FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

EFFECTIVENESS OF A 6-MONTH NUTRITION INTERVENTION TARGETING PREDIABETES IN PEOPLE LIVING WITH HIV (PLWH) AND PREDIABETES

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DEDICATION

This dissertation is dedicated to everyone who has made this journey possible. I would like to first thank my late parents, May Abdelnour Sneij and Albert Abdelmasih Sneij for raising me with great aspirations and a special love for Nutrition. I would also like to thank my siblings, Waleed, Kameel, Nabeel and Rhonda Sneij for all their love and support along the way, strengthening me when the road got tough, especially when our parents were called home. Last but not least, a special thanks to my dear husband, Reynaldo Alberto Perez, who entered into my life during this journey and supported me towards its completion.

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ABSTRACT OF THE DISSERTATION

EFFECTIVENESS OF A 6-MONTH NUTRITION INTERVENTION TARGETING PREDIABETES IN PEOPLE LIVING WITH HIV (PLWH) AND PREDIABETES

by

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Miami, Florida

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The objective of this study was to assess the effectiveness of a 6-month randomized, controlled nutrition intervention targeting prediabetes in people living with HIV (PLWH) and have prediabetes. Participants (n=38) were randomized into the intervention group (n=20) or the control group (n=18). Participants randomized into the intervention group met once a month for approximately 1 hour to receive medical nutrition therapy, nutrition counseling and nutrition education; participants randomized into the control group received educational material at baseline. Fasting blood glucose (FBG) for the 6-month follow-up for the intervention group was significantly reduced compared to baseline (p=0.03). No significant difference was found in the control group between the baseline and 6-month blood glucose values (p=0.11). A significant reduction in body mass index (BMI) was also observed within the intervention group (p=0.03) at the end of the 6-month intervention; but not in the control group (p=0.10). No significant difference was observed for inflammation as measured by high sensitivity C-reactive protein (hs-CRP) in either the intervention group (p=0.40) or the control group (p=0.12). There was a significant improvement in oxidative stress as measured by 8-hydroxyguanosine (8OHdG) in the intervention group (p=0.04); but no improvement was seen in the control

group (p=0.43). Furthermore, significant improvement in stage of behavioral change was observed in the intervention group for physical activity, fruit/vegetable intake and fiber intake. Significant improvement was also observed for nutrition knowledge and self-efficacy in the intervention group; but not in the control group. Participants with high compliance with treatment, were more able to achieve better fruit and vegetable intake, fiber intake, nutrition knowledge and self-efficacy than those with poor compliance with study visits. The results from this intervention support the notion that a nutrition intervention is effective in low-income PLWH and prediabetes to lower diabetes risk by significantly lowering fasting blood glucose, BMI and oxidative stress (8OHdG), as well as improving participants through the stages of behavioral change. This pilot study also demonstrated that a 6-month intervention, provided adherence and attendance, is feasible to improve prediabetes condition and this type of intervention could be implemented into a larger scale.

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ABBREVIATIONS AND ACRONYMS

PLWH	People Living with HIV
HIV	Human Immunodeficiency Disease
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
MASH	Miami Adult Studies on HIV
BMI	Body Mass Index
WHR	Waist to Hip Ratio
FBG	Fasting Blood Glucose
HbA1C	Hemoglobin A1C
8OHdG	8-hydroxydeoxyguanosine
Hs-CRP	High sensitivity C-reactive protein
DNA	Deoxyribonucleic Acid
CVD	Cardiovascular Disease
IGT	Impaired Glucose Tolerance
IFG	Impaired Fasting Glucose
MNT	Medical Nutrition Therapy
REDCap	Research Electronic Data Capture
ELISA	Enzyme Linked ImmunoSorbent Assay
SD	Standard Deviation
IQR	Interquartile Range

CHAPTER I: INTRODUCTION

Statement of Problem

Prediabetes is a state of hyperglycemia in which blood glucose levels are above normal but still below the diabetes threshold [1]. Because prediabetes prevention does not fall squarely into the domains of primary or secondary interventions, it was previously often inadequately addressed [2]. However, prediabetes is currently considered an important public health concern, as prediabetes is known to increase risk for co-morbidities including diabetes and cardiovascular diseases, as well as increasing healthcare cost and mortality rate [3]. Although prediabetes is not necessarily a diagnosis of diabetes, it is an intermediate transient state of elevated glycemic parameters, with current estimates suggesting that up to 70% of individuals with prediabetes will eventually develop diabetes [4].

People with prediabetes are at a higher risk of developing type 2 diabetes within 10 years without any intervention [4]. Considering the increased risk for type 2 diabetes, people with prediabetes are the ideal target population for the development and implementation of intervention programs to prevent the further progression to diabetes [4]. Studies have shown that incidence rates of diabetes in people with prediabetes have been significantly reduced with effective interventions [3] [5-7].

