AN EXAMINATION OF INFLUENTIAL FACTORS IN DIABETES PREVENTION EFFORTS

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DEDICATION

This dissertation is dedicated to my family, whose unwavering support helped made this possible.

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I would like to thank my committee members for their guidance, patience, and encouragement throughout.

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ABSTRACT

Type 2 Diabetes Mellitus (hereafter referred to as "diabetes") is a growing public health concern in the United States (U.S.), making prevention a priority. An estimated 79 million U.S. adults (35% of adults) have pre-diabetes, a health condition that denotes a high risk for diabetes, surpassing the number of adults who have diabetes. Clinical trials have shown that diabetes can be prevented in individuals with pre-diabetes through lifestyle health behaviors including weight loss, physical activity, and diet/nutrition. Understanding the factors that influence diabetes prevention is important in efforts to improve the health of at-risk individuals.

This three-part dissertation aimed to better understand the influential factors in diabetes prevention efforts and the implications for chronic disease prevention. Through a secondary data analysis of the National Health and Nutrition Examination Survey (NHANES), the first study quantitatively examined the impact of risk awareness on physical activity and diet in pre-diabetic individuals. The second study used survival/time-to-event analysis and data from the epidemiological Kohala Health Study to investigate the predictive ability of the metabolic syndrome in Native Hawaiians at risk for diabetes. The third study used qualitative methods to identify the salient factors that influence the perceptions of potential adopters on lifestyle interventions, and how the identified issues affect the implementation of lifestyle interventions.

Together, these three studies suggest that in order to decrease diabetes incidence, prevention efforts will need to extend beyond the education and awareness efforts at the individual-interpersonal level (i.e. prevention programs), and address the broader environmental context (i.e. public policies, community norms, organizational values). Individual-level prevention programs will need to be complemented by population-based strategies that seek to minimize the underlying causes of diabetes.

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LIST OF ABBREVIATIONS

A1C	Hemoglobin A1C
BRFSS	Behavioral Risk Factor Surveillance Survey
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CVD	Cardiovascular Disease
DIT	Diffusion of Innovations Theory
DPP	Diabetes Prevention Program
HR	Hazard Ratio
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
KHS	Kohala Health Study
METS	Metabolic Syndrome
NHANES	National Health and Nutrition Examination Survey
PA	Physical Activity
U.S.	United States

CHAPTER 1: INTRODUCTION

Problem Statement

The occurrence of type 2 diabetes mellitus (hereafter referred to as "diabetes") is increasingly becoming a serious public health concern in the United States (U.S.), with current national estimates showing 25.8 million, or 8.3% of the population, with diagnosed diabetes (1). This epidemic of diabetes is having profound effects on the nation's health and health care costs (2-5). Estimates provided by the Centers for Disease Prevention and Control (CDC) show diabetes costs the nation $174 billion in 2007, with $116 billion in direct healthcare costs and another $58 billion in indirect costs associated work productivity loss and premature mortality, among others (1).

Diabetes is a complex condition, with many health ramifications, including micro- and macrovascular complications (6-8). Individuals with diabetes have a 2- to 4-fold increased risk for cardiovascular disease (CVD) (9-11), and up to 80% of diabetic persons will experience some form of macrovascular disease, including coronary artery disease, peripheral arterial disease, and stroke (12). Complications from microvascular changes are also common, including diabetic retinopathy (a leading cause of blindness), diabetic nephropathy (a leading cause of renal failure), and diabetic neuropathy (damage of the nerves) (7).

As diabetes is a serious health condition that poses numerous challenges once it develops, prevention is crucial, especially among those at high-risk for developing diabetes (12). "Pre-diabetes," a condition that identifies persons at high risk for developing diabetes, is defined by the American Diabetes Association (ADA) as either impaired fasting glucose (IFG) of 100-125 mg/dl, impaired glucose tolerance (IGT) of 140-199 mg/dl, or elevated hemoglobin A1C (A1C) of 5.7-6.4% (13). Pre-diabetes is considered a risk factor not only for diabetes, but also for microvascular complications (14) and CVD (15-18). As such, the need to identify and prevent pre-diabetes is essential.

Currently in the U.S., the estimated number of individuals with pre-diabetes vastly exceeds the number of diabetic individuals, with an estimated 79 million adults,

or more than a third of U.S. adults (35%), with pre-diabetes (1). The significant number of adults with pre-diabetes is a public health problem because, although these individuals do not yet have forthright diabetes, they are at considerable increased risk for micro- and macrovascular complications compared to normoglycemic individuals (19-23). IFG and IGT place the individual at high risk for CVD, even if they do not lead first to diabetes (24). If not adequately identified and treated, pre-diabetes will progress to diabetes for a third of individuals with IFG or IGT, and for more than two-thirds of individuals with both IFG and IGT (25). However, if pre-diabetes is detected and treated early, progression to diabetes may be reduced or delayed, and risk for CVD and microvascular disease may also be reduced (14, 16, 26).

Prevention is key to stemming the diabetes epidemic and improving health outcomes (27). Preventing diabetes by controlling pre-diabetes would significantly decrease morbidity and mortality, and is feasible because it may be many years before pre-diabetes develops into diabetes, providing a wide window of opportunity for prevention (28, 29). It is for this reason that the ADA has developed standards of "treatment" for pre-diabetes, consisting primarily of lifestyle modification involving weight loss, physical activity, diet, and smoking cessation (13). The recommended lifestyle health behaviors are effective for many people at keeping blood glucose, blood pressure, and lipids under control, minimizing CVD risk. Medications such as metformin may also be used in treatment.

Diabetes prevention has been recognized by the U.S. Department of Health and Human Services as being an important part of its broad goal in improving the health of the nation (30). Supporting this goal are favorable outcomes from diabetes prevention trials (31), the most notable being decreased diabetes incidence (32) and potential cost-effectiveness and cost-savings of primary lifestyle prevention programs (33-36). Calculations from Herman et al. show that a primary prevention lifestyle intervention would cost $1,100/quality-adjusted life-years (QALY) (35), well within a proposed standard of less than $20,000/QALY for a program to be an appropriate use of resources (37). A diabetes simulation model developed by the CDC and RTI International further

provides evidence that broad prevention efforts would be beneficial, projecting that a nationwide community-based diabetes prevention program would be cost efficient, preventing 885,000 cases of diabetes in 25 years and saving $5.7 billion in health care costs (38). In light of the growing epidemic of diabetes, such promise supports primary preventive efforts.

Diabetes prevention is especially appropriate in the state of Hawaii, as diabetes is the fifth leading cause of mortality in Hawaii (39). Also, primary prevention is needed for Hawaii's diverse population. Although incidence rates of diagnosed diabetes are lower than the national average (6.6 cases per 1000 in Hawaii compared to 8.8 cases per 1000 in the nation in 2009), the state has a high percentage of ethnic minorities at increased risk for diabetes (1, 12). Hawaii BRFSS statistics indicate that, compared to Whites, Native Hawaiians, Filipinos, and the Japanese have a higher prevalence of diabetes (40). Specifically, Whites in the state have a 3.4% prevalence of diabetes, compared to the 7.9% prevalence for Native Hawaiians, 7.5% for Filipinos, and 6.6% for Japanese.

Literature Review

The evidence for lifestyle behaviors in the prevention of diabetes first emerged from observational epidemiological studies that suggested that certain risk factors, including physical inactivity and obesity, increased the risk for diabetes development and occurrence of diabetes-related health complications (41-43). The epidemiological studies brought forth the possibility of diabetes prevention for those at risk. Subsequently, three significant clinical trials provided scientific evidence for diabetes prevention with lifestyle changes.

The first clinical trial that showed it was possible to prevent diabetes with lifestyle modifications was the DaQing Impaired Glucose Tolerance (IGT) and Diabetes Study (44). After screening and identifying adults at-risk for diabetes from clinics in DaQing, China, 577 persons were randomized by clinic blocks to one of four intervention arms: physical activity, diet, physical activity and diet, or control. At the end of the 6-year study, diabetes incidence was lower in the three intervention arms, compared to

the control arm, and reductions in risk for diabetes ranged from 31-46%. Similar findings were seen in the Finnish Diabetes Prevention Study (DPS), the first diabetes prevention RCT to randomize at the individual level (45). In the Finnish DPS, IGT subjects were randomized into either an intervention or control group, with the 3-year intervention consisting of a personalized diet and physical activity plan provided with ample professional support and structured exercise classes. The DPS resulted in a 58% reduced risk for diabetes. Both studies also found sustained health benefits and diabetes prevention in their follow-up (46, 47).

The Diabetes Prevention Program (DPP) was the first diabetes prevention trial in the U.S. (48). In addition to supporting the findings from the Chinese DaQing IGT and Finnish DPS studies, it showed that diabetes prevention was possible in an ethnically diverse population. Moreover, similar to the China DaQing and Finnish DPS trials, the benefits of lifestyle changes to prevent diabetes were sustained years after the end of the initial trial, with a low incidence of diabetes in participants that received the lifestyle intervention (49).

In spite of the promising results from the RCTs, translation to public health remains a nascent field, and more research is needed for broad application of best strategies for addressing primary prevention of diabetes. The “high-risk” approach focuses on individuals who are at-risk for diabetes and offers several advantages, including a cost-effective use of limited resources, whereas the “population” strategy takes on a traditional public health approach and aims to benefit entire populations (50). The high-risk approach has been utilized in several pilot interventions, with some specifically incorporating the DPP protocol into programs for communities at high risk (51). The DEPLOY study is an example of this, partnering with the YMCA, a community agency with broad reach, and with a health care system, in this case the Indiana University School of Medicine (52). DEPLOY took place at two YMCAs in Indianapolis with similar populations. One of the sites was randomly assigned to receive the intervention. Significant decreases in weight and cholesterol were seen in the intervention site. An extension of the pilot study showed sustained benefits (53),

although further research is needed on the sustainability of the program, as well as its effectiveness in different contexts.

Other high-risk approach interventions adapt the DPP protocol to meet the cultural needs of communities (54). The PILI 'Ohana project, a culturally adapted weight prevention program for Native Hawaiians and Pacific Islanders, is an example of a community-based lifestyle intervention. Pili 'Ohana follows a substantially amended DPP protocol to promote weight loss in Native Hawaiians and Pacific Islanders, and is primarily targeted towards decreasing health disparities in obesity experienced by these populations (55, 56). Similarly to the high-risk interventions that strictly follow the DPP protocol, the long-term benefits of these culturally tailored interventions are unknown thus far.

To address the complex nature of preventing diabetes, it is likely that both high-risk and population-based approaches will be needed in primary prevention efforts (57). Regardless of the approach used, understanding the components that shape the approaches and their roles in primary prevention is important in efforts to control the causes of diabetes incidence.

Conceptual Framework

The conceptual framework for this dissertation is structured by the components identified in the literature as being important in primary prevention efforts. These components, consisting of awareness of diabetes risk, effective identification of risk status, and lifestyle interventions, highlight important steps that lead to the promotion of recommended health behaviors proven to minimize diabetes incidence. The model is shown in Figure 1.

Figure 1.1. Conceptual Framework for dissertation research

The first component, awareness of diabetes risk, describes how risk is conceptualized, assessed, and communicated. As in the case of diabetes management, this crucial first step is necessary to start individuals to consider engaging in lifestyle interventions and proven treatments (58). Low levels of risk awareness, as is currently the case among U.S. adults (59, 60), have the potential to hinder adoption of healthy lifestyle behaviors. Awareness among diagnosed diabetic individuals has been shown to influence risk-reducing behaviors (61), lending credence for increasing awareness among pre-diabetic individuals who require similar lifestyle modifications.

Effective identification of risk describes how those at risk are detected and treated. Effective identification methods are necessary for public health prevention efforts, allowing for the prescription of evidence-based interventions by providers (62). While the main prevention trials identified at-risk individuals with blood glucose tests, most notably the oral glucose tolerance test (OGTT) to check for IGT, such inconvenient and expensive tests are not feasible in real-world settings. Other identification strategies that have been investigated include the use of BMI in combination with IFG (63), or a predictive model based on a combination of clinical and non-clinical information such as age, sex, ethnicity, family history, BMI, glucose, blood pressure, and cholesterol values (64). The potential use of the Metabolic Syndrome (MetS) to detect pre-diabetes also has been examined (65-67). As questions remain about the best method to identify persons for interventions, more research is needed to investigate prospective strategies and their applicability to diverse populations (68).

In addition to increasing awareness and finding effective identification strategies, access to lifestyle interventions is important in reducing risk. It is likely that increasing availability and improving access to lifestyle interventions would aid in treatment of affected individuals (62). However, while clinical trials such as the DPP have clearly shown diabetes and diabetes-related health complications to be preventable in those at-risk with lifestyle modifications, the effective widespread translation of lifestyle interventions into public health has not yet been optimized (62). Evidence suggesting

that translated interventions are potentially cost-effective and cost-saving (69, 70) promote the need to further research for viable methods to widely disseminate, offer, and enroll individuals in lifestyle interventions.

Purpose and Research Questions

As previously discussed, treatment for pre-diabetic individuals is important in order to stem the growing diabetes epidemic. But even with scientific evidence providing support for primary prevention (48), many are still not aware of their risk status (60), and treatment in the form of public health lifestyle interventions is limited (62). The goal of this three-study dissertation is to understand how treatment can be effectively disseminated in public health by: 1) better understanding the role of risk status awareness in preventive behavior; 2) investigating prospective identification methods for diverse populations; and 3) delineating the factors that influence diffusion of lifestyle interventions.

Study 1 addressed the research question: *How does awareness of risk status impact lifestyle health behaviors among pre-diabetic individuals?* Data from the National Health and Nutrition Examination Survey (NHANES) and quantitative methods were used to investigate how awareness of risk status influences lifestyle health behaviors (diet and physical activity) in pre-diabetic individuals. The findings shed light on the public health implications of increasing awareness of pre-diabetes.

Study 2 examined if the *metabolic syndrome (MetS) in conjunction with impaired fasting glucose (IFG) is a better predicator of diabetes in Native Hawaiians than IFG alone*. Data from the Kohala Health Study (KHS), an epidemiological study assessing diabetes and cardiovascular risks in the multiethnic Hawaii island community, and survival analysis (time to event analysis) were used to determine if metabolic syndrome (MetS), paired with IFG, is a significant predictor of diabetes incidence in Native Hawaiians, an ethnic group at increased risk for obesity and diabetes. The results from this study provide an understanding of alternative, effective methods for identification of at-risk individuals from diverse populations.

Study 3 qualitatively explored *which factors influence the broad dissemination of diabetes lifestyle interventions*. Using interviews from key informants, themes emerging from the data identified the salient barriers and facilitators to widespread dissemination of lifestyle interventions. The goal of Study 3 was to provide an in-depth identification of issues that affect the diffusion of lifestyle interventions for diabetes.

Community

Community partners for this dissertation include the Kohala Health Study (KHS), an epidemiological study that assesses diabetes and cardiovascular risks in the community of North Kohala on the island of Hawaii, and organizational and community advocates who have expressed interest in primary diabetes prevention. Advocates include relevant personnel from the DPP-Hawaii site, health insurance providers in Hawaii, the Hawaii branch of the American Diabetes Association, the Hawaii Primary Care Association, The Queen's Medical Center, the Hawaii Department of Health Diabetes Prevention and Control Program, and community leaders.

CHAPTER 2: STUDY 1

Abstract

Background. Lifestyle health behaviors such as physical activity and diet have been shown in clinical trials to be effective in halting the progression from pre-diabetes to diabetes. Increasing awareness of diabetes risk may initiate lifestyle health behaviors in pre-diabetes; however, only a small percentage of U.S. adults with pre-diabetes are aware of their risk status. It is unclear how this low prevalence of diabetes risk awareness impacts lifestyle health behaviors.

Purpose. This study aimed to determine the predictors of diabetes risk awareness and the role diabetes risk awareness plays in diet and physical activity behavior in pre-diabetic adults.

Methods. Cross-sectional data from 1,770 non-pregnant adults aged 20 years or older with clinically defined pre-diabetes in the 2007-2010 National Health and Nutrition Examination Survey (NHANES). Multivariate logistic regressions were used to identify: 1) the variables that predict awareness of diabetes risk and 2) the impact of risk awareness on diet behavior (saturated fat and dietary fiber intake) and physical activity.

