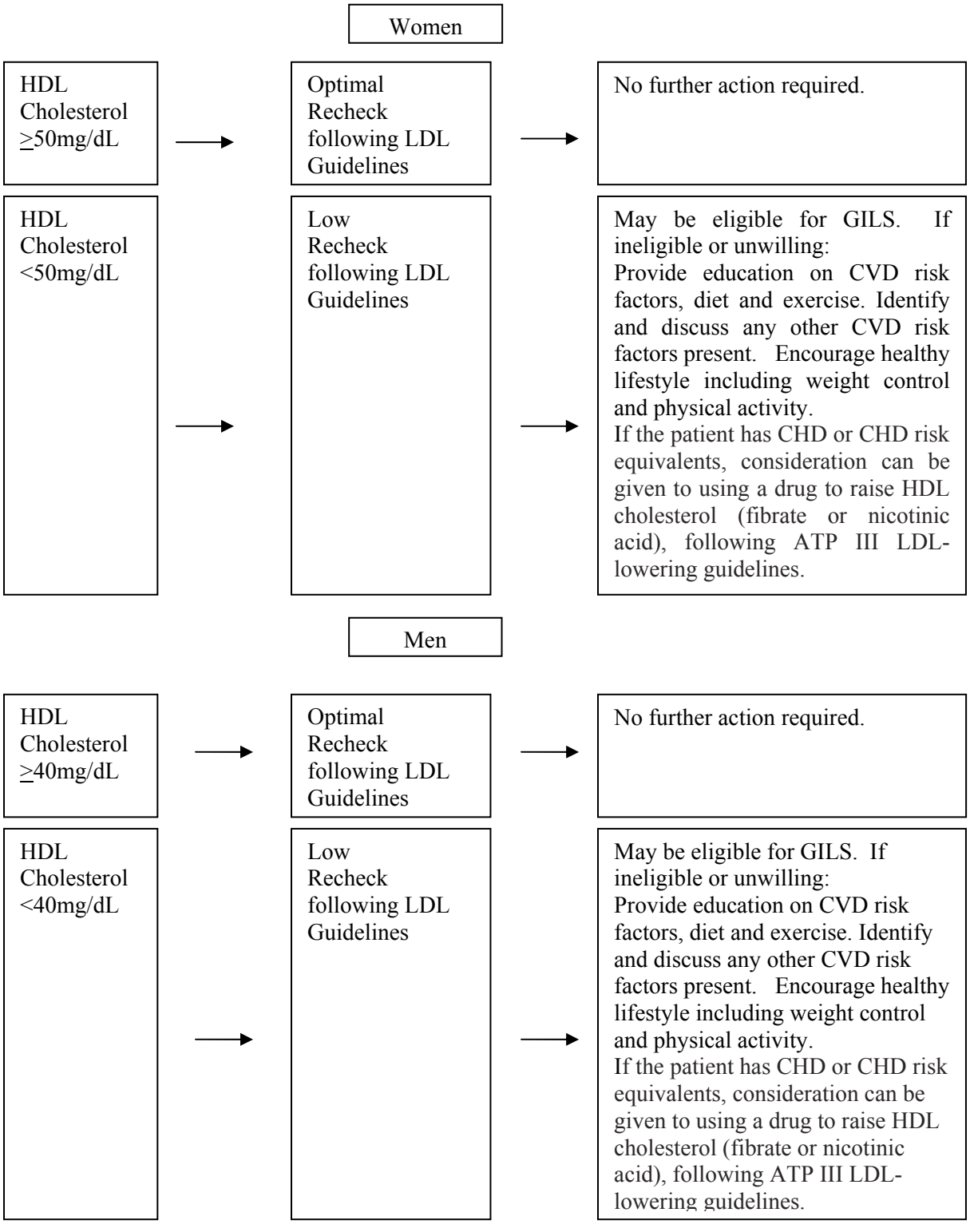
1. Therapy for these atherogenic dyslipidemic states begins after the LDL goal has been achieved and starts with TLC alone or simultaneously with initiation of more intensive LDL-lowering therapy with drugs.
2. Non-HDL cholesterol=Total Cholesterol-HDL Cholesterol and may be determined in the non-fasting state.