Although no population group may be immune to the development of prediabetes, there are some population groups that have a higher risk of developing prediabetes due to multiple factors. Studies show an increased prevalence of prediabetes in people living with HIV (PLWH) [8-9] with rates ranging between 22.4 to 43.1% [10-12] [20], which is more than double that of the general population [10]. Moreover, studies have shown an early onset of morbidities in PLWH compared to the general non-HIV infected population [21-22]. Although numerous successful interventions have been conducted in the general population to lower diabetes risk [5-7] [13-14], there are currently no interventions that have been conducted in PLWH to lower diabetes risk, a group which is at high-risk for developing the condition.

Significance

Multiple nutrition interventions have been conducted to prevent diabetes in the general population [5-7] [13-14] and have proven to be successful in lowering HbA1C levels, [14] diabetes risk [14-15] and diabetes incidence [5] [7] [15]. Prevention and treatment of diabetes is an increasingly important part of long-term care in PLWH [16]; however, these intervention studies have not been conducted in PLWH, who are at high risk of developing diabetes [8] due to multiple factors, including but not limited, to HIV infection, chronic ART use and/or body composition changes, among other factors [17-19].

Due to this gap in the literature, nutrition interventions that target prediabetes in PLWH to prevent the development of diabetes are needed. In addition, oxidative stress and inflammation associated with elevated glucose levels, as well as HIV infection and/or chronic ART use increase the risk for non-HIV/AIDS related co-morbid diseases such as cardiovascular disease and diabetes mellitus. Therefore, implementing and evaluating interventions in this high-risk population to control glycemic parameters is necessary to effectively reduce risk for non-HIV co-morbid diseases.

Specific Aims and Hypotheses:

- AIM 1: To assess the effectiveness of a 6-month lifestyle/nutrition intervention to reduce blood glucose, oxidative stress and inflammation in PLWH on stable ART with undetectable HIV viral load who were diagnosed with prediabetes.
  - <u>Hypothesis 1a</u>: The 6-month nutrition intervention will be effective in significantly lowering fasting blood glucose levels in prediabetic PLWH on stable ART and with undetectable HIV viral load.
  - <u>Hypothesis 1b</u>: The 6-month nutrition intervention will be effective in significantly lowering oxidative stress, as measured by 8OHdG, in prediabetic PLWH on stable ART and with undetectable HIV viral load.
  - <u>Hypothesis 1c</u>: The 6-month nutrition intervention will be effective in significantly lowering inflammation, as measured by hs-CRP, in prediabetic PLWH, on stable ART and with undetectable HIV viral load.

- AIM 2: To assess the effectiveness of a 6-month lifestyle/nutrition intervention in progressing participants through the *stages of change* and promoting self-efficacy, as measured by domains and instruments of the Health Belief Model and the Transtheoretical (Stages of Change) Model.
  - <u>Hypothesis 2a:</u> The 6-month lifestyle/nutrition intervention will be more effective in progressing participants to more advanced *stages of change* in prediabetic PLWH on stable ART and with undetectable HIV viral load than the control group.

- Hypothesis 2b: The 6-month lifestyle/nutrition intervention will be more effective in improving *self-efficacy* in prediabetic PLWH on stable ART with undetectable HIV viral load than those in the control group.

- AIM 3: To assess the association of compliance with monthly lifestyle/nutrition intervention sessions with biological markers and behavioral scores (*stages of change* and *self-efficacy*).
  - Hypothesis 3a: Those who are compliant with the intervention visits (≥4 visits) will have better glycemic control measured by significant reductions in fasting blood glucose, 8OHdG and hs-CRP than those that are not compliant with intervention visits.
  - Hypothesis 3b: Those who are compliant with the intervention visits (≥4 visits) will have significantly higher advancements of *stages of change* compared to those that are not compliant with intervention visits.
  - Hypothesis 3c: Those who are compliant with the intervention visits (≥4 visits) will have significantly improved *self-efficacy* scores compared to those that are not compliant with intervention visits.

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CHAPTER II: LITERATURE REVIEW

A. INTRODUCTION

Prediabetes is a state of hyperglycemia in which blood glucose levels are above normal but still below the diabetes threshold [1]. Because prediabetes prevention does not fall into the domains of primary or secondary interventions, it is often inadequately addressed [2]. Although prediabetes is not necessarily a diagnosis of diabetes, it is an intermediate transient state of elevated glycemic parameters, estimates suggest that up to 70% of individuals with prediabetic conditions will eventually develop diabetes [3].