Results. In 2007-2010, 46.9% of adults in the U.S. had pre-diabetes and 15.8% were aware of their risk status. Multivariate models identified a family history of diabetes and presence of co-morbid health conditions such as hypertension and dyslipidemia as significant predictors of risk awareness. Risk awareness was not a significant predictor of diet or physical activity behavior in pre-diabetic adults.

Conclusions. Awareness of diabetes risk alone will likely not result in recommended health behaviors in pre-diabetic adults; other factors will need to be incorporated.

Introduction

Currently in the United States, an estimated 25.8 million people, or 8.3% of the population, have diabetes (1). That number continues to grow, and in 2010, there were 1.9 million new cases of diabetes among adults age 20 years or older. To add to this public health epidemic is the number of pre-diabetic individuals, individuals at increased risk for diabetes. An estimated 79 million adults, or more than a third of U.S. adults (35%), have pre-diabetes (1).

Major randomized controlled trials have demonstrated the possibility of preventing diabetes in persons at risk, i.e., those with pre-diabetes (44, 45, 48). Preventive lifestyle behaviors such as weight loss, physical activity, and diet (e.g., reduced saturated fat intake and increased dietary fiber intake) have been shown in clinical trials to be effective in halting the progression to diabetes. Given this, increasing awareness of risk and encouraging proven lifestyle behavioral changes in pre-diabetic individuals is likely to help stem the burgeoning burden of diabetes.

In diagnosed diabetes, low awareness about diabetes is often associated with unfavorable health outcomes (58, 71). It is unknown if low awareness in pre-diabetes is associated with poor lifestyle health behaviors that can lead to detrimental health outcomes. But as awareness precedes initiation of preventive health behaviors in pre-diabetes (59), improving awareness of the health implications and risks of pre-diabetes may aid in diabetes prevention efforts.

In 2005-2006, only a small percentage of U.S. adults with pre-diabetes were aware of their risk status. National estimates show that on average, only 4.8-7.3% of pre-diabetic adults are aware of their risk for diabetes (59, 60), a trend consistently observed across the individual states (72). It is unclear how this low prevalence of diabetes risk awareness impacts lifestyle health behaviors. This study aims to address this knowledge gap by determining: 1) the predictors of diabetes risk awareness; and 2) the role diabetes risk awareness plays in diet and physical activity behavior in pre-diabetic adults (Figure 1.1).

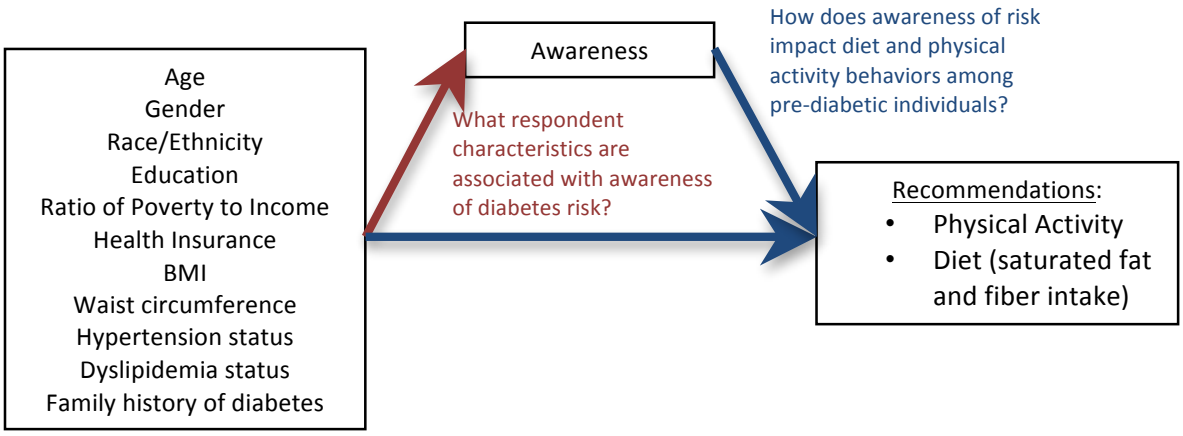

Figure 2.1. Conceptual Framework for Study 1

Methods

Research Design

Cross-sectional data from the 2007-2010 National Health and Nutrition Examination Survey (NHANES) (73) was used for this study. NHANES is a survey of the civilian non-institutionalized population of the U.S., uses a complex, multistage, probability sampling method to select respondents. Starting in 1999, the survey switched to a "continuous" format, sampling approximately 5,000 individuals in 15 counties across the country each year. NHANES is a two-component survey, consisting of an interview as well as an examination. The interview component collects data pertaining to demographic characteristics, dietary behavior, and health conditions and behaviors. The examination component collects data on medical and physiological measurements, dental conditions, and laboratory assessments.

The survey has above a 75% response rate for both the interview and examination components (Table 2.1). The response rates for the two continuous datasets used in this analysis are as follows:

Table 2.1. NHANES response rates, 2007-2008 and 2009-2010

Total, all ages	Screened sample	Interviewed sample	Examined sample
2007-2008	12,943	10,149 (78.4%)	9,762 (75.4%)
2009-2010	13,272	10,537 (79.4%)	10,253 (77.3%)

Data for NHANES is publicly available from the CDC website (http://www.cdc.gov/nchs/nhanes.htm). Data from the continuous surveys are released in two-year intervals (e.g. 2007-2008 and 2009-2010). The continuous format allows for the combining of two-year datasets to increase sample size, and most variables are held constant. Changes in variables are noted on each page of the data release.

Each two-year data release is organized in sections, and the five main sections are: demographics, dietary, examination, laboratory, and questionnaire. The demographics section contains data on demographic (e.g., gender, age) and socioeconomic (e.g., education, poverty) characteristics. The dietary section contains data on diet/nutrition intake and behavior. The examination section contains data on physiological measures, such as blood pressure, height, weight, and waist circumference. The laboratory section contains data on laboratory assessments, including blood glucose levels and cholesterol assessments. The questionnaire section contains information from the interview section on self-reported health conditions (e.g., diabetes) and health-related behaviors (e.g., physical activity).

Measures & Definitions

Risk awareness was assessed by two questions: 1) *Have you ever been told by a doctor or other health professional that you have any of the following: prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes, or that your blood sugar is higher than normal but not high enough to be called diabetes or sugar diabetes?* and 2) *Have you ever been told by a doctor or other health professional that you have health conditions or a medical or family history that increases your risk for diabetes?* Subjects answering in the affirmative for either of these questions were classified as being aware of risk status. These questions were found in the Diabetes Questionnaire section of NHANES.

The diet-related dependent variables for the second part of the analysis, meeting recommended saturated fat and fiber intake, were obtained from dietary assessment data found in the Dietary section of NHANES. The dietary component in NHANES, referred to as *What We Eat in America* (WWEIA) (74), is comprised of two 24-hour food recalls. The first is administered in the examination portion of the survey by a dietary interviewer, and the second is administered by phone 3-10 days following the first interview. Dietary intake was collected using the USDA Automated Multiple-Pass Method (75), and the USDA's Food and Nutrient Database for Dietary Studies tool was used to calculate individual food intakes and estimates of energy and nutrients (76). Per analysis recommendations (77), a single 24-hour recall was used to assess saturated fat and fiber intake for this study. Participants that provided reliable intake information (determined by the dietary recall status code, DR1DRSTZ=1) were included in the analysis. More than 90% of participants provided reliable intake information. Participants were classified as either meeting or not meeting ADA dietary recommendations for reducing the risk for diabetes: saturated fat intake less than 10% of total daily calories and daily fiber intake of 14g/1000kcal (13).

The physical activity dependent variable was obtained from the Physical Activity Questionnaire section of NHANES. The NHANES physical activity questionnaire is based on the World Health Organization (WHO)'s Global Physical Activity Questionnaire (GPAQ) (78), and its survey items correspond to the GPAQ (Appendix A). The measurement of physical activity took into account three forms of activity--occupational, recreational, and transport-related--as well as the intensity, duration, and frequency of each. Participants were classified as inactive/sedentary and not meeting ADA recommendations for physical activity if they did not report engaging in any occupational, recreational, or transport-related activity, or if their level of physical activity did not reach the cutoff for high or moderate levels. Using the GPAQ Analysis Guide (79), participants engaging in moderate or vigorous/high activity (Table 2.2) were classified as meeting ADA recommendations for physical activity.

Table 2.2. Criteria for Physical Activity levels

Level	Criteria
High	≥3 days of vigorous-intensity activity resulting in a minimum of ≥1,500 MET-minutes/week OR 7 days of any combination of transport, moderate- or vigorous-intensity activity resulting in a minimum of ≥3,000 MET-minutes/week
Moderate	Not meeting criteria for High levels of activity, but achieving either of the following: ≥3 days of vigorous-intensity activity of at least 20 minutes/day OR ≥5 days of moderate-intensity or transport activity of at least 30 minutes/day OR ≥5 days of any combination of transport, moderate- or vigorous-intensity activity results in a minimum of ≥600 MET-minutes/week
Low/Sedentary	Not meeting criteria for Moderate or High levels or not reporting any activity at all

Demographic and socioeconomic covariates such as age, gender, race/ethnicity, education, and poverty were all self-reported and obtained from the Demographics section of NHANES. Age was presented in years as a continuous variable, ranging from 0 to 79, with participants 80 years and older coded as 80 years. For this study, age was grouped into three categories: 20-39, 40-59, and 60 and over. The 20-39 category was used as the reference group. Race/ethnicity was presented as either Non-Hispanic (NH) White, NH Black, Mexican American, Other Hispanic, or Other including multi-race. For this study, race/ethnicity was grouped into four categories: NH White, NH Black, Mexican American, or Other. The reference group was NH Whites. Education for adults ≥20 years was presented as five options: <9th grade, 9-11th grade, High school/GED, Some college/AA degree, ≥College graduate. For this study, education was grouped into three categories: <high school, high school/GED, and >high school. The reference group was less than high school. Poverty was presented as a continuous variable, as the ratio of family income to poverty.

Family history of diabetes also was self-reported and obtained from the Diabetes questionnaire section. Health insurance coverage was self-reported and obtained from

the Health Insurance questionnaire section. BMI and waist circumference were obtained from the Body Measures examination section. BMI was calculated from height and weight measurements (kg/m^2), and waist circumference was measured in centimeters. For this study, BMI was grouped into four categories: Underweight (BMI<18.5), Normal weight (18.5<BMI<24.9), Overweight (25<BMI<29.9), and Obese (BMI≥30). The normal weight group was used as the reference group. Hypertension was defined as the mean of 3 blood pressure readings ≥140/90 or use of hypertension medication. Dyslipidemia/high cholesterol was defined as a total cholesterol ≥240 mg/dL or use of dyslipidemia medication.

Study Protocol

Data for this study were retrieved from the NHANES website (http://www.cdc.gov/nchs/nhanes.htm). For this analysis, 4 years of the continuous NHANES survey was used, 2007-2010. To prepare the work dataset, the data files were appended and merged, and the dataset checked for missing data, skip patterns, distributions, and influential outliers. A subset of the population of interest (i.e., pre-diabetic adults, as detailed below in the "Sample" section) was created for use in the analyses.

Sample

Figure 2.2 presents the sample for this study. The total number of participants in the four continuous years of NHANES, 2007-2010, was 20,686. The analyses were restricted to non-pregnant adults ≥20 years who completed both the interview and examination portions (n=11,756), and who were not diagnosed diabetics (if they were ever told by a doctor or other health professional that they have diabetes or sugar diabetes, n=10,316). Inclusion criteria consisted of a morning exam session (to ensure valid fasting times), valid fasting times (between 8 and 24 hours), and complete OGTTs. Undiagnosed diabetics based on blood glucose levels (n=366) were excluded. In all, the

total non-diabetic population (n=3,526) consisted of 1,756 normoglycemic and 1,770 pre-diabetic individuals.

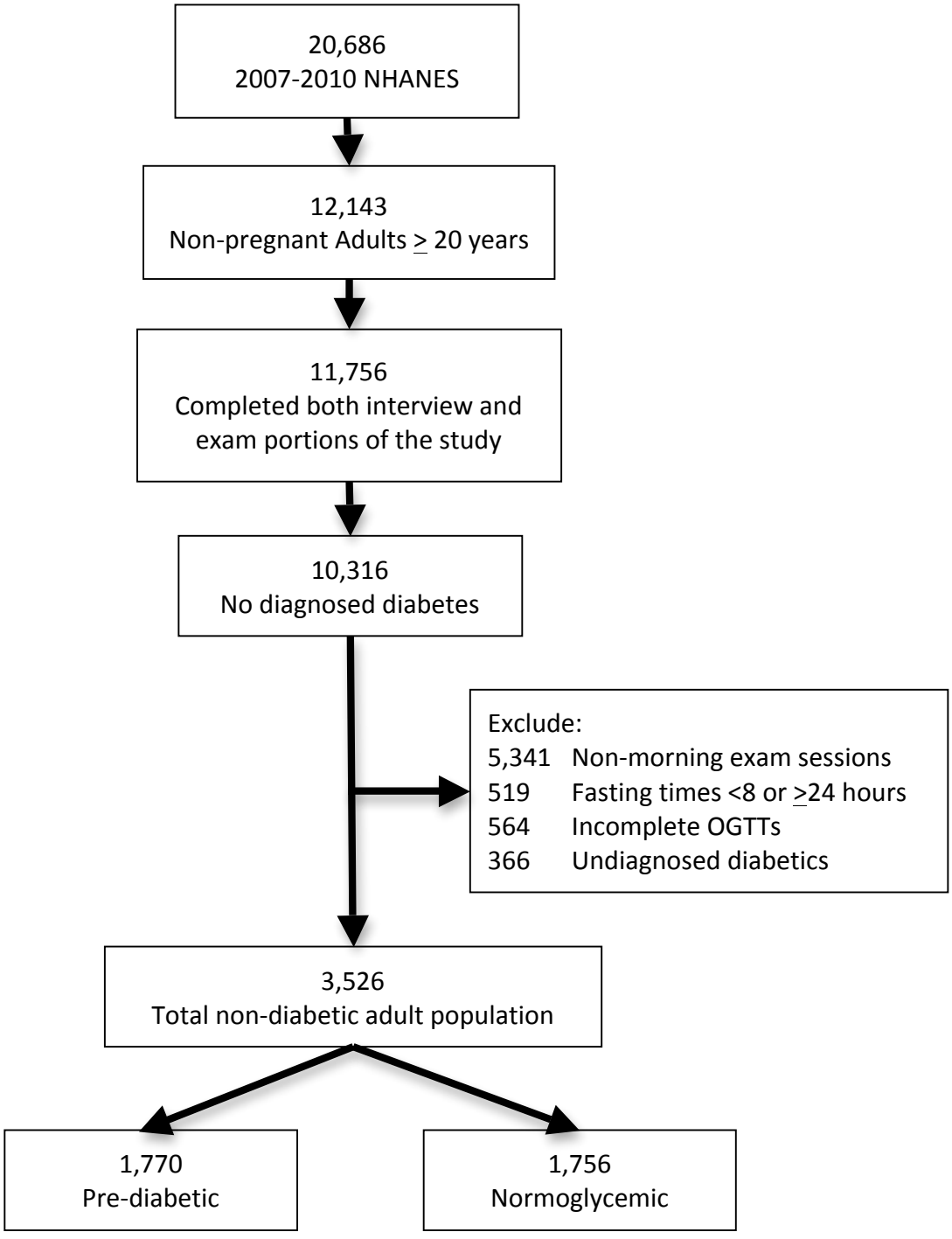

Figure 2.2. Sample for NHANES analysis

Statistical Analysis

Using bivariate analysis techniques, differences between groups were determined by chi-square tests and t-tests. To determine population estimates (i.e. counts and percentages of the U.S. non-institutionalized population that have pre-diabetes), relevant population totals from the Current Population Surveys (CPS) (available on the NHANES website) were used. Briefly, the process entails using *proc surveymeans* in SAS to first calculate the prevalence of pre-diabetes, then combining the appropriate CPS population totals of the subpopulation of interest, and finally multiplying the estimated prevalence with the corresponding CPS population totals. All estimates provided in this study are weighted population estimates.