Triglycerides

Triglycerides <150 mg/dl	Optimal Recheck based on LDL Guidelines	No additional action required.
Triglycerides ≥150-199 mg/dl	Borderline High Recheck based on LDL Guidelines	May be eligible for GILS. If ineligible or unwilling: Provide education on CVD risk factors, diet and exercise. Identify and discuss any other CVD risk factors present. Encourage healthy lifestyle including weight control and physical activity.
Triglycerides ≥200-499 mg/dl	High Recheck within 3-6 months	Non-HDL cholesterol becomes a secondary target of therapy. Goals for non-HDL cholesterol are 30 mg/dL higher than those for LDL cholesterol. First the LDL cholesterol goal is attained, and if non-HDL remains elevated, additional therapy may be required to achieve the non-HDL goal. Consider higher doses of statin or add fibrate or niacin. May be eligible for GILS. If ineligible or unwilling in addition to above, provide education on CVD risk factors, diet and exercise. Identify and discuss any other CVD risk factors present and provide pamphlet as appropriate.
Triglycerides ≥500 mg/dl	Very High Evaluate as soon as possible, recheck within 3 months	Treat with fibrate or niacin to reduce risk of pancreatitis, then following ATP III. May be eligible for GILS. If ineligible or unwilling in addition to above, provide education on CVD risk factors, diet and exercise. Identify and discuss any other CVD risk factors present and provide pamphlet as appropriate..

****** If Triglycerides ≥ 150mg/dl may be eligible for GILS.**

HDL Cholesterol



****** If HDL< 40mg/dl for MEN or <50mg/dl for WOMEN may be eligible for GILS.**

STEP UP **METABOLIC SYNDROME, PRE-DIABETES AND GILS ELIGIBILITY GUIDELINES**

1. Determine if patient has at least two of the following risk factors:
   - Triglycerides ≥150mg/dl OR history of treated (with medication) triglycerides
   - Blood Pressure ≥130 OR ≥85 OR previous diagnosis with hypertension (treated with medication)
   - HDL Cholesterol
     a. Men <40mg/dl
     b. Women <50mg/dl
   - Waist circumference
     a. Men >102 cm (>40 inches)
     b. Women>88cm (>35 inches)

   If yes, proceed with #2.
   If no, patient does not meet criteria for metabolic syndrome nor is eligible for GILS. Proceed as outlined above for individual risk factors identified.

2. Does patient have previous diagnosis with diabetes? If yes, not eligible for GILS, provide info on metabolic syndrome. If no, continue and examine patient's fasting glucose results:
   a. If fasting glucose ≥ 110mg/dL and <126 mg/dL, patient is confirmed to meet criteria for the metabolic syndrome and may be eligible for the GILS, proceed to #3.
   b. If fasting glucose ≥100mg/dL and <110mg/dL, patient may be offered oral glucose tolerance test, repeat FBG or HbA1c according to the physician preference to determine eligibility. If two-hour result >140 and <200, patient may be eligible for the GILS. Proceed to #3.

3. Women only: Is patient currently pregnant or lactating?
   a. If no continue with question #4
   b. If yes, patient is not eligible for the GILS; provide appropriate counseling and health pamphlets.

4. Is BMI ≥ 25kg/mc2?
   a. If yes, patient is eligible for GILS, physician should confirm and refer. Continue with question #5
   b. If no, patient is not eligible for GILS. Provide appropriate counseling and health pamphlets. Proceed to question #5.

STEP UP FURTHER CARDIAC TESTING:

5. Consider ECG and/or ABI for the following:

Pulse Rate <50 OR >100, OR irregular rhythm	→	Abnormal, ECG may be considered to assist in treatment considerations for blood pressure and/or lipids.

Review completed Rose Angina and Claudication Questionnaire results:

Undetermined chest pain on Rose Questionnaire	→	Abnormal, ECG may be considered to assist in treatment considerations for blood pressure and/or lipids.
Rose Questionnaire positive for claudication	→	Abnormal, ABI may be considered to assist in treatment considerations for blood pressure and/or lipids.

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APPENDIX B: MODIFIED RPS-DD SURVEY

ATTITUDES ABOUT HEALTH

This survey will provide important information about how people feel about the risk of getting a chronic disease, like diabetes. There are no right or wrong answers. We are interested in *your* opinions and attitudes. Please answer each question as best as you can.

1. General Attitudes

For each item, please circle the number below the response which BEST DESCRIBES YOUR OPINION.