People with prediabetes are at a higher risk of developing type 2 diabetes within 10 years without any intervention [3]. In addition, the risk for cardiovascular disease (CVD) is substantially increased with prediabetic conditions [3]. Considering the increased risk for type 2 diabetes and CVD, people with prediabetes are the ideal target population for the development and implementation of early intervention programs to prevent further progression to diabetes [3]. In fact, prediabetes has been reversed with proper intervention in a previous study, where glucose tolerance was normalized in >50% of subjects in a study conducted by Eriksson and Lindgarde [4]. Moreover, studies have shown that incidence rates of diabetes in people with prediabetes have been significantly reduced with effective interventions [5-7].

Because prediabetes is often asymptomatic, as a result, many people with prediabetes are unaware of their condition. According to the U.S. Department of Health and Human Services (DHHS) and the American Diabetes Association (ADA), an estimated 41 million Americans between 40-74 years of age are prediabetic, and most are unaware, underlining the importance of increasing screening to promote awareness of prediabetes

[3]. Although no population group may be immune to the development of prediabetes, there are some population groups that have a higher risk of developing prediabetes due to multiple factors.

According to analyses based on the 2003-2006 US National Health and Nutrition Examination Survey (NHANES) data, approximately 3.5% of people 20 years and older had prediabetes, which increased with age to 7.2% in people aged 40-59 years and 10.6% in those aged 60-74 years [8]. Studies show an even higher prevalence of prediabetes among people living with HIV (PLWH) [9-10] with rates ranging between 22.4 to 43.1%[8][11-12]. The prevalence of prediabetes is 2-3 times higher in PLWH compared with the general population. Although numerous successful interventions have been conducted in the general population to lower diabetes risk [4-7][13] there are currently no interventions that have been conducted in prediabetic PLWH to lower diabetes risk in this particularly high-risk population.

B. BACKGROUND AND SIGNIFICANCE

Prediabetes

Prediabetes is defined to be the state of hyperglycemia with glycemic measures above normal levels, but still below the diabetes threshold [1]. This is due to the defects in insulin secretion and/or insulin action [14]. Insulin resistance is the condition in which more insulin is required to achieve a normal metabolic response, or in which a normal amount of insulin fails to produce a normal metabolic response, resulting in hyperglycemia [14].

The World Health Organization (WHO) and the American Diabetes Association (ADA) have specified criteria for the diagnosis of prediabetes, but they are not uniform. The WHO has defined prediabetes with 2 parameters: impaired fasting glucose (IFG) defined to be fasting blood glucose between 110 and 125 mg/dL and impaired glucose tolerance (IGT) defined as 2-hour plasma glucose of 140-200mg/dL after consuming 75 grams of oral glucose [1]. In contrast, the American Diabetes Association (ADA) has defined prediabetes with the same cut-off point for IGT, but with lower cut-off parameter for IFG (100 and 125 mg/dL) and an additional criteria of hemoglobin A1C (HbA1C) between 5.7 and 6.4% [1].

Prevalence of prediabetes in PLWH

While no population group is exempt from developing prediabetes, defined by impaired glucose tolerance, impaired fasting glucose or elevated HbA1C, there are certain populations that may be at an increased risk compared to others. Studies reveal prevalence rates of prediabetes in PLWH to be higher than the rates of the general non-infected population [11] [15].

A study conducted by Gebreyesus [16] assessed the prevalence of prediabetes among PLWH (n=134) with a median age of 40 years and found a prevalence rate of 22.4%. All the participants were receiving antiretroviral therapy (ART) with a median duration of therapy of 58 months. Another study conducted by Srivanich *et al.* [17] also examined the rate of prediabetes among PLWH (n=149) with a mean age of 42.2 years. The majority of the participants was receiving ART (92%) for a mean duration of 0.8 years. Among the study participants, 27.5% were prediabetic. These prevalence rates are seen to be more than twice the prevalence in the general non-infected population. A recent study by Arafath *et al.* conducted a retrospective, cross-sectional study in an outpatient multidisciplinary HIV Clinic (n=249) and found a rate of prediabetes of approximately 30%, with BMI being a major risk factor for diabetes [18].

Oxidative stress and HIV

HIV infection is associated with increased oxidative stress, where reactive oxygen species (ROS) are produced during different stages of the HIV life cycle [19]. An oxidative stress biomarker that is found to be elevated in PLWH is 8-hydroxy-2-deoxyguanosine (8OHdG), which is a marker of DNA damage due to oxidative stress [20]. 8OHdG is the product of DNA base modification produced by the oxidation of deoxyguanosine, which is considered to be the most sensitive and useful marker of DNA oxidative damage [21]. Changes in 8OHdG levels may be sensitive due to the susceptibility of the guanine base to oxidative damage as a result of its inherent chemical structure [21], making the oxidative hydroxylation of guanine in the 8-position to be the most frequent and mutagenic base of nuclear DNA. Upon repair of oxidized DNA bases, 8OHdG is removed and released into circulation, and excreted in the urine [21].