In the first analysis, multiple logistic regression was used to assess the strength of potential predictors of risk awareness (the dependent variable), including gender, age, race/ethnicity, education, poverty, BMI, waist circumference, hypertensive status, dyslipidemia status, health insurance status, and family history of diabetes (independent variables). In the second analysis, risk awareness as considered as an independent variable (along with gender, age, race/ethnicity, education, poverty, BMI, waist circumference, hypertensive status, dyslipidemia status, health insurance status, family history of diabetes) in predicting diet behaviors (fiber and saturated fat intake) and physical activity behavior among pre-diabetic individuals.

To select the covariates for the statistical models, the *Purposeful Selection* method was used (80). Each of the steps are briefly described below:

1) Fit univariate models for each covariate.
2) Include in the multivariate model all variables with $p<0.25$ from the univariate analyses, as well as any variables not selected with this criterion but deemed to be of clinical and/or conceptual importance.

3) Use p-values from the Wald test to determine which covariates to delete from the multivariate model and the partial likelihood ratio test to confirm that the deleted covariate was not significant.
4) Assess if the removed covariates are important confounders (produces a 20% or greater change in parameter estimates). Important confounders are added back to the model.
5) Repeat steps 3 and 4 for variables excluded in the initial multivariate model until a preliminary final model contains only significant covariates and/or confounders.
6) If interactions are deemed necessary, assess significance of the interaction term in the model by using the partial likelihood ratio test.
7) Assess model adequacy (for logistic regression, by examining influential cases, and model fit with the likelihood ratio, Hosmer-Lemeshow, and c-statistic tests).

In lieu of manual procedures, the *%PurposefulSelection* macro by Bursac, Gauss, Williams, and Hosmer (81) designed to automate the model-building process was used. Because the macro does not assess for interactions, interactions were not included in the analyses. The *%PurposefulSelection* macro consists of three sub-macros that culminate in a final model: *%ScanVar*, which scans the individual covariates; *%UniFit*, which fits the univariate models; and *%MVFit*, which fits the multivariate models iteratively (82).

All analyses were conducted using SAS v9.3 (Cary, NC), using the *proc surveymeans* and *proc surveylogistic* procedures to account for the complex sampling survey design.

Results

In 2007-2010, 46.9% (95% CI=44.4, 49.4), or 93 million, of U.S. adults 20 years or older had pre-diabetes (defined as the presence of either IGT, IFG, or both). The prevalence of pre-diabetes among males was 54.6% (95% CI=51.4, 57.8), and 39.9% (95% CI=37.0, 42.7) among females. Of adults with pre-diabetes, only 15.8% (95%

CI=13.5, 18.0) were aware of their risk status. In addition, less than half (48.9%, 95% CI=46.0, 51.8) had a blood test for diabetes or high blood sugar in the past 3 years.

The characteristics of pre-diabetic adults aware and not aware of their risk status are presented in Table 2.3. The populations were similar in age, race/ethnicity, and educational attainment, though adults aware of their risk status were more likely to be female (54.4% among those aware, compared to 43.3% of those not aware). Adults aware of their risk status were also more likely to have higher BMIs (mean BMI of those aware=31.8, mean BMI of those not aware=29.1) and waist circumferences (mean of those aware=105 cm, mean of those not aware=101 cm). In comparison to adults not aware of their risk status, aware adults were more likely to be hypertensive (45.1% vs. 31.4%) and have high cholesterol (38.3% vs. 26.1%). In addition, 67.4% of adults aware of their risk status reported a family history of diabetes, compared to 30.2% of those not aware.

Table 2.3. Characteristics of U.S. adults with pre-diabetes by risk awareness

	Aware n=285		Not Aware n=1,485		p-value*
	n	Prevalence	n	Prevalence	
Gender					
Male	126	45.6 (3.63)	852	56.7 (1.29)	
Female	159	54.4 (3.63)	633	43.3 (1.29)	**0.0018**
Age					
20-39	79	29.0 (3.06)	363	26.1 (2.36)	
40-59	112	45.4 (3.63)	569	46.6 (2.24)	
≥60	94	25.6 (3.04)	553	27.3 (0.96)	0.7702
Mean	285	49.0 (1.13)	1485	50.1 (0.66)	0.3824
Race/Ethnicity					
NH White	127	64.8 (3.8)	774	73.0 (2.82)	
NH Black	51	11.5 (2.15)	207	7.81 (0.97)	
Mexican American	58	10.0 (2.05)	280	9.1 (1.57)	
Other	49	13.7 (2.49)	224	10.0 (1.58)	0.0529
Education					
<High School	72	18.5 (2.98)	442	19.8 (1.4)	
High School/GED	70	24.8 (3.62)	353	24.8 (1.46)	
>High School	138	56.6 (4.01)	687	55.3 (2.2)	0.8946
BMI					

Underweight	3	0.95 (0.57)	17	1.11 (0.29)	
Normal	35	12.5 (2.90)	328	22.0 (1.85)	
Overweight	92	33.6 (2.99)	574	39.1 (1.61)	
Obese	151	51.3 (3.24)	537	35.6 (1.56)	**0.0005**
Mean	283	31.8 (0.59)	1471	29.1 (0.18)	**0.0001**
Waist circumference (mean)	277	105 (1.11)	1464	101 (0.57)	**0.0014**
Systolic Blood Pressure					
<120	125	48.5 (4.13)	662	48.3 (1.62)	
120-139	102	37.2 (3.89)	546	37.0 (1.58)	
140-159	37	10.1 (1.33)	191	10.7 (0.94)	
≥160	11	1.8 (0.61)	50	2.5 (0.34)	0.8893
Mean	277	121 (1.04)	1460	122 (0.51)	0.2742
Diastolic Blood Pressure					
<80	217	75.3 (3.19)	1207	80.7 (1.31)	
80-89	48	18.8 (2.48)	184	13.9 (1.20)	
90-99	7	2.5 (1.22)	41	2.9 (0.61)	
≥100	3	0.68 (0.40)	9	0.62 (0.29)	0.4468
Mean	277	71.1 (0.55)	1451	70.6 (0.40)	0.2742
Hypertension					
Yes	132	45.1 (2.78)	515	31.4 (1.83)	
No	144	53.2 (2.93)	942	67.4 (1.76)	**<0.0001**
Total cholesterol (mean)	283	199 (2.82)	1481	201 (1.13)	0.3805
LDL (mean)	274	119 (2.37)	1454	122 (1.01)	0.3016
HDL (mean)	283	50.3 (1.01)	1481	51.9 (0.50)	0.1503
Triglycerides (mean)	282	148 (5.27)	1481	140 (3.18)	0.2586
Dyslipidemia					
Yes	101	38.3 (2.73)	377	26.1 (1.07)	
No	130	48.5 (2.80)	668	47.0 (1.42)	**0.0009**
Family history of diabetes					
Yes	201	67.4 (2.79)	457	30.2 (1.83)	
No	83	32.5 (2.80)	987	67.2 (1.84)	**<0.0001**
Health Insurance					
Yes	214	82.3 (2.18)	1102	80.9 (1.37)	
No	71	17.7 (2.18)	380	18.8 (1.33)	0.6283
Poverty Ratio (mean)	256	3.04 (0.13)	1364	3.02 (0.08)	0.8723

Boldface indicates significance at the $p<0.05$ level

*Determined by chi-square and t-tests

As shown in Table 2.4, gender was strongly associated with diabetes risk awareness; specifically, compared to females, males were less likely to be aware of their risk status (0.60, 95% CI=0.44, 0.83). Participants with 30 or greater BMIs were also 2.50 times (95% CI=1.39, 4.52, p=0.0024) more likely to be aware of their risk status, compared to participants with normal BMIs. Similarly, elevated waist circumference was associated with diabetes risk awareness, and a one-centimeter increase in waist circumference conferred a 2% increase in the odds of being aware of risk. The odds of being aware of their risk status for participants with hypertension and dyslipidemia compared to those without the health conditions were 1.84 (95% CI=1.41, 2.39, p<0.0001) and 1.42 (95% CI=1.16, 1.75, p=0.0008), respectively. Finally, having a family history of diabetes was strongly associated with awareness of diabetes risk (OR=4.55, 95% CI=3.19, 6.50, p<0.0001).

Table 2.4. Bivariate analyses of pre-diabetic adults who are aware of diabetes risk

	Risk Awareness	p-value*
Gender		
Male	0.60 (0.44-0.83)	**0.0017**
Female	1.00 (reference)	
Age		
20-39	1.00 (reference)	
40-59	0.89 (0.56-1.41)	0.6212
≥60	0.86 (0.61-1.22)	0.4052
Race/Ethnicity		
NH White	1.00 (reference)	
NH Black	1.63 (1.00-2.68)	0.0525
Mexican American	1.23 (0.81-1.87)	0.3271
Other	1.58 (0.97-2.58)	0.0689
Education		
<High School	1.00 (reference)	
High School/GED	1.03 (0.61-1.72)	0.9182
>High School	1.09 (0.71-1.68)	0.6839
BMI		
Underweight	1.36 (0.30-6.25)	0.6898
Normal	1.00 (reference)	
Overweight	1.43 (0.76-2.69)	0.2676
Obese	2.50 (1.39-4.52)	**0.0024**
Waist circumference	1.02 (1.01-1.03)	**0.0002**
Hypertension	1.84 (1.41-2.39)	**<0.0001**

Yes	1.00 (reference)	
No		
Dyslipidemia		
Yes	1.42 (1.16-1.75)	**0.0008**
No	1.00 (reference)	
Family history of diabetes		
Yes	4.55 (3.19-6.50)	**<0.0001**
No	1.00 (reference)	
Health Insurance		
Yes	1.00 (reference)	
No	0.92 (0.67-1.28)	0.6274
Poverty Ratio	1.01 (0.91-1.12)	0.8716

Boldface indicates significance at the p<0.05 level

The multivariate model selected by the *Purposeful Selection* procedure to explain diabetes risk awareness included the variables of gender, age, race/ethnicity, BMI, waist circumference, hypertension, dyslipidemia, and family history (Table 2.5). Family history of diabetes remained a strong predictor of diabetes risk awareness in the multivariate model (p<0.0001), as did gender (p=0.0002), and the presence of hypertension (p=0.0053) and dyslipidemia (p=0.0054). Pre-diabetic adults with hypertension, dyslipidemia, and a family history of diabetes were 1.45-4.04 times more likely to be aware of their risk status. After multivariate adjustment, those who identified themselves as other/mixed race/ethnicity were more aware of their risk status than Non-Hispanic Whites (OR=2.09, 95% CI=1.14, 3.85). The multivariate model also showed that age was a significant predictor; older pre-diabetic adults (≥60 years) were less likely to be aware of their risk status (OR=0.50, 95% CI=0.27, 0.92).

Table 2.5. Multivariate analysis of pre-diabetic adults who are aware of diabetes risk

	Risk Awareness	p-value
Gender		
Male	0.56 (0.36-0.87)	**0.0002**
Female	1.00 (reference)	
Age		
20-39	1.00 (reference)	
40-59	0.61 (0.33-1.15)	0.1290
≥60	0.50 (0.27-0.92)	**0.0269**
Race/Ethnicity	1.00 (reference)	0.6537

NH White	1.17 (0.59-2.32)	0.3700
NH Black	1.30 (0.73-2.29)	**0.0176**
Mexican American	2.09 (1.14-3.85)	
Other		
Education		
<High School	-	-
High School/GED		
>High School		
BMI		
Underweight	0.78 (0.07-9.20)	0.8410
Normal	1.00 (reference)	
Overweight	1.69 (0.91-3.16)	0.0966
Obese	1.82 (0.82-4.01)	0.1409
Waist circumference	1.01 (0.99-1.03)	0.2295
Hypertension		
Yes	1.78 (1.19-2.67)	**0.0053**
No	1.00 (reference)	
Dyslipidemia		
Yes	1.45 (1.12-1.89)	**0.0054**
No	1.00 (reference)	
Family history of diabetes		
Yes	4.04 (2.64-6.19)	**<0.0001**
No	1.00 (reference)	
Health Insurance		
Yes	-	-
No		
Poverty Ratio	-	-

--, not selected as a significant covariate or confounder for the final model
Boldface indicates significance at the p<0.05 level

The role of diabetes risk awareness in dietary and physical activity behavior of pre-diabetic adults was also examined. Table 2.6 presents the mean saturated fat and fiber intake of pre-diabetic adults, as well as their average daily physical activity. On average, there were no differences in saturated fat intake of those aware of their risk status and those not aware (27.9 grams vs. 27.7 grams, p=0.5562). Similarly, no differences existed in fiber intake between the awareness groups (16.7 grams vs. 16.3 grams, p=0.9327). Pre-diabetic adults not aware of their risk status on average reported

a higher amount of daily physical activity (108 minutes), though they did not significantly differ from those aware of their risk status (95.6 minutes, p=0.2570).

Table 2.6. Average dietary intake and physical activity of pre-diabetic adults in the U.S.

Intake	Aware	Not aware	p-value
Saturated Fat (g)	27.9 (1.33)	27.7 (0.69)	0.5562
Fiber (g)	16.7 (0.65)	16.3 (0.40)	0.9327
Physical Activity* (minutes)	95.6 (0.56)	108 (5.94)	0.2570

Data presented as Means (S.E.)
*Total daily Physical Activity in minutes, including recreation, transportation, and work-related activity

The prevalence of pre-diabetic adults meeting dietary intake and physical activity recommendations are shown in Table 2.7. Similar to assessments of average dietary intake and physical activity, there were no significant differences in awareness groups ($p \geq 0.10$ for comparisons of aware and not aware groups). A slightly lower percentage of pre-diabetic adults aware of their risk status met recommended saturated fat intakes (41.6% vs. 42.1%), and a higher percentage met fiber intake recommendations (11.2% vs. 10.0%). However, slightly more pre-diabetic adults not aware of their risk status met physical activity recommendations (55.2% vs. 52.8%).

Table 2.7. Percent of pre-diabetic adults meeting dietary intake and physical activity recommendations

Recommendation	Aware	Not aware
Saturated Fat	41.6 (3.64)	42.1 (1.79)
Fiber	11.2 (2.14)	10.0 (1.09)
Physical Activity	52.8 (3.81)	55.2 (2.18)

Data presented as % (SE)

Three multivariate models were used to assess the role of diabetes risk awareness in meeting recommendations for 1) saturated fat intake, 2) fiber intake, and 3) physical activity. Again, variables included in the models were selected using the *Purposeful Selection* method.

The association of diabetes risk awareness with meeting saturated fat intake recommendations disappeared after adjustment for age, race/ethnicity, education, BMI, waist circumference, dyslipidemia status, health insurance, and awareness (OR=0.89, 95% CI=0.63, 1.26) (Table 2.8). In this multivariate model, race/ethnicity was significantly associated with meeting saturated fat intake recommendations, with NH Blacks (OR=2.29, 95% CI=1.55, 3.36), Mexican-Americans (OR=1.80, 95% CI=1.27, 2.56), and Other/Mixed (OR=2.13, 95% CI=1.37, 3.29) more likely to meet saturated fat intake recommendations compared to NH Whites. In addition, pre-diabetic adults with health insurance were 73% more likely to meet saturated fat intake recommendations compared to those without health insurance.

Risk awareness was also not significantly associated with meeting fiber intake recommendations (OR=0.92, 95% CI=0.51, 1.66) after adjustments for gender, age, race/ethnicity, education, poverty, BMI, waist circumference, hypertension status, and family history of diabetes. Race/ethnicity and education were significant predictors of meeting fiber intake recommendations. Specifically, Mexican-Americans (OR=2.07, 95% CI=1.08, 3.93) and pre-diabetic adults with greater than a high school education (OR=1.85, 95% CI=1.14, 3.00) were more likely to meet fiber intake recommendations.