	Strongly Agree	**Agree**	**Disagree**	**Strongly Disagree**
1. I feel that I have little control over risks to my health.	1	2	3	4
2. If I am going to get diabetes, there is not much I can do about it.	1	2	3	4
3. I think that my personal efforts will help control my risks of getting diabetes.	1	2	3	4
4. People who make a good effort to control the risks of getting diabetes are much less likely to get diabetes.	1	2	3	4
5. I worry about getting diabetes.	1	2	3	4
6. Compared to other people of my same age and sex (gender), I am *less* likely than they are to get diabetes.	1	2	3	4
7. Compared to other people of my same age and sex (gender), I am *less* likely than they are to get a serious disease.	1	2	3	4
8. Worrying about getting diabetes is very upsetting.	1	2	3	4

Continue with next page.

2. Your Attitudes about Health Risks

Below is a list of health problems and diseases. For each one, please circle the number below the words to tell us if you think **your own personal health** is at "almost no risk," "slight risk," "moderate risk" or "high risk" from these problems.

If you, or a family member, already have the disease (or had the disease in the past), please *also* check (√) the appropriate line on the right.

⇓

	Almost No Risk	**Slight Risk**	**Moderate Risk**	**High Risk**	**Have(or had) this disease:** **Myself**	**Family member**
9. Arthritis	1	2	3	4	_____	_____
10. Heart Disease	1	2	3	4	_____	_____
11. Cancer	1	2	3	4	_____	_____
12. High blood pressure	1	2	3	4	_____	_____
13. Hearing loss	1	2	3	4	_____	_____
14. Asthma	1	2	3	4	_____	_____
15. Diabetes	1	2	3	4	_____	_____
16. Osteoporosis (bone disease)	1	2	3	4	_____	_____
17. Stroke	1	2	3	4	_____	_____
18. Blindness	1	2	3	4	_____	_____
19. Foot amputation	1	2	3	4	_____	_____
20. Infections needing treatment by a doctor	1	2	3	4	_____	_____
21. Impotence(only in men)	1	2	3	4	_____	_____
22. Kidney failure	1	2	3	4	_____	_____
23. AIDS	1	2	3	4	_____	_____

Continue with next page

3. Environmental Health Risks

Below is a list of possible hazards or dangerous conditions in the environment around most of us.

For each one, please circle the number below the words to tell us if your **own personal health** is at "almost no risk," "slight risk," "moderate risk" or "high risk" from each of the following hazards or conditions.

	Almost No Risk	**Slight Risk**	**Moderate Risk**	**High Risk**
24. Medical X-rays (radiation)	1	2	3	4
25. Violent crime	1	2	3	4
26. Extreme weather (hot or cold)	1	2	3	4
27. Driving/riding in an automobile	1	2	3	4
28. "Street" drugs (illegal drugs)	1	2	3	4
29. Air pollution	1	2	3	4
30. Pesticides	1	2	3	4
31. Household chemicals	1	2	3	4
32. Cigarette smoke from people smoking around you	1	2	3	4

Continue with next page

4. Individual Risk and Lifestyle Behaviors

Lifestyle behaviors include such things as eating, exercising, smoking and dealing with stress. Please give us your best answer for the following questions about lifestyle behaviors:

A. If you do not change any of your current lifestyle behaviors, what is your chance of getting diabetes within the **next ten years**? (Choose one answer)

____ Almost no chance of getting diabetes

____ Slight chance of getting diabetes

____ Equal chance of getting diabetes

____ Moderate chance of getting diabetes

____ High chance of getting diabetes

B. If you do not change any of your current lifestyle behaviors, what is your chance of getting diabetes within the **next year**? (Choose one answer)

____ Almost no chance of getting diabetes

____ Slight chance of getting diabetes

____ Equal chance of getting diabetes

____ Moderate chance of getting diabetes

____ High chance of getting diabetes

C. Have you made any lifestyle behavior changes that you believe will lower your chance of getting diabetes? (Choose one answer)

_____ Yes _____ No

If yes, are you continuing those lifestyle changes at the current time?

_____ Yes _____ No

D. Do you plan to make any lifestyle behavior changes to prevent diabetes in the near future? (Choose one answer)

_____ Yes _____ Maybe _____ No

5. Treatments to Prevent Diabetes:

For each item below, please circle the number below the response that BEST DESCRIBES YOUR OPINION.

	Strongly Agree	**Agree**	**Neither Agree nor Disagree**	**Disagree**	**Strongly Disagree**
Doing regular exercise and following a diet take a lot of effort.	1	2	3	4	5
Regular exercise and diet will prevent diabetes from developing.	1	2	3	4	5
The benefits of following a diet and exercise program outweigh the effort to do it.	1	2	3	4	5

Thanks!

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