A randomized, case-control study aimed to examine the relationship of insulin resistance and 8OHdG in PLWH (n=600) found that levels of 8OHdG were significantly higher in PLWH with/without receiving ART (n=300) than HIV-seronegative controls (n=300). Moreover, they found that PLWH receiving ART (n=200) had significantly higher levels of 8OHdG compared with PLWH not receiving ART (n=100), suggesting an additional adverse effect of ART on oxidative stress [22].

Inflammation

HIV infection is commonly characterized with increased inflammation and decreased immune cell proliferation due to the oxidative stress that results from the different stages of the viral life cycle, which includes viral replication [23]. Independent of HIV infection, prediabetes and elevated glucose levels are also associated with increased levels of inflammation [24]. Due to the impaired glucose metabolism characteristic of the prediabetic condition, people with prediabetes tend to be in a hyperglycemic state and have increased levels of inflammation.

Elevated levels of inflammatory biomarker, hs-CRP, have been reported in PLWH and have been associated with HIV disease progression independent of HIV viral load and/or CD4 lymphocyte counts [25]. Moreover, it has been reported that regardless of HIV disease progression to AIDS, hs-CRP has been found to significantly increase over time in PLWH [25]. Minimizing oxidative stress attributed to elevated glycemic parameters, such as in prediabetes, may reduce the inflammation experienced by PLWH, thereby preventing and/or delaying the development of non-HIV related comorbidities.

Interventions

Because PLWH are at higher risk of developing diabetes, therefore, the Academy of Nutrition and Dietetics asserts that dietary intervention are necessary to reduce risk associated with prediabetes in this population [26]. While prediabetes is a risk factor for developing diabetes, there are studies that report a 40 to 70% efficacy of a lifestyle-based intervention in reducing the risk in adults with prediabetes [1].

In addition, according to the Academy of Nutrition and Dietetics, implementing nutrition interventions that promote healthy behavioral habits has the potential to significantly slow HIV disease progression, decrease the severity of the disease and improve longevity [26]. Although PLWH have different needs specific to their HIV infection, the goals for diabetes prevention and management are the same for HIV infected and non-infected individuals. Regular physical activity (~150 minutes per week) has been shown beneficial in HIV non-infected as well as HIV-infected individuals [27].

Nutrition Interventions in General Population

Salas-Salvado *et al*. [28] conducted a large scale randomized, controlled clinical nutrition intervention on non-diabetic adults (n=418) with high cardiovascular risk, such as hypertension, dyslipidemia and high BMI for the course of 6 years. The objective of the study was to test the effectiveness of two Mediterranean diet interventions compared to a low-fat diet on incidence of diabetes in high risk adults. The participants were randomized into 3 study arms: education on a low-fat diet (control), Mediterranean meals (MedDiet) supplemented with olive oil (1 liter/week) or nuts (30 grams/day). The diets were ad libitum and no advice regarding physical activity was given. The main outcome was incidence of diabetes based on the American Diabetes Association criteria for diagnosis. After a median follow-up of 4 years, diabetes incidence was 10.1% in the MedDiet with olive oil, 11.0% in the MedDiet with nuts and 17.9% in the control group. The incidence rate for diabetes was reduced 52% when the two MedDiet groups were pooled together and compared to the control group. They also found that adherence to the MedDiet was inversely associated with diabetes incidence. Although diabetes risk was reduced with the consumption of a MedDiet, there were no significant changes in physical activity or body weight [28]. This study demonstrates the effectiveness of diet modification for diabetes risk reduction, regardless of increasing physical activity and/or observing considerable weight loss.

The Diabetes Prevention Program (DPP) [5] conducted a 27-center randomized clinical study to determine if lifestyle intervention would prevent the incidence of diabetes in people with impaired glucose tolerance (IGT). The intervention incorporated a multifaceted approach providing various ways to reduce diabetes risk. Through an extensive network of training, feedback and clinical support, they had frequent contact with the participants with the assistance of individual case managers or “lifestyle coaches.” The investigators utilized a structured 16-session core-curriculum that taught the participants behavioral self-management to promote weight loss and physical activity. They also provided supervised physical activity sessions, which encouraged and guided the participants to exercise more. The intervention framework was fairly flexible with the implementation of the maintenance program, where group and individual sessions were provided in accordance to the needs of the participant. Behavior maintenance was encouraged using an individualized “toolbox” of adherence strategies. Finally, the flexibility of the intervention allowed accommodations for ethnic diversity. Participants (n=1079) were overweight or obese, consisting of 55% Caucasian, 20% African American and 16% Hispanic. The main goals of the intervention were a minimum of 7% weight loss and a minimum of 150 minutes of moderate intensity physical activity per week. They found that lifestyle modifications decreased the incidence of type 2 diabetes by 58% [5].

Similarly, a study conducted by Tuomilhto *et al.,* [7