Table 2.8. Multivariate analyses of dietary intake among pre-diabetic adults

	Diet: Saturated Fat	p-value	Diet: Fiber	p-value
Gender				
Male	-	-	0.76 (0.50-1.17)	0.2086
Female			1.00 (reference)	
Age				
20-39	1.00 (reference)		1.00 (reference)	
40-59	0.74 (0.49-1.13)	0.1586	1.38 (0.67-2.85)	0.3865
≥60	1.19 (0.89-1.57)	0.2387	1.95 (0.82-4.62)	0.1285
Race/Ethnicity				
NH White	1.00 (reference)		1.00 (reference)	
NH Black	2.29 (1.55-3.36)	**<0.0001**	1.01 (0.47-2.17)	0.9899
Mexican American	1.80 (1.27-2.56)	**0.0010**	2.07 (1.08-3.93)	**0.0275**
Other	2.13 (1.37-3.29)	**0.0007**	1.09 (0.51-2.33)	0.8322
Education				

<High School	1.00 (reference)		1.00 (reference)	
High School/GED	0.74 (0.45-1.21)	0.2300	0.99 (0.57-1.71)	0.9731
>High School	0.81 (0.47-1.38)	0.4271	1.85 (1.14-3.00)	**0.0135**
BMI				
Underweight	0.15 (0.03-0.86)	**0.0334**	0.45 (0.07-3.06)	0.4179
Normal	1.00 (reference)		1.00 (reference)	
Overweight	0.81 (0.51-1.27)	0.3556	1.01 (0.48-2.10)	0.9835
Obese	0.70 (0.41-1.21)	0.1990	1.13 (0.33-3.95)	0.8432
Waist circumference	0.98 (0.97-1.00)	0.0609	1.00 (0.97-1.03)	0.9720
Hypertension				
Yes	-	-	1.72 (0.93-3.19)	0.0867
No			1.00 (reference)	
Dyslipidemia				
Yes	1.12 (0.89-1.41)	0.3152	-	-
No	1.00 (reference)			
Family history of diabetes				
Yes	-	-	1.20 (0.70-2.08)	0.5048
No			1.00 (reference)	
Health Insurance				
Yes	1.73 (1.04-2.86)	**0.0337**	1.61 (0.82-3.15)	0.1658
No	1.00 (reference)		1.00 (reference)	
Poverty Ratio	-	-	1.06 (0.89-1.28)	0.5034
Risk Awareness				
Yes	0.89 (0.63-1.26)	0.5105	0.92 (0.51-1.66)	0.7803
No	1.00 (reference)		1.00 (reference)	

--, not selected as a significant covariate or confounder for the final model

Similarly to dietary recommendations, diabetes risk awareness was not a significant predictor of meeting physical activity recommendations after adjustment for gender, age, race/ethnicity, education, poverty, BMI, waist circumference, hypertension and dyslipidemia status (Table 2.9). However, males were significantly more likely to meet physical activity recommendations (OR=2.24, 95% CI=1.56, 3.22). Pre-diabetic adults over the age of 60 were less likely than younger pre-diabetic adults to meet physical activity recommendations (OR=0.41, 95% CI=0.23, 0.72), as well as those with BMIs less than 18.5 (OR=0.10, 95% CI=0.02, 0.49).

Table 2.9. Multivariate analysis of physical activity among pre-diabetic adults

	Physical Activity	p-value
Gender		
Male	2.24 (1.56-3.22)	**<0.0001**
Female	1.00 (reference)	
Age		
20-39	1.00 (reference)	
40-59	0.66 (0.38-1.16)	0.1501
≥60	0.41 (0.23-0.72)	**0.0021**
Race/Ethnicity		
NH White	1.00 (reference)	
NH Black	0.88 (0.62-1.27)	0.5017
Mexican American	0.96 (0.60-1.54)	0.8598
Other	0.63 (0.35-1.12)	0.1129
Education		
<High School	1.00 (reference)	
High School/GED	0.83 (0.51-1.35)	0.4488
>High School	1.08 (0.74-1.57)	0.6939
BMI		
Underweight	0.10 (0.02-0.49)	**0.0048**
Normal	1.00 (reference)	
Overweight	0.89 (0.59-1.34)	0.5743
Obese	0.93 (0.50-1.72)	0.8072
Waist circumference	0.98 (0.96-1.00)	0.0582
Hypertension		
Yes	0.88 (0.58-1.33)	0.5328
No	1.00 (reference)	
Dyslipidemia		
Yes	1.09 (0.80-1.50)	0.5890
No	1.00 (reference)	
Family history of diabetes		
Yes	0.82 (0.56-1.22)	0.3275
No	1.00 (reference)	
Health Insurance		
Yes	-	-
No		
Poverty Ratio	1.00 (0.91-1.10)	0.9777
Risk Awareness		
Yes	1.17 (0.78-1.75)	0.4485
No	1.00 (reference)	

Discussion

In 2007-2010, 46.9% of U.S. adults had pre-diabetes, placing them at high risk for diabetes. Less than 20% of those at risk were aware of their increased risk status. These numbers indicate a rise in the prevalence of pre-diabetes, as in 2005-2006, 29.6% of U.S. adults had pre-diabetes (59). The proportion of pre-diabetics who were aware of their elevated risk status was greater, 15.8% in comparison to 7.3% in 2005-2006. However, the increased awareness may be a result of the differences in risk awareness assessment; in 2005-2006, awareness was specifically knowledge of a pre-diabetic condition, while in this analysis, a more comprehensive assessment was used to capture overall diabetes risk awareness. Here, awareness was defined as knowledge of a pre-diabetic condition or knowledge of health/medical conditions and/or a family history that raises risk for diabetes. Regardless, the results indicate that overall awareness of diabetes risk is low among U.S. adults at increased risk for diabetes. Considering the increasing prevalence of pre-diabetes in the U.S., these findings suggest that low awareness continues to be a problem, possibly causing delays in treatment and prevention of micro- and macrovascular complications (58).

This is the first study to examine the predictors of pre-diabetes risk awareness. Other studies have focused on awareness for diagnosed diabetes. For diagnosed diabetes, education is a significant predictor of awareness, with higher levels of education conferring in higher levels of awareness (83, 84). Tang et al (85) also found higher levels of education to affect awareness levels by influencing health literacy. Conversely, this study did not find education to be a significant predictor of diabetes risk awareness in pre-diabetic adults. Gender, however, was a significant predictor, with males significantly less likely to be aware of their risk status in comparison to females. In contrast, the inverse is true in the case of diagnosed diabetes, with males more likely to be aware of their condition (83, 86). The multivariate results from this study also indicate that older age (i.e. $\geq$60 years) is a significant predictor of risk awareness, with older pre-diabetic adults significantly less likely to be aware of their risk. Similar observations are seen in awareness analyses in diagnosed diabetics; older adults with

diagnosed diabetes have low levels of awareness of their condition (87-89).

Co-morbid conditions and a family history of diabetes are also significant predictors of risk awareness for pre-diabetic adults. The results suggest that having co-morbid conditions such as hypertension and dyslipidemia is strongly associated with awareness (hypertension incurs a 78% increase in the odds of being aware, dyslipidemia a 45% increase). Additionally, a family history of diabetes also increases the odds of being aware of risk status by more than 4 times. In contrast, co-morbid conditions and family history are not significant predictors of awareness in diabetes (83). The results suggest that co-morbid conditions and family history play a more important role in knowledge of diabetes risk rather than knowledge of diagnosed diabetes.

Such associations are not surprising, as hypertension, dyslipidemia, and family history are common risk factors for diabetes, and are used in estimating diabetes risk (90). Hence, it is reasonable to assume that the presence of these risk factors increases the likelihood of at-risk individuals being aware of their risk status, further validating their role in not only risk estimation, but also risk awareness. However, the results also signify the need to increase awareness of pre-diabetic adults that do not have these indicators, as pre-diabetic individuals may not necessarily have obvious co-morbid risk factors.

In the second part of the analysis, the role of risk awareness in diet and physical activity behavior in pre-diabetic adults was examined. Previous studies were unable to do this due to sample size constraints (59). There were no differences in diet and physical activity between pre-diabetic adults who are aware of their risk status and those who are not aware; less than half of both groups (aware and not aware) met recommendations for saturated fat intake, and about 90% in both groups did not meet recommendations for dietary fiber intake. Similar proportions were also seen in physical activity behavior, with about half of each group meeting physical activity recommendations. These results show that awareness does not affect dietary and physical activity behavior, a finding that was confirmed in the multivariate analysis,

where risk awareness was not a significant predictor of either dietary or physical activity behavior. While the results indicate that overall intervention is needed to help pre-diabetic individuals meet dietary and physical activity recommendations, it also suggests that other factors beyond awareness alone are important in diet and physical activity behavior of at-risk individuals. This is consistent with health behavior research that presents awareness as one step in several that lead to behavior change (91).

Other factors beside risk awareness, such as health insurance, were significant in predicting whether pre-diabetic individuals met diet and physical activity recommendations. Although this study did not delineate how health insurance impacts saturated fat intake, it may be that health insurance leads to physician advice, which has been shown in the literature to be associated with adoption of healthy behaviors (92, 93). Additionally, higher levels of education significantly increased the odds of meeting fiber intake by 85%. Males were also more likely to meet physical activity recommendations, a finding echoed by a previous study that used self-reported data from the Medical Expenditure Panel Survey (94). These variables highlight factors that are associated with meeting dietary and physical activity recommendations; however, these are not the only ones. Additional research will be needed to determine effective ways to encourage risk-reducing behaviors.

Strengths and Limitations

The major strengths of this study include the nationally representative sample, examinations by medical professionals, and standard measures of physiological (e.g. BMI, waist circumference, blood pressure) and laboratory (e.g. blood glucose and cholesterol levels) data. Also, this study provides data from the most current NHANES, and has a larger sample size than previous studies, allowing for more detailed analyses on the role of risk awareness. However, the results of this study are also subject to limitations. First, NHANES is a cross-sectional survey, so causality cannot be determined, only associations. Because of the lack of a temporal component, the cause-and-effect is unknown, and whether risk awareness preceded health behaviors or vice-

versa. Second, the measures of physical activity and dietary intake, while standardized, were reliant on self-reports and subject to biases. Such reporting limitations are especially evident in dietary intake assessments, and NHANES notes that the measurement error in the dietary recall data includes both random error and biases (95). Random error occurs because recall data is only a snapshot of intake and may not reflect usual dietary intake; however, the variability is assumed to cancel out. Biases occur because there is a generalized tendency towards under under-reporting of total energy, which may or may not be differential. Analyses with dietary recall data operate with the assumption that there is no bias (that is, that there is no under-reporting). Finally, this study used the statistical software package SAS. While both statistical software packages SAS and SUDAAN produce identical beta coefficients and odds ratio estimates, estimates of the confidence intervals and variance may differ between the two programs. Both SAS and SUDAAN produce the Wald statistic and its corresponding p-value, but the logistic regression procedure in SUDAAN also produces the Satterthwaite χ^2 or the Satterthwaite F and their corresponding p-values. The Satterthwaite adjustment produces a more conservative result, though this adjustment effect decreases as sample sizes increase (96).

Conclusion

In conclusion, awareness of diabetes risk remains low with less than a fifth of pre-diabetic adults in the U.S. aware of their risk status. More than half of pre-diabetic adults did not meet saturated fat intake recommendations for prevention of diabetes, and nearly 90% did not meet fiber intake recommendations. In addition, only about half of at-risk individuals met the physical activity recommendations for diabetes prevention. This study identified gender, family history, and co-morbid conditions as predictors of risk awareness, which is important in efforts to increase awareness of diabetes risk. However, increasing risk awareness is only a first step in diabetes prevention; as this study showed, awareness alone is not a significant predictor of at least some types of preventative behavior. Awareness will likely be a part of overall diabetes prevention efforts.

CHAPTER 3: STUDY 2

Abstract

Background. Translating the Diabetes Prevention Program (DPP) would most likely benefit at-risk individuals and aid in efforts to decrease diabetes incidence. While the DPP used the expensive and inconvenient OGTT to identify diabetes risk, more practical methods that effectively predict diabetes risk in Native Hawaiians, a group at increased risk for diabetes, are needed.

Purpose. To examine: 1) the predictive ability of the metabolic syndrome and its comparability to IFG in assessing diabetes risk in Native Hawaiians and 2) the combined effect of the metabolic syndrome and IFG on diabetes prediction.

Methods. Secondary data analysis of the Kohala Health Study that included 283 Native Hawaiians at risk for diabetes. Cox proportional hazards models were used to estimate the effect of the metabolic syndrome on diabetes development, and to assess the combined effect of the metabolic syndrome and IFG on diabetes development.

Results. The metabolic syndrome was significantly predictive of diabetes development in both Native Hawaiian men (HR=5.95, 95% CI=1.18, 29.98) and women (HR=19.17, 95% CI=2.48, 147.9). In comparison, IFG alone was not a significant predictor of diabetes development in Native Hawaiian men, and was comparable to the metabolic syndrome for Native Hawaiian women. The metabolic syndrome combined with IFG was predictive of diabetes (HR=5.77, 95% CI=2.51, 13.27), although both the metabolic syndrome excluding IFG and IFG alone did not significantly increase risk for developing diabetes.

Conclusions. The metabolic syndrome significantly increases the risk of diabetes in Native Hawaiians, although it is not independent of IFG. Adding the metabolic syndrome criteria to IFG also significantly predicts diabetes risk. The metabolic syndrome is a potential tool to identify Native Hawaiians at risk for diabetes.

Introduction

Clinical trials such as the Diabetes Prevention Program (DPP) have provided evidence that diabetes is preventable (48). Translating the DPP would most likely benefit at-risk individuals and aid in efforts to decrease diabetes incidence. However, one of the challenges in translating the DPP is the identification of persons at-risk. Diabetes risk identification is typically reliant on plasma glucose, and the DPP used fasting plasma glucose (FPG) and 2-hour 75-gram oral glucose tolerance test (OGTT) values to identify at-risk individuals (48). This poses a barrier in translation efforts, as the OGTT to detect impaired glucose tolerance (IGT) is costly, inconvenient, and arduous (97) and not practical in real-world settings. FPG to detect impaired fasting glucose (IFG) can be used to identify risk status, and compared to the OGTT, is a more convenient laboratory assessment. However, studies have shown IGT to be a stronger predicator of diabetes (25, 98-100), and up to 60% of persons with IGT do not have IFG (100-102). Thus, it is important to investigate if other methods may be used to identify at-risk individuals that would benefit from prevention programs.

The metabolic syndrome is a cluster of related cardiovascular disease (CVD) risk factors that includes measures of impaired fasting glucose along with central adiposity, dyslipidemia, and elevated blood pressure (103). Research indicates that it plays a significant role in diabetes and CVD development (104), and thus may be a helpful tool in assessing diabetes risk (65, 66, 104-111). Further, the components that constitute the metabolic syndrome (waist circumference, blood pressure, triglycerides, HDL cholesterol, and fasting plasma glucose) may offer a more practical and convenient alternative to OGTTs. However, because the metabolic syndrome includes IFG as part of its criteria, it is unclear whether the metabolic syndrome offers predictive value beyond IFG alone (66, 104, 108, 109). In addition, while previous studies have shown the metabolic syndrome to be comparable to IFG in predicting diabetes risk in Mexican Americans (64) and Asian populations (67), it is unknown if the metabolic syndrome effectively predicts diabetes risk in Native Hawaiians, an ethnic group at increased risk for diabetes (112), and whether it offers comparability to IFG in predicting diabetes

development. Effective identification of Native Hawaiians at-risk is especially crucial, given the prevalence of risk factors in the population: obesity, elevated BMI, and central adiposity (113).

The purpose of this study is to examine 1) the predictive ability of the metabolic syndrome and its comparability to IFG in assessing diabetes risk in Native Hawaiians and 2) the combined effect of the metabolic syndrome and IFG on diabetes prediction. This is a retrospective study using data from the Kohala Health Study, conducted between 1993 and 2000. The Kohala Health Study provides temporal data on the development of diabetes, as well as relevant anthropometric and blood glucose measures, that can be used to examine the predictive ability of the metabolic syndrome in Native Hawaiians.

Methods

Study Design and Sample

The Kohala Health Study (KHS) was an epidemiological study assessing diabetes and cardiovascular risks in the multiethnic Hawaii island community of North Kohala. The design of the study has been previously described in detail (114). Briefly, the Kohala Study's multiethnic population consisted of 295 Caucasians, 186 Filipinos, 190 Japanese, 255 Other/Mixed not including Native Hawaiians, and 526 Native Hawaiians with 10 who reported 100% Native Hawaiian ancestry. Although findings on the prevalence of impaired glucose tolerance and metabolic syndrome in the Kohala Study multiethnic population have been reported (112, 115, 116), the potential of the metabolic syndrome in predicting diabetes development has not yet been examined. This study was a secondary data analysis to examine the metabolic syndrome as a diabetes predictive tool in Native Hawaiians from the Kohala Health Study. For this study, a panel (cohort) design with two time-points, baseline and follow-up, was used.

The sample for the secondary data analysis were Kohala residents of Native Hawaiian ethnicity (n=526) who completed initial examinations in the Native Hawaiian Health Research (NHHR) study between 1993 and 1995. Of the 526 Native Hawaiians

that participated in the NHHR study, 359 came from the Kohala area, and were invited to participate in the follow-up, the Kohala Health Study (KHS). The KHS collected data between 1997 and 2000. Of the 359 Native Hawaiians residing in the Kohala area that participated in the initial examination, 335 (93%) participated in the follow-up. After excluding 76 participants who did not complete the follow-up examination and/or were diagnosed diabetics, 283 Native Hawaiian subjects were included in the present study. Baseline characteristics were used to predict diabetes development at follow-up. This study was approved by the University of Hawaii IRB (CHS #20303).

Measures

Study participants completed OGTTs and plasma blood tests after fasting overnight for a minimum of 8 hours. Diabetic participants or participants taking insulin/oral glucose medications were excluded from the OGTT. Blood for the plasma glucose tests were obtained through venipuncture. American Diabetes Association (ADA) criteria were used to determine IFG (100-125 mg/dL) and IGT (140-199 mg/dL).

Waist circumference was measured at the umbilical level of the participant in a standing position. Blood pressure was measured with a mercury sphygmomanometer on the right arm. Waist and blood pressure measurements were taken three times each and averaged for a final measurement. Lipid levels were obtained through blood results.

Questionnaires were used to gather information on demographics, medical history including family history of diabetes, and participant health behaviors such as diet, smoke and alcoholic drink status, and physical activity.

Definitions

The metabolic syndrome was defined by the 2009 harmonized criteria proposed by: the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart

Federation; International Atherosclerosis Society; and International Association for the Study of Obesity (103). Metabolic syndrome is defined as the presence of three or more of the five factors: elevated waist circumference (≥102 cm for men and ≥88 cm for women, AHA/NHLBI (ATP III) definitions for the United States population), elevated triglycerides (≥150 mg/dL), reduced HDL cholesterol (<40 mg/dL for men and <50 mg/dL for women), elevated blood pressure (SBP ≥130 mmHg and/or DBP ≥85 mmHg), and elevated fasting glucose (≥100 mg/dL).

Statistical Analysis

As time-to-event data was available, survival analysis was used to assess diabetes development in at-risk Native Hawaiians (117). When time-to-event data is available, survival analysis offers an advantage over other methods that only examine whether an outcome occurs or not by accounting for censoring. Censoring allows for the inclusion of individuals who leave the study early (e.g. due to drop out or death).

Survival times and censoring variables were created prior to running the analysis. Survival time was defined as the time from the start of the study (the baseline examination date) to when one of three things occurred: 1) the participant develops the event of interest, diabetes; 2) another event occurs that excludes the participant from being at risk for diabetes (i.e. drop out from the study or death); or 3) the end of the study occurs. Ties in survival times were handled with the Exact partial likelihood method, which assumes that the ties are due to a lack of precision in measuring survival time. Censoring variables were created to indicate whether a participant's survival time represents time to event, time to exclusionary event, or time to end of study.

The Kaplan-Meier/product limit estimator method was used to examine the survival distribution functions, which provided information on whether the "survival" of the participants differed on incidence of diabetes by their risk status (i.e. no metabolic syndrome or IFG, metabolic syndrome only, IFG only, both metabolic syndrome and IFG). The non-parametric log-rank test was used to compare the survival functions.

Unadjusted and adjusted hazard ratios (HRs) for the outcome, development of diabetes, were obtained using the semi-parametric Cox proportional hazards model (hereafter referred to as "Cox model"). The Cox model was used to determine covariate effects on survival function while leaving the dependence on time unspecified (117). The counting-process form of the Cox model was used to accommodate for interval censoring (that is, the event time is not directly observed and the event is only known to have occurred within a time interval), which was observed in this study.

The *Purposeful Selection of Covariates* method proposed by Hosmer, Lemeshow, and May (2008) was used to develop the statistical models (117). The method considers both statistical and clinical/conceptual significance and consists of eight steps, briefly described below:

8) Fit univariate models for each covariate.
9) Include in the multivariate model all variables with $p<0.25$ from the univariate analyses, as well as any variables not selected with this criterion but deemed to be of clinical and/or conceptual importance.
10) Use p-values from the Wald test to determine which covariates to delete from the multivariate model and the partial likelihood ratio test to confirm that the deleted covariate was not significant.
11) Assess if the removed covariates are important confounders (produces a 20% or greater change in parameter estimates). Important confounders are added back to the model.
12) Repeat steps 3 and 4 for variables excluded in the initial multivariate model until a preliminary final model contains only significant covariates and/or confounders.
13) Examine the scale of continuous covariates. Test if the effect of the covariate is linear in the log hazard. Use transformations for non-linear continuous covariates.

14) If interactions are deemed necessary, assess significance of the interaction term in the model by using the partial likelihood ratio test.
15) Assess model adequacy by verifying the statistical significance of covariates, the assumption of linearity in the Cox model, the assumption of proportional hazards, influential subjects, and overall model goodness-of-fit (117).

All analyses were conducted using SAS v9.3 (Cary, NC) and R (http://www.r-project.org/).

Results

Following a recommended rule for including a minimum of 10 outcome events per covariate included in the statistical model (118, 119), the identified significant covariates ascertained from the *Purposeful Selection of Covariates* model-building process were Age and Body Mass Index (BMI). The results are presented with and without adjustment for these confounders. Unadjusted HRs are provided, as the harmonized criteria for metabolic syndrome diagnosis does not indicate age- or BMI-specific criteria.

Characteristics of the 283 study participants are shown in Table 3.1. During the follow-up, 23 subjects developed diabetes (10 males and 13 females). Subjects who developed diabetes were on average older in age, had a family history of diabetes, and had higher average glucose and total cholesterol and triglycerides at baseline. Incident diabetic subjects also had lower mean HDL cholesterol levels, and higher BMIs, blood pressure, and central adiposity. Subjects who did not develop diabetes were also less likely to be current smokers and reported more physical activity.

Table 3.1. Baseline characteristics of Kohala Health Study participants that did not and did develop diabetes by follow-up.

	Developed Diabetes	
	No (n=260)	**Yes** (n=23)
Age	43.3 ± 11.4	53.7 ± 9.1
Men	42%	43%
Family history of diabetes	59%	65%
Fasting plasma glucose (FPG) (mg/dL)	97.6 ± 9.2	110.4 ± 8.9
2-hour postload glucose (mg/dL)	105.7 ± 32.1	138.6 ± 34.1
Total cholesterol (mg/dL)	196.7 ± 42.3	218.6 ± 36.2
Triglycerides (mg/dL)	128 ± 106.3	228.5 ± 187.1
HDL cholesterol (mg/dL)	43.1 ± 13.6	34.9 ± 13.8
Systolic blood pressure (SBP) (mmHg)	125 ± 16.4	135.7 ± 20.8
Diastolic blood pressure (DBP) (mmHg)	80.4 ± 11.5	84.1 ± 15.4
BMI	28.8 ± 5.5	33.4 ± 6.3
Waist circumference (cm)	92.6 ± 14.3	103.6 ± 14.1
Waist-hip ratio	0.87 ± 0.1	0.89 ± 0.1
Current smoker	31%	35%
Physical Activity (mean MET-hours)	31.9 ± 39.3	22.2 ± 28.7

Data presented as Mean±S.D. or prevalent percent

Kaplan-Meier/product-limit survival plots of diabetes incidence are displayed in Figure 3.1. The log-rank test indicated statistically significant differences ($p<0.0001$) in the incidence of diabetes among the 4 categories (absence of the metabolic syndrome and IFG, presence of the metabolic syndrome, presence of IFG, and presence of both the metabolic syndrome and IFG).

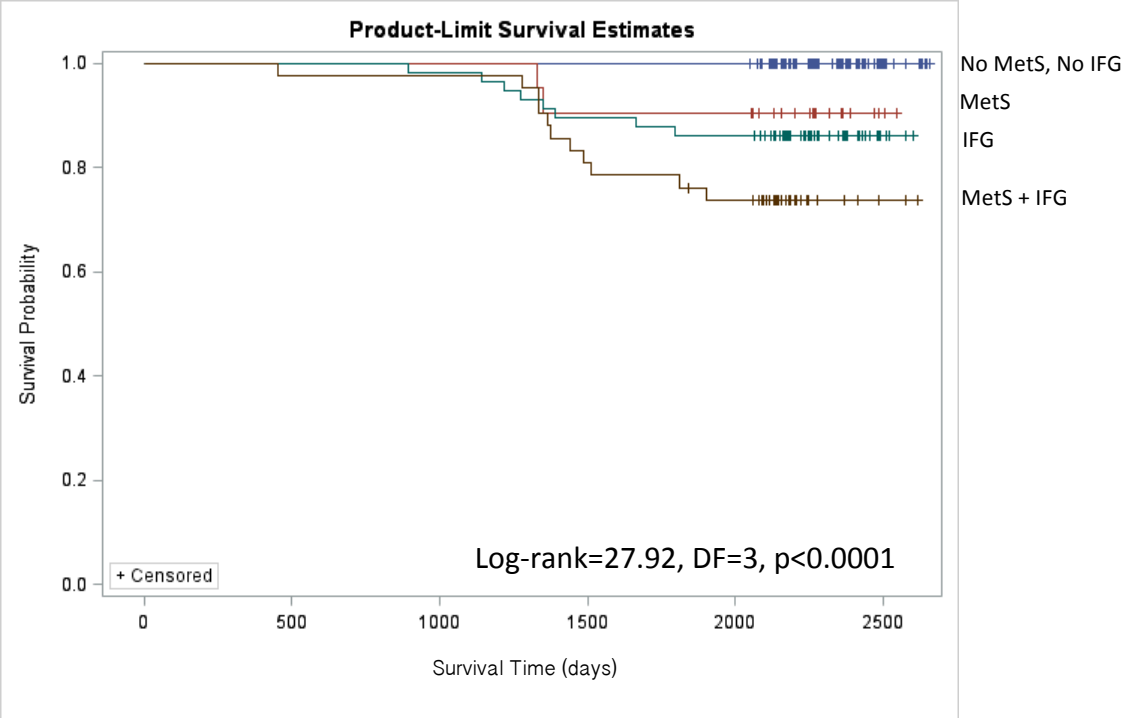

Figure 3.1. Kaplan-Meier survival distribution function of diabetes incidence

Due to the sex-specific criteria for males and females of waist circumference and HDL cholesterol, the metabolic syndrome and each individual component were assessed by sex (Table 3.2). The metabolic syndrome was a significant risk factor for diabetes in both sexes, and remained a significant risk factor for females even after adjustment for the identified confounders of age and BMI. Among males with the metabolic syndrome, the rate of developing diabetes is 5.95 times larger than among males who do not have the metabolic syndrome ($HR_{unadjusted}$=5.95, 95% CI=1.18-29.98, p<0.05). Females with the metabolic syndrome develop diabetes at about 19 times the rate of females without the metabolic syndrome ($HR_{unadjusted}$=19.17, 95% CI=2.48-147.9, p<0.05). After adjustment for age and BMI, the metabolic syndrome remains a significant risk factor for diabetes in females ($HR_{unadjusted}$=12.33, 95% CI=1.57-99.09, p<0.05). None of the HRs for the individual components of the metabolic syndrome indicated significant predictions for males, though all, with the exception of reduced HDL cholesterol, were significantly associated with risk of diabetes development in females. Of the individual components, impaired fasting glucose (IFG) was the strongest

predictor of diabetes development for both males and females, and it was significantly predictive in females ($HR_{unadjusted}$=19.72, 95% CI=2.55-152.9, p<0.05). For males, the metabolic syndrome was a stronger predictor of diabetes development than IFG, but for females, IFG was a stronger predictor.

Table 3.2. Hazard Ratios (HRs) for the development of diabetes associated with the Metabolic Syndrome and its individual components by Sex

	Population at risk (n)	Number of events	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Male				
Metabolic Syndrome (Harmonized criteria)				
(-)	66	2	1.00 (reference)	1.00 (reference)
(+)	54	8	5.95 (1.18-29.98)*	3.76 (0.66-21.60)
Elevated waist circumference				
(-)	90	6	1.00 (reference)	1.00 (reference)
(+)	30	4	1.77 (0.50-6.32)	0.75 (0.15-3.87)
Elevated triglycerides				
(-)	74	4	1.00 (reference)	1.00 (reference)
(+)	46	6	2.10 (0.59-7.47)	2.09 (0.57-7.63)
Reduced HDL cholesterol				
(-)	46	2	1.00 (reference)	1.00 (reference)
(+)	74	8	2.80 (0.59-13.24)	2.42 (0.46-12.86)
Elevated blood pressure				
(-)	67	4	1.00 (reference)	1.00 (reference)
(+)	53	6	1.75 (0.43-7.12)	1.08 (0.24-4.96)
Elevated fasting glucose				
(-)	71	2	1.00 (reference)	1.00 (reference)
(+)	48	8	4.67 (0.58-37.45)	5.48 (0.59-50.51)
Female				
Metabolic Syndrome (Harmonized criteria)				
(-)	98	1	1.00 (reference)	1.00 (reference)
(+)	65	12	19.17 (2.48-147.9)*	12.33 (1.57-99.09)*
Elevated waist circumference				
(-)	77	1	1.00 (reference)	1.00 (reference)
(+)	86	12	9.93 (1.29-76.51)*	4.34 (0.43-43.39)
Elevated triglycerides	127	7	1.00 (reference)	1.00 (reference)
(-)	36	6	3.16 (1.05-9.43)*	1.93 (0.57-6.53)

(+)				
Reduced HDL cholesterol				
(-)	50	1	1.00 (reference)	1.00 (reference)
(+)	113	12	5.06 (0.66-39.01)	8.18 (0.89-75.59)
Elevated blood pressure				
(-)	64	5	1.00 (reference)	1.00 (reference)
(+)	99	8	3.00 (0.98-9.20)*	1.78 (0.50-6.32)
Elevated fasting glucose				
(-)	52	2	1.00 (reference)	1.00 (reference)
(+)	109	11	19.72 (2.55-152.9)*	15.72 (2.01-122.6)*

*significant at the p<0.05 level
Multivariate adjustment made for age and body mass index. Elevated waist circumference defined as ≥102cm for males and ≥88cm for females (AHA/NHLBI (ATP III) recommended threshold for the United States); elevated triglycerides defined as ≥150mg/dL; reduced HDL cholesterol defined as <40mg/dL for males and <50mg/dL for females; elevated blood pressure defined as SBP≥130mmHg and/or DBP≥85mmHg; elevated fasting glucose defined as ≥100mg/dL.

Because IFG has been shown to be a strong predictor of diabetes development, the individual components of the metabolic syndrome with and without IFG were examined (Table 3.3). For subjects without IFG, no events occurred with one to two individual metabolic syndrome components, and 1 event each occurred with three or four components. Subjects without IFG but with 4 components of the metabolic syndrome saw a non-significant higher rate of diabetes development within the study period ($HR_{unadjusted}$=3.24, 95% CI=0.43-24.45). However, subjects with IFG significantly increased their risk for developing diabetes with increasing number of metabolic syndrome components (one component: 1.49 (0.44-5.05), two components: 1.90 (0.70-5.18), three components: 3.32 (1.39-7.93), four components: 3.32 (1.39-7.93), unadjusted P_{trend}<0.05).

Table 3.3. Hazard Ratios (HRs) for diabetes development in association to number of Metabolic Syndrome components excluding IFG

IFG status	# of MetS components excluding IFG	Population at risk (n)	Number of events	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
(-)	0	28	0	1.00 (reference)	1.00 (reference)
	1	49	0	-**	-**
	2	50	0	-**	-**
	3	20	1	0.62 (0.08-4.58)	0.15 (0.02-1.43)
	4	8	1	3.24 (0.43-24.45)	2.75 (0.36-20.96)
(+)	0	13	0	1.00 (reference)	1.00 (reference)
	1	22	3	1.49 (0.44-5.05)	2.47 (0.69-8.85)
	2	35	5	1.90 (0.70-5.18)	2.28 (0.81-6.40)
	3	43	10	3.32 (1.39-7.93)	2.07 (0.85-5.01)
	4	12	3	4.26 (1.25-14.48)*	3.29 (0.93-11.66)

*P_{trend} significant at the <0.05 level
**No events; HR could not be computed.
Multivariate adjustment made for age and body mass index.

Finally, the separate predictive abilities of the metabolic syndrome excluding IFG, as well as the combined effect of the metabolic syndrome and IFG, were assessed (Table 3.4). For this analysis, the metabolic syndrome was defined as the presence of 3 or more components excluding IFG. The analysis showed IFG to be a consistent, though non-statistically significant, predictor of diabetes development during the study period ($HR_{unadjusted}$=1.40, 95% CI=0.59-3.32, $HR_{adjusted}$=2.37, 95% CI=0.93-6.04). The singular presence of the metabolic syndrome excluding IFG was not a significant predictor of incident diabetes for Native Hawaiians. However, the presence of both the metabolic syndrome (defined as any 3 components excluding IFG) and IFG were significantly associated with diabetes development during the study period. The adjusted HR for incident diabetes during the study period was significantly higher in subjects with the combined effect of the metabolic syndrome (defined as any 3 components excluding IFG) and IFG ($HR_{adjusted}$=3.46, 95% CI=1.46-8.17, p<0.01). The same trend was observed in the unadjusted HR ($HR_{unadjusted}$=5.77, 95% CI=2.51-13.27, p<0.0001). The rate of diabetes development during the study period among Native Hawaiians with either the metabolic syndrome or IFG, or both, was higher than the rate for those with neither.

Table 3.4. Hazard Ratios (HRs) for the development of diabetes

	Population at risk	**Number of events**	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
No Metabolic Syndrome, No IFG	114	0	1.00 (reference)	1.00 (reference)
Metabolic syndrome	21	2	1.06 (0.25-4.52)	0.35 (0.06-1.90)
IFG	59	8	1.40 (0.59-3.32)	2.37 (0.93-6.04)
Metabolic syndrome + IFG	44	13	5.77 (2.51-13.27)*	3.46 (1.46-8.17)**

*significant at the p<0.0001 level
**significant at the p<0.01 level
Multivariate adjustment made for age and body mass index.

Discussion

This study is the first to demonstrate the predictive utility of the metabolic syndrome in assessing diabetes risk among a population of Native Hawaiian ethnicity. Using the harmonized criteria for the metabolic syndrome (103), we determined that the metabolic syndrome was an independent risk factor for diabetes development in both men and women, a finding echoed by previous studies. For example, in a meta-analysis of relative risk (RR) estimates for the metabolic syndrome and incident diabetes by Ford, Li, and Sattar (120), the risk for developing diabetes in the presence of the metabolic syndrome was significant, ranging from a RR of 3.53 to 5.17, depending on the metabolic syndrome definition used. The San Antonio Heart Study with Non-Hispanic Whites and Mexican-Americans also found the metabolic syndrome to be an independent risk factor for diabetes, with the metabolic syndrome conferring a 6-fold higher risk for diabetes development (66, 121). Among Asian-Japanese, the metabolic syndrome results in a 2.58 higher risk for diabetes development in men, and a 3.69 higher risk for women (67). Similarly, among an Asian-Chinese population, the HR for incident diabetes ranged from 3.5 to 4.5, depending on the metabolic syndrome definition used (110, 122).

In comparison, our study found the hazard risk of developing diabetes within the study period to range from 5.95 for men to 19.17 for women. The significant risk for incident diabetes in Native Hawaiians who have the metabolic syndrome may reflect its prevalence in this ethnic group (42%) (115). Our findings also indicate that the metabolic syndrome may be a significant predictive tool for Native Hawaiians, whose diabetes is likely attributed to insulin resistance rather than impaired insulin secretion as observed in Asian populations (123). Nonetheless, the study findings corroborate with previous studies that find the metabolic syndrome to be useful in predicting diabetes development, and indicates that the metabolic syndrome is effective is predicting diabetes risk in heterogeneous populations.

Individually, several components of the metabolic syndrome were also observed to increase risk for developing diabetes in Native Hawaiian women. With the exception of reduced HDL cholesterol, the presence of any of the other four components (elevated waist circumference, triglycerides, blood pressure, and fasting glucose) resulted in a significantly increased hazard of developing diabetes for women. Similar analyses in Asian-Chinese and Japanese populations showed individual metabolic factors to be significantly predictive of incident diabetes (110, 122). However, individual metabolic factors did not significantly predict diabetes for Native Hawaiian men. Although men in this study experienced higher hazards for diabetes in the presence of individual metabolic syndrome components, the results were not statistically significant. Our results suggest that the cumulative effect of metabolic factors may be important for predicting diabetes in Native Hawaiian men, a finding supported by research showing an increased risk of diabetes incidence with the accumulation of metabolic factors (120, 124).

Our findings indicate the importance of IFG in predicting incident diabetes in Native Hawaiians. Including IFG in the metabolic syndrome definition results in IFG and the metabolic syndrome being comparable predictors of diabetes, whereas excluding IFG from the metabolic syndrome definition shows IFG to be a better predictor. Other

studies have presented similar findings, with the metabolic syndrome excluding IFG either comparable or inferior to IFG in predicting diabetes incidence (67, 104, 108, 109, 122). In contrast, several studies have not shown IFG to be a significant contributor to the prevalence of the metabolic syndrome, possibly due in part to the low prevalence of IFG in their study populations (121, 125). IFG may be a significant contributor to the prevalence of the metabolic syndrome in Native Hawaiians because of high fasting glucoses in this population (112), supporting the significance of IFG in diabetes prediction for this population. This is further substantiated in our stratified analysis that examined diabetes risk both in the presence and absence of IFG; a higher risk for diabetes was observed in the presence of IFG, suggesting that the metabolic syndrome without IFG is not an independent risk factor for incident diabetes in Native Hawaiians. Other studies, however, have found it to be an independent risk factor (67).

Adding the metabolic syndrome to IFG significantly increases the risk for incident diabetes. Our study showed that IFG and any three metabolic factors increased the risk for diabetes nearly 6-fold, while the metabolic syndrome alone and IFG alone did not significantly predict diabetes development. This is consistent with studies that have found the coexistence of IFG and the metabolic syndrome to be useful in predicting diabetes incidence; for example, Lorenzo et al (66) found that the addition of the metabolic syndrome to IFG predicted diabetes beyond IFG alone. Other studies have demonstrated similar results (126-128), and two have also showed that the predictive power of the metabolic syndrome in addition to IFG is comparable to IGT (121, 129).

Strengths and Limitations

This study has several strengths, including the longitudinal design with a high follow-up rate and comprehensive laboratory and examination measures. This was also the only study to investigate the utility of the metabolic syndrome in predicting diabetes risk for Native Hawaiians. However, the limitations of the study include a limited sample size and single follow-up examination. These limitations may have contributed to the wide confidence intervals observed in the results, although trends across the

sexes and metabolic components remained consistent. Additional studies may help to confirm the findings. In addition, the observed times may have biases, as participants did not provide exact dates of diabetes diagnosis in 13 cases.

Conclusion

Clinical trials such as the DPP have shown that diabetes is preventable in individuals at high risk. However, one of the barriers in translating the DPP is the use of OGTTs to determine diabetes risk, as OGTTs are inconvenient and costly. To facilitate the translation of the DPP, more convenient and less expensive methods of identification that perform well in diverse populations are needed. This study showed that the metabolic syndrome is such a potential identification tool, predicting incident diabetes in Native Hawaiians. The study findings also showed that the metabolic syndrome adds to the predictive power of IFG, as the metabolic syndrome excluding IFG in addition to IFG conferred a higher risk of diabetes development than either measure alone. As the metabolic syndrome is a more practical and convenient method than the OGTT, using the measure to identify individuals at risk for diabetes may help facilitate translation of diabetes prevention programs.

CHAPTER 4: STUDY 3

Abstract

Background. Understanding how the DPP can be effectively translated into communities will be an important part of primary prevention efforts. Accomplishing this goal will require an understanding of the dissemination process and the factors, including opinion leader perceptions, which have the potential to influence the adoption of lifestyle interventions. The Diffusion of Innovations Theory (DIT) offers a useful framework that provides insight into the adoption of diabetes preventive innovations.

Purpose. To identify the salient factors that influence the perceptions of opinion leaders on lifestyle interventions for their respective organizations, and to consider how the identified issues affect the diffusion process.

Methods. Information was collected from semi-structured key informant interviews with eight opinion leaders. The data were analyzed using qualitative research methods including thematic analysis.

Results. Leaders were aware of lifestyle interventions as well as general population-based primary prevention efforts. Both lifestyle interventions and population-based primary prevention efforts were deemed important for public health, although leaders were not entirely convinced of the relative advantage of lifestyle interventions. Leaders also expressed reservations on the adoptability of population-based primary prevention and lifestyle interventions, perceiving them to be not only very complex ideas, but also not compatible with the needs of the populations their organizations serve and the current values of the medical system.

Conclusions. The findings suggest that opinion leader perceptions of the relative advantage, complexity, and compatibility of primary prevention and lifestyle interventions for diabetes are important in understanding the factors that mediate persuasion of the ideas.

Introduction

The urgency of primary prevention of diabetes is substantiated by the increasing incidence of newly diagnosed diabetics in the United States (130, 131), and the projected gravity of 39 million diagnosed diabetics by the year 2050 if current trends continue (132, 133). Despite evidence from clinical trials showing the possibility of primary prevention (36, 44, 48), a significant gap still exists in translating the results to public health (134, 135). More than a decade after the Diabetes Prevention Program results were published, access to prevention programs (also referred to as lifestyle interventions) remains limited, as evidenced by the registry of recognized primary preventive programs (136). The registry provided by the National Diabetes Prevention Program (NDPP), a CDC-led diabetes prevention program that aims to provide evidence-based lifestyle programs to pre-diabetic individuals, shows that 14 states, including the state of Hawaii, do not have a recognized program. This is cause for concern, as affected individuals in states without programs may not have access to proven treatment.

Prevention for diabetes has largely focused on secondary prevention and less so on primary prevention. Secondary prevention focuses on the effective control of forthright diabetes to stem the progress of the condition, and does so through glycemic control and prevention or control of co-morbid conditions such as hypertension and hypercholesterolemia (137). In contrast, primary prevention is aimed at preventing diabetes from ever occurring. Primary prevention of diabetes consists primarily of avoiding obesity, increasing physical activity, and dietary modifications. The greater attention and access to secondary prevention services has led to concerns about the gains made in the public health fight against diabetes; though health complications have decreased for diagnosed diabetic individuals, these improvements are offset by the increase in incidence of diabetes (138). It is unclear how the balance between secondary and primary prevention may be remedied, but given the projected enormity of rising incidence (132, 139), efforts toward primary prevention of diabetes needs to be increased.

Understanding how the DPP can be effectively translated so that they are accepted and implemented in communities will be important in the primary prevention of diabetes (134). Accomplishing this goal will require an understanding of the dissemination process and the factors that influence the adoption of primary prevention interventions, including identifying the barriers and facilitators to translation (134). The Diffusion of Innovations Theory (DIT) may be useful for this purpose by offering a framework that provides insight into the factors that potentially affect adoption of diabetes preventive innovations. Rogers (140) defines preventive innovations, such as lifestyle programs for diabetes, as "new ideas that require action at one point in time in order to avoid unwanted consequences at some future time."

According to the DIT, which explains the diffusion process and spread of innovations among systems, an innovation is spread ("diffused") with time through communication among social systems (140). The diffusion process occurs through five steps, from knowledge to persuasion, decision, implementation, and confirmation (140). It is during the persuasion step, which is preceded by acquired knowledge of an innovation from prior conditions, that attitudes and beliefs towards the innovation are developed. The attitudes and beliefs formed during this stage lead to decisions regarding the adoption of the innovation. Persuasion is mediated by the attributes of the innovation, which are identified by the theory as the innovation's relative advantage, compatibility, complexity, trialability, and observability (Table 4.1) (140). Research suggests that the relative advantage, compatibility, and complexity of the innovation are especially relevant, and that innovation adoption is more likely to occur if the innovations are perceived to have a higher relative advantage, compatibility, trialability, observability, and lower complexity (or higher simplicity) (141). Because preventive health innovations typically have low immediate relative advantage, previous research indicates that the relative advantage factor critically affects adoption rates (141).

Table 4.1. Five factors affecting persuasion in the DIT

	Definitions Rogers, E.M. (2003) (140)
Relative Advantage	*Degree to which an innovation is perceived as being better than the idea it supersedes.*
Compatibility	*Degree to which an innovation is perceived as consistent with the existing values, past experiences, and needs of potential adopters.*
Complexity/Simplicity	*Degree to which an innovation is perceived as relatively difficult to understand and use.* Complexity is negatively correlated to the rate of adoption; Simplicity is positively correlated
Trialability	*Degree to which an innovation may be experimented with on a limited basis.*
Observability	*Degree to which the results of an innovation are visible to others.*

To accelerate the diffusion of lifestyle interventions and propose strategies for adoption, attributes of the innovation must first be examined. Diffusion research indicates that on average, half of the variance in the rate of adoption of an innovation is explained by the five perceived attributes of an innovation (relative advantage, compatibility, complexity, trialability, and observability) (140).

Potential adopters of an innovation also affect the innovation's rate of adoption. Rogers (140) notes the importance of considering the characteristics of "innovators" in the diffusion process and proposes five categories based on the innovator's adoption action: innovators, early adopters, early majority, late majority, and laggards. Opinion leaders, a potential subset of early adopters, are especially influential in the diffusion process (140, 142). Their position in social networks allow them to serve as

communication catalysts (142-144), and their support for an innovation is likely to influence its diffusion, referred to in the literature as "the gating function of variables influencing adoption" (142), pertaining to the weight of opinion leaders in determining innovation adoption. Opinion leaders that are aware of the evidence pertaining to the innovation and cognizant of the value of the innovation are more likely to support the innovation (145).

To date, no studies have investigated the thoughts of opinion leaders regarding the attributes of diabetes prevention programs. The purpose of this study is to identify the salient factors that influence the leaders' opinions on lifestyle interventions for their respective organizations. The findings from this study should contribute to the understanding of, and provide recommendations for, the attributes that mediate persuasion for diabetes lifestyle interventions.

Methods

Study Design

This study used qualitative methods in the form of semi-structured key informant interviews to gain an understanding of opinion leaders' awareness and knowledge of diabetes prevention programs, their perceptions of the persuasiveness of the evidence, and the salient concepts that might influence the diffusion of diabetes primary lifestyle interventions. This study was approved by the University of Hawaii IRB (CHS #20303).

Sample

Eight key informant interviews were conducted. Participants were selected based on their importance in general diabetes efforts and potential influence in primary prevention efforts. They represented various organizations, including the original DPP clinical trial-Hawaii site, health care providers in Hawaii, the Hawaii branch of the American Diabetes Association, and the Department of Health, Diabetes Prevention and

Control Program. Key informants were contacted either by email or phone requesting their participation in the study, and the interview was conducted at times and places convenient for the participants.

Measures

The interview guide was developed using the DIT framework and addressed the diffusion process of diabetes primary prevention. Specifically, the initial steps in diffusion (knowledge and persuasion) and the attributes of the innovation that contribute to persuasion (relative advantage, compatibility, complexity, trialability, and observability) were addressed (Table 4.2). The interview question guide used in this study is available in Appendix C.

Table 4.2. Measures for key informant interviews

DIT facet addressed	Measure
Knowledge	Assess awareness and knowledge of primary prevention of diabetes and diabetes lifestyle programs
Persuasion	Assess opinion of primary prevention of diabetes and diabetes lifestyle programs
Persuasion: Relative Advantage	Assess perceived advantages and disadvantages of primary prevention efforts Assess advantage of diabetes lifestyle programs over other methods, and the benefits versus the cost Assess beliefs and attitudes towards primary prevention
Persuasion: Compatibility	Assess fit of diabetes lifestyle programs with organization Assess priority of primary prevention and investment in diabetes lifestyle programs
Persuasion: Complexity/Simplicity	Assess perceived difficulty of primary prevention and implementation of diabetes lifestyle programs
Persuasion:	Assess the testability of primary prevention efforts and diabetes

Trialability	lifestyle programs
Persuasion: Observability	Assess the visible and measurable results of primary prevention and diabetes lifestyle programs

Data Collection

Of the eight semi-structured interviews, six were conducted in-person at the interviewee's workplace, one was conducted by phone, and another took place at a convenient meeting place outside of the workplace. The duration of the interviews ranged from half an hour to an hour. Before the interview began, a description of the study purpose and goals were explained, and informed consent was obtained (Appendix B).

All interviews were audio-recorded. Transcriptions of the interviews were done within a week of the interview by the interviewer. No problems were experienced during the transcription process, as all the interviews were done in private and the digital recordings were clear. Field notes also were taken, and supplemental materials provided by the interviewees were included in the analysis.

Data Analysis

Qualitative coding was done to identify the salient themes related to the research question. The investigator coded all the transcripts in the same manner. An inductive approach was taken for the analysis, allowing codes and themes to emerge from the data instead of determined a priori (146). Coding began with structural/holistic coding, and proceeded to line-by-line coding where every line of the transcripts was examined and coded. In-vivo codes were also used during the coding process (147).

Following the coding process, thematic analysis was used to identify the main, recurrent, or most important themes that arose from the data (148). As defined by Boyatzis, a theme is "a pattern in the information that at minimum describes and

organizes the possible observations and at maximum interprets aspects of the phenomenon" (p.161) (148). Several steps were involved in the thematic analysis. In the first step, themes were initially generated and kept simple to accommodate for possible modifications. The initial themes were then defined, by re-examining the data to see how each code was assigned to the theme. Themes were preliminarily named and defined, and the data were re-examined for relevancy to the themes using the generated preliminary themes. The final version of the themes were assembled and reported.

Results

While the main objective of the study was to examine leader persuasion on lifestyle interventions at the individual-interpersonal level for those at high risk (i.e. pre-diabetics), leaders clearly felt that general primary prevention efforts, the gamut of policy, community, organization, interpersonal, and individual factors that intervene on populations, also needed to be addressed. That is, leaders felt both the high-risk, individual-level (lifestyle interventions) and population approaches (general primary prevention) were necessary (50). Thus, in addition to discussing lifestyle interventions, leaders also discussed their knowledge and perceptions toward the attributes of general primary prevention efforts. While general primary prevention is not technically considered an "innovation," the DIT framework is still useful in understanding the relevant attributes that influence persuasion of the idea. Hence, leader knowledge and perceptions toward general primary prevention of diabetes were also analyzed using the DIT framework.

Four main themes emerged from the key informant interviews to describe the opinion leaders' views on primary prevention of diabetes, public health efforts, and lifestyle interventions. The themes are presented below.

We are generally aware and knowledgeable about the DPP/lifestyle interventions, but we are not as knowledgeable about how to translate the DPP or on the best way to accomplish primary prevention of diabetes.

When asked, 7 of the 8 opinion leaders were knowledgeable about the DPP and its main outcome, of the intensive lifestyle intervention being very successful in decreasing diabetes incidence in pre-diabetic (at high risk) individuals. One of the leaders stated he had no prior knowledge of pre-diabetes or the DPP, and was only recently introduced to the concept and discussion through professional work partnerships.

Of the seven aware leaders, all said their awareness of the DPP came from their job responsibilities, and that they followed efforts to translate the program because their jobs required them to do so. Two of the key informants confessed to not keeping up with program translation efforts once their job positions and responsibilities shifted, no longer requiring upkeep in knowledge of program translation efforts. Knowledge of the DPP/lifestyle interventions was also attained through scientific journals and medical professional sources.

Leaders expressed interest in program translation efforts. However, they were unable to provide specific knowledge on the process. Acknowledging the difficulty of the task, most had limited, if any, experience in direct diabetes program translation efforts. Two of the leaders were aware of, but not personally involved in, the National Diabetes Prevention Program. One of these leaders was also aware of the recent availability of United Healthcare, a health insurance company participating in the national program and reimbursing for certified lifestyle interventions, in Hawaii. However, the leader also stressed that she was aware United Healthcare only reimbursed for certified programs, so even though the insurance is available in Hawaii, there are no certified programs to take advantage of the reimbursement. Four of the leaders mentioned that the only diabetes-related prevention program they knew of was the local Pili ‘Ohana program, and they also stressed that its prevention focus was on

obesity, not diabetes. Similarly, leaders stated that the direction of health care was starting to steer in the direction of diabetes primary prevention through indirect ways such as obesity prevention. However, most noted the fragmented focus and the lack of broad, concerted efforts to increase the availability of lifestyle interventions. Because leaders were not personally involved in any translation efforts, they were only able to offer suggestions and not any specifics pertaining to the translation of the DPP.

Leaders were also aware that general, population-based primary prevention would involve many factors. However, they were not personally involved in any primary prevention activities beyond education and awareness efforts and as a result, were only able to offer suggestions but not specific ideas for population-based primary prevention.

We think primary prevention of diabetes and lifestyle program implementation are complex endeavors.

Leaders were concerned about the potential complex nature of population-based primary prevention of diabetes. While they felt that the approach used in the smoking cessation/tobacco initiative a generation ago was effective in decreasing smoking rates, they also pointed out that it was effective because it was multifaceted and involved many factors, such as policy changes and organizational, community, and interpersonal/social norm shifts in favor of smoking cessation. To the leaders, this meant that a similar multifaceted, population-based approach would be needed in order for the same success to be replicated with primary prevention of diabetes. Specifically, leaders stressed the need for a multifaceted approach based on the social-ecological model, with: support from top-level administrators; medical paradigm, reimbursement, and outcomes reporting shifts in favor of primary prevention; public health policies; social norm changes; and infrastructure/systems changes. While leaders were in support of these changes that they perceived to be necessary for diabetes prevention, they also felt that it would be very difficult to accomplish. For example, leaders felt that shifting social norm in health-promoting behavior such as weight loss would be hard since, as two of the leaders explained, overweight/obesity has become

the norm in certain places, to the detriment of diabetes prevention: "I think here and in like many places that I lived…there's a tendency to just accept that this is just the way life is." Similarly, shifting the medical paradigm toward primary prevention would be difficult, because of the ingrained policies and way of thinking: "There needs to be a paradigm shift. But the whole health care system is based on reimbursement and treatment of conditions…So that means the doctor has to find something wrong with you…the whole system, is set up to treat sickness, not health. It's all backwards." Further, leaders pointed out that changing public health policies and environmental factors so that they support diabetes prevention would "break down the barriers that currently exist for a lot of people" but that such a task would be difficult in the current climate:

> "It's about looking at the here and now, and as long as we continue to do that, and nobody looks at ten years down the road, twenty, these problems, "the can" will continue to be kicked down the road. But people don't realize, that as you kick that can down the road, the can is getting bigger. It doesn't stay the same size, it's actually becoming a bigger can, which people don't talk about. They just talk about kicking the can down the road, but the can is going to become more cumbersome, and harder to kick. And eventually, you're not going to be able to kick it down the road, it's going to be in your face, and now it's going to be your immediate concern, way worse."

Similarly, leaders were also concerned with the complexity of issues in translating prevention programs for communities at-risk. As one of the leaders observed, while the DPP showed efficacy, "…the issue is how do you translate that into real-world? I believe it's still a question mark." Another leader concurred, stating that for primary prevention, "the translation still is in a state where I don't think people are still quite aware of what needs to be done and how to translate it and what's worthwhile." Specifically, leaders cited a number of factors that demonstrated why they believe the translation process to be complicated, including: cultural needs,

program acceptability, accessibility, affordability, and the identification of at-risk individuals. All of the leaders stressed the importance of culturally appropriate methods and outcome measurement evaluation, and cultural tailoring for Hawaii-based interventions, citing the diverse needs of the state's population. Leaders were against generic education and programs that would not resonate with Hawaii's population. However, leaders pointed out culturally appropriate programs and messages would take some effort, given the many cultures in the state. Further, leaders were concerned about logistics, such as the accessibility and availability of programs in rural areas and on the neighbor islands, as well as how to translate programs so that they are resonate with at-risk individuals: "because it's not just knowing how many are pre-diabetic, it's also a matter of knowing how many will cooperate." These variables contribute to the uncertainty in program translation, which in turn contribute to the difficulty of obtaining funding for programs, since, as leaders note, given the current budget constraints, funding cuts to public health, and competing priorities, funding and enthusiasm for programs is contingent on evidence of effectiveness.

We consider the advantages and disadvantages of primary prevention and lifestyle interventions.

All 8 leaders interviewed had at least a general knowledge of primary prevention, and as a result, believe that primary prevention of diabetes is important, justifying that primary prevention is necessary because "we can't afford diabetes" and morally, "it's the right thing to do." Fueled by the continued increasing prevalence of diabetes, leaders believe that not only is primary prevention important, but that there is a certain urgency, as diabetes is a major risk factor for many health problems such as cardiovascular disease. As diabetes is a risk factor for detrimental health conditions such as cardiovascular disease, six of the leaders also view primary prevention to be beneficial in preventing many chronic diseases: "…if we can prevent diabetes, we can prevent a lot of other diseases." Furthermore, leaders consider primary prevention to be necessary, citing the unsustainability of the healthcare system's focus on secondary

prevention: "I don't think it's a question of if it's impossible or not, I think it's a question of, can we afford not to do it. Because ultimately, if we don't get into primary prevention, it's not sustainable."

While not disputing the benefits of and need for primary prevention, many leaders expressed reservations on the effect of treatment (i.e. lifestyle interventions) on diabetes prevention, questioning if the results are a true "prevention" rather than a mere "delay" in diabetes incidence. One of the leaders suggested that it is "prevention" if affected individuals view diabetes as a serious condition; otherwise it is only a "delay" in incidence. Leaders were also not entirely convinced a prevention program by itself would be effective in changing behaviors, noting external influences and the difficulties of intense behavioral modifications required for success in programs. Despite their reservations, leaders were still in support of increasing the availability of evidence-based lifestyle interventions, citing that programs are necessary and "you need these lifestyle programs to address a disease."

While leaders agree that lifestyle programs are necessary to stem the diabetes epidemic, they do not believe programs alone would be sufficient, and that a population-based approach would also be needed. However, the extent of influence from external factors was a source of debate among leaders. Half of the leaders believe environmental factors, such as access to safe communities and affordable produce and policies regulating unhealthy habits, to be very important in determining treatment (i.e. lifestyle program) success: "the social issue, the social determinants piece has to be resolved and that's a pretty big issue." Yet the other half were unconvinced that such factors would exert much influence, with one of the leaders questioning the effects of regulatory policies: "how much of this stuff can we keep mandating people to do?" Instead, these leaders emphasized the importance of individual responsibility and motivation: "I think a lot of it, is up to the individual and what their belief system is, what they're willing to work at." For example, these leaders regard the debate over the role that fast food and sugar-sweetened beverages play in diabetes development as

being of minimal consequence, pointing out that the hazard is not the food or drink itself, but its overconsumption by individuals and "the absence of personal responsibility." These leaders believe that prevention programs are enough to facilitate diabetes prevention, and that population-based strategies are not required. In the end, however, leaders asserted that both environmental and policy interventions as well as individual responsibility warrant consideration: "there are individual choices but they're especially hard."

Primary prevention and lifestyle interventions are not currently compatible with the needs of the populations we serve and the existing medical system.

The current forefront priority of diabetes prevention is secondary prevention, and minimizing complications in diagnosed diabetics. Leaders were more aware and knowledgeable about secondary prevention, a consequence of their job and organization's focus on secondary prevention. While leaders would like to invest more in primary prevention and lifestyle interventions, two reasons prevent this from occurring. First, the priorities of the organizations are determined by the needs of the populations they serve, and for some, their populations seek care when they already have forthright diabetes: "I think in the populations that we serve…the focus is more heavily toward secondary preventions." Second, the current medical paradigm's focus on disease treatment places secondary prevention as a priority and not primary prevention. Secondary prevention is the main focus of diabetes efforts because reimbursement and coverage from Medicare and health insurance exists, whereas funding for identification and treatment of at-risk individuals is limited. One of the leaders points out that the "…challenge for primary prevention is that funding does not exist…the way the system is set up now, it's really to provide sick care…most of the reimbursement is heavily weighted toward providing services for those that already have diagnoses." For those reasons, treatment (i.e. programs) for primary prevention of diabetes takes a backseat to secondary services. Leaders did note that if reimbursement were not an issue, treatment for at-risk individuals (i.e. lifestyle

interventions) would be a good fit for their organizations' goals and objectives. Despite these reasons, many leaders said primary prevention was a priority, albeit shadowed by secondary prevention: "It's a priority because it's a complex disease and it's preventable."

Discussion

This study examined leader opinions and attitudes toward primary prevention and lifestyle interventions for diabetes. The DIT model delineates five attributes that influence persuasion and subsequently the rate of adoption of the innovation: relative advantage, complexity, compatibility, trialability, and observability. Of the five, relative advantage, complexity, and compatibility appear to be especially pertinent for the diffusion of primary prevention and lifestyle interventions for at-risk individuals.

For the opinion leaders interviewed in this study, the relative advantage of primary prevention of diabetes is obvious; leaders view primary prevention in general as a worthy venture and very much needed, given the current epidemic. Primary prevention was unanimously deemed advantageous over the preceding idea of focusing on secondary prevention to stem the diabetes epidemic. For these leaders, primary prevention offers sustainability as well as economic and social advantages, which are factors often shown in diffusion research to be conducive to its adoption (142). Based on the DIT, this perception should facilitate primary prevention of diabetes; however, this is stymied by the less obvious relative advantage of lifestyle interventions. Leaders, while convinced of the overall argument for primary prevention, were hesitant on the advantage of diabetes lifestyle programs over other, population-based strategies. Research indicates that lifestyle interventions suffer from a lack of perception of relative advantage; because outcomes do not occur immediately and may be obscure, it is often difficult to gauge the advantages (141). This was the case here, as leaders questioned if lifestyle programs were enough to guarantee a decrease in diabetes incidence, and if other extenuating circumstances influenced results. The lack of knowledge on translation of lifestyle programs and concerns about maintaining fidelity of programs

also contributed to low perceptions of relative advantage. Such views led leaders to express reservations on the relative advantage of lifestyle interventions, confirming the relative advantage as a non-negligible factor for diffusion of lifestyle interventions.

The complexity of primary prevention and diabetes lifestyle interventions was also a key factor in leaders' persuasion on the innovations' diffusibility. Previous research indicates that leaders that are aware of the evidence and value of an innovation are more likely to support the innovation (145). While this was true among the leaders in this study, their hesitance to provide full support for primary prevention actions and adopt diabetes lifestyle interventions appeared to stem from the complex nature of the innovations. Rogers (140) refers to the complexity of an innovation as its perceived ease in comprehension and practice. Though leaders had no problems understanding the general premise behind primary prevention, utilizing primary prevention was judged by leaders to be very complex, due to the myriad of social, economic, and political issues surrounding it. For primary prevention, complexity plays an important role in leaders' persuasion.

Similar notions were also seen in regards to leaders' assessments on the complexity of lifestyle programs. While leaders could understand the benefits of lifestyle programs for diabetes, the complexity associated with implementing them in practice affected their persuasion. Much of the complexity seemed to derive from concerns over challenges in the translation of the DPP to communities, especially in regards to ensuring a balance between maintaining program fidelity and cultural needs. While such challenges are common in translating lifestyle interventions to communities (149), they also lead to perceptions of complexity, which are regarded in the DIT as barriers to adoption (140). Hence, complexity is also an important factor for lifestyle interventions.

Diffusion research also points to the importance of compatibility; Katz (150) suggests that compatibility between an innovation and the adopter allows diffusion to occur more readily. Indeed, the interviews indicate that compatibility is a significant

attribute in determining leaders' persuasion for primary prevention and lifestyle programs. Leaders, while interested in primary prevention and lifestyle interventions, did not perceive them to be entirely compatible with the current priorities and needs of their organizations. As leaders noted, the priorities of their organizations reflect the medical model, which currently emphasizes secondary prevention rather than primary prevention. Additionally, primary prevention and lifestyle programs do not align with the needs of the populations the leaders and their organizations serve, as the majority of their populations already have diagnosed diabetes and require secondary preventive treatment. According to the DIT, such conflicts in priorities and needs lead to perceptions of low compatibility, which imparts a degree of uncertainty on the innovation and consequently limits persuasion and the rate of adoption (140). Thus, efforts to promote primary prevention and lifestyle programs may benefit by addressing issues that affect compatibility.

The attributes of observability and trialability did not appear to be as relevant to opinion leaders in this study, a finding backed by diffusion literature that notes that unlike the attributes of relative advantage, compatibility, and complexity, observability and trialability are not consistently significant across all types of innovations (151). However, further research may find observability and trialability to be important attributes, as past diffusion research suggests that that the observability of outcomes is important for ambiguous ideas such as primary prevention which involve a myriad of variables (142), and trialability is important for newer innovations such as translated lifestyle interventions (140).

In this study, the five perceived innovation attributes of relative advantage, complexity, compatibility, observability, and trialability were important in determining adoption of primary prevention and lifestyle interventions. Relative advantage is consistently shown in diffusion research to be one of the strongest predictors of adoption rate. This is particularly true in the case of preventive interventions in which an innovation is adopted to prevent the occurrence of an undesired event in the future

(141, 152), such as diabetes prevention. However, the results from this study indicate that, in the case of diabetes prevention, complexity was also a critical attribute, rivaling relative advantage, as leaders appeared to be more concerned about the complexity of primary prevention and lifestyle interventions than its relative advantage. For the leaders in this study, the relative advantage of primary prevention was obvious, and while the relative advantage of lifestyle interventions was less clear, leaders still felt that programs are necessary. In comparison, both primary prevention and lifestyle interventions were perceived to be complex, with leaders citing complexity to be an influential issue in their persuasions. Complexity has been found in prior research to be an important attribute for new innovations (140). Diffusion research indicates that new innovations are often more affected by perceptions of complexity than of relative advantage and compatibility.

Emphasizing attributes that are identified to be important by adopters help expedite the diffusion process (153). As the study results indicate, relative advantage, complexity, and compatibility are crucial attributes in the assessment of primary prevention and lifestyle intervention. It may be that increasing favorable perceptions of these attributes will facilitate the rate of adoption of these innovations.

Limitations

The study limitations include the inherent biases of the model used; the DIT has pro-innovation and individual blame biases (140). In addition, the five attributes used in the study's framework (relative advantage, complexity, compatibility, observability, and trialability) are not the only possible attributes that describe an innovation. However, research has shown that these five attributes explain the majority of the variance in the rate of adoption of an innovation (154).

The limitations of this study also include the limited generalizability; a select group of key informants were interviewed, and their thoughts and perceptions may not necessarily reflect the perspectives of other key informants in the field. Further, this

study focused on factors within the knowledge and persuasion steps of the diffusion process, and the diffusion process in its entirety was not examined.

Conclusion

Knowing which factors might affect the diffusion of primary prevention and lifestyle interventions is important, as despite the release of evidence for primary prevention of diabetes more than a decade ago (48), translation of the results to public health have not been widespread, and diabetes incidence in the U.S. continues to rise. The results of this study indicate that leader knowledge and perceptions of the relative advantage, complexity, and compatibility of primary prevention and lifestyle interventions are potentially important. Intervening in these areas may help to facilitate the diffusion of primary prevention of diabetes and translation of lifestyle interventions.

CHAPTER 5: CONCLUSION

How Findings Compare and Extend the Literature

The findings from the three studies in this dissertation provide new information for diabetes prevention. Based on the findings, we can draw three main conclusions regarding the dissemination of diabetes prevention: 1) awareness of diabetes risk alone is not sufficient in predicting risk-reducing behaviors; 2) prevention programs may benefit from less costly measures of risk, such as the metabolic syndrome, to identify at-risk individuals; and 3) perceptions of the relative advantage, complexity, and compatibility are especially relevant in influencing the persuasion of opinion leaders on primary prevention of diabetes and lifestyle interventions, and subsequently, the diffusion of these ideas.

Study 1 showed that awareness of diabetes risk continues to be low among individuals at-risk. However, the low prevalence of awareness did not appear to be the defining factor in diet and exercise behavior among at-risk individuals, as the proportion of those meeting dietary and physical activity recommendations did not differ by whether or not individuals were aware of their risk, nor was awareness significant in predicting the likelihood of meeting diabetes preventive recommendations. These findings stress the need for additional research to determine effective ways of encouraging the adoption of recommended risk-reducing behavior among at-risk individuals.

Study 2 presented findings that offer alternative methods for identifying at-risk individuals. The findings add to the growing body of literature that indicates less costly and more convenient forms of risk measurement are comparable to the more arduous 2-hour glucose tolerance test in detecting diabetes risk. The results demonstrate the effectiveness of the metabolic syndrome in predicting diabetes risk in Native Hawaiians, corroborating previous studies conducted with Mexican American (66) and Japanese (67) populations on the potential value of using the metabolic syndrome to predict risk.

Study 3 illustrates the perceptions and opinions of potential adopters of diabetes prevention. While many factors affect the adoption of an innovation, research suggests that the perceptions by potential adopters on the attributes of the innovation are especially influential in determining how fast an innovation is diffused. The findings from the study show the importance of the innovation attributes, and also show that for diabetes prevention innovations, perceptions of complexity are especially relevant in determining adoptability, along with perceptions of relative advantage, and compatibility with organizational goals and priorities. These findings suggest that intervening in these areas (for example, reducing the perceived complexity) may aid in diffusion efforts for diabetes prevention. The perceived attributes also point to the importance of population-based strategies to decrease diabetes incidence; for example, the compatibility of diabetes prevention innovations with their organizations was perceived by the potential adopters to be contingent on policies that support diabetes prevention.

Taken together, the study conclusions suggest that a variety of factors are necessary for diabetes prevention. Thus, a socio-ecological approach encompassing the spectrum of policy, community, organizational, interpersonal, and individual interventions will be needed (155). The social-ecological approach may be effective for diabetes prevention, because it uses both high-risk and population-based strategies to address the factors that put people at risk for diabetes (50). Interventions occur at the individual level, addressing an individual's susceptibility to diabetes, and offering interventions to promote knowledge, attitudes, beliefs, and behaviors that decrease their risk for getting diabetes. Population-based strategies complement the high-risk strategies by helping to identify and address the underlying influences of diabetes incidence, including policies at the national, state, and local levels, community norms and values, organizational roles, and interpersonal relationships with family, friends, and health providers. Similar to the smoking cessation model (156), multi-level interventions are needed to promote diabetes prevention at every front. By addressing

multiple levels of influential factors, the social-ecological approach is more likely to sustain diabetes prevention efforts than if only a single level was addressed.

The practice implications of these findings suggest that a myriad of issues need to be considered. First, prevention programs are necessary in diabetes prevention, but it is simply not feasible to identify everyone at risk using OGTTs. Other effective ways of identification must be determined. However, whether or not programs using the alternative identification methods will yield similar results to the DPP, which used IGT as a key inclusion criterion, is unknown, and will also need to be taken into consideration. Second, because education and awareness programs at the individual-interpersonal level alone will not create significant change, efforts at the policy-organization-community levels need to be increased. As Yach et al (157) and Garfield et al (134) note, such efforts include raising awareness of diabetes prevention in policymakers and providing scientific evidence in support of broad, public health changes.

Limitations of the studies

The focus of this dissertation was primarily on individuals at-risk for diabetes, with limited analysis on the awareness and knowledge of health care providers, systems, payers, and policymakers, all of which have a significant role in diabetes prevention. While health care providers and payers were represented in Study 3, the sample was too small to be generalizable.

In addition, the studies did not examine in detail prevention efforts at all levels, and the main focus was on the individual-interpersonal levels. Efforts at the community-organizational and policy levels were briefly discussed; however, specific policy recommendations and community and organizational relationships were not investigated.

Directions for future research

The strongest evidence for diabetes prevention comes in the form of interventions for high-risk individuals. Yet, as the results from these studies indicate, the high-risk approach alone will not yield substantial results in decreasing diabetes incidence. Current research on diabetes prevention has primarily focused on the high-risk approach, with less research on the population-based approach. Thus, recommendations for future research include investigating components of the population-based approach.

Additional informant interviews will be important in diabetes prevention efforts. As policy is a crucial component in diabetes prevention, validated in the literature (158) as well as indicated in Study 3, interviews with key policymakers to investigate their perceptions of diabetes prevention may be helpful in determining the policy component.

What is missing from the literature is a network analysis to investigate communication and interactions between organizations that have significant roles in diabetes prevention. Wejnert (142) notes that network-influenced decisions have a positive effect on innovation adoption. Thus, understanding the relationships between organizations that are involved in diabetes prevention is potentially helpful in understanding how diabetes prevention is addressed at the organization and community levels. Data from the network analysis may also be used in network interventions, which uses network data to provide practical information on how to facilitate change among organizations (159).

In addition, a comprehensive literature review using the social-ecological model as a framework to delineate how diabetes prevention operates at multiple levels may be helpful in understanding how the variables interact across levels, that is, the "connectedness" across levels (160). The review would synthesize research from all pertinent domains (e.g. medicine, behavioral science, urban planning and policies, health economics). Such a framework exists in the field of physical activity promotion

(161), though there is currently not one specifically for diabetes prevention.

Conclusions

The dissemination of primary prevention of diabetes in public health is important, given the growing epidemic. Despite clinical trials such as the Diabetes Prevention Program showing the efficacy of lifestyle interventions in preventing diabetes (48), more than a decade after the DPP, a gap still remains in its translation to the broader community (155). The findings from the three studies in this dissertation suggest that, to decrease diabetes incidence, prevention efforts will need to extend beyond the education and awareness efforts at the individual-interpersonal level (i.e. prevention programs), and address the broader environmental context (i.e. public policies, community norms, organizational values). Prevention programs are necessary, but they are only one component in the overall diabetes prevention scheme and do not address external influences. In essence, high-risk strategies (individual level prevention programs) will need to be complemented by population-based strategies that seek to minimize the underlying causes of diabetes.

Appendix A: Study 1 NHANES Physical Activity Survey

Correspondence of the NHANES Physical Activity Questionnaire (NPAQ) items with the WHO Global Physical Activity Questionnaire (GPAQ)

	Global PAQ	NHANES PAQ	Recommended MET values
Work	P1	PAQ605	Moderate=4.0 Vigorous=8.0
	P2	PAQ610	
	P3	PAD615	
	P4	PAQ620	
	P5	PAQ625	
	P6	PAD630	
Transport	P7	PAQ635	Cycle, Walk=4.0
	P8	PAQ640	
	P9	PAQ645	
Recreation	P10	PAQ650	Moderate=4.0 Vigorous=8.0
	P11	PAQ655	
	P12	PAD660	
	P13	PAQ665	
	P14	PAQ670	
	P15	PAD675	
Sedentary	P16	PAD680	N/A

Appendix B: Study 3 Informed Consent

Consent to Participate in Research Project:
An examination of influential factors in diabetes prevention efforts

My name is Laura Hsu, and I am a public health doctoral student at the University of Hawaii. The research I am conducting is part of my doctoral dissertation.

Project Description: The purpose of this research is to investigate what factors influence diabetes prevention efforts. Diabetes prevention programs have been shown to be effective at preventing diabetes, yet they are not widely available in communities for people at risk for diabetes. This study will assess what you view as barriers and facilitators to translating diabetes prevention programs into communities. Data from this interview will help identify important factors that may be useful in diabetes prevention efforts. You have been selected to participate because you have a role in this process.

Procedures: If you agree to participate in this study, you will be asked ten main questions. This in-person interview should take about 45 minutes. The interview will take place at a location that is convenient, maintains your privacy, and acceptable to you. The interview will consist of questions about diabetes prevention programs, your views on their effectiveness, and the factors that play a role in translating prevention programs into communities. Some examples of questions are: Have you been involved in any diabetes prevention efforts? How important do you think diabetes preventions programs that promote lifestyle health behaviors are in preventing diabetes? If you or your organization wanted to implement a program focused on preventing diabetes, what do you think would facilitate/help that endeavor? You are free to not answer any questions you do not wish to answer and to stop the interview at any time. Participation is strictly voluntary. With your permission, the interviews will be audio-recorded.

Benefits and Risks: I believe there are no direct benefits to you in participating in my research project. However, the results of this project might help me and other researchers learn more about factors that affect diabetes prevention efforts. I believe there is little or no risk to you in participating in this project. If, however, you are uncomfortable answering any of the interview questions, we will skip the question, or take a break, or stop the interview, or withdraw from the project altogether.

Confidentiality and Privacy: During this research project, I will keep all data from the interviews in a secure location. Only I will have access to the data, although legally authorized agencies, including the University of Hawai'i Human Studies Program, have the right to review research records. After I transcribe the interviews, I will erase the audio-recordings. When I report the results of my research project, and in my typed transcripts, I will not use your name or any other personally identifying information. Instead, I will use a pseudonym (fake name) for your name. If

you would like a summary of the findings from my final report, please contact me at the number listed near the end of this consent form.

Voluntary Participation: Participation in this research project is voluntary. You can choose freely to participate or not to participate. In addition, at any point during this project, you can withdraw your permission without any penalty of loss of benefits.

Questions: If you have any questions about this project, please contact me at via phone 808-956-5757 or e-mail (lhsu@hawaii.edu). If you have any questions about your rights as a research participant in this project, you can contact the University of Hawai'i, Human Studies Program, by phone at 808-956-5007 or by e-mail (uhirb@hawaii.edu).

A copy of this form will be provided. Please keep the copy for your records. If you agree to participate in this project, please sign this form and return it.

Signature for Consent:
I agree to participate in the research project entitled, *"An examination of influential factors in diabetes prevention efforts."* I understand that I can change my mind about participating in this project, at any time, by notifying the researcher.

_____ ***Please initial here if you agree to be audio-recorded.***

Name (Print): _____

Signature: _____

Date: _____

Appendix C: Study 3 Key Informant Interview Guide

Thank you for taking time out for this interview. The purpose of this interview is to gather your insight on diabetes prevention. Preventing diabetes has become a public health priority, especially in light of clinical trials such as the Diabetes Prevention Program in the United States that has shown diabetes prevention to be possible with lifestyle health behaviors such as weight loss and physical activity.

What do you know about diabetes prevention (primary prevention of diabetes)? Diabetes lifestyle prevention programs? Please elaborate.

Have you/your organization been involved in any diabetes prevention efforts? Please describe.

Is diabetes prevention (primary prevention) a priority for you/your organization? Why or why not?

In your opinion, do you think diabetes can be successfully prevented with lifestyle health behaviors such as diet/nutrition and physical activity, or do you think there are other more effective ways to prevent diabetes?

(If other methods mentioned)

What are these other methods? Why do you think they are more effective?

How important do you think diabetes lifestyle prevention programs are in promoting health behaviors that prevent diabetes? Please elaborate.

Do you think diabetes lifestyle prevention programs would be a good fit for your organization?

Have you/your organization tried to or implemented diabetes lifestyle prevention programs?

If YES:	If NO:
What helped to facilitate the implementation of that prevention program? What were the barriers in the implementation of that program? Costs (hiring personnel, providing resources, program materials, etc)? For example, think about other similar health programs that you/your organization has implemented – what were the barriers there? Do you foresee those same barriers affecting diabetes lifestyle prevention programs? What are the barriers for the continuation and sustainability of that program? Will you continue your organization's diabetes prevention program? Why/why not?	Are you/your organization interested in diabetes lifestyle prevention programs for the communities your organization serves? Why/why not? If you/your organization wanted to implement a program focused on preventing diabetes, what would facilitate/help that endeavor? What would prevent/hinder that endeavor? Barriers? Costs (implementing and disseminating DPPs, e.g. hiring personnel, providing resources, program materials)? Would these barriers be difficult to overcome? Please elaborate.

That's all – do you have any additional questions or comments?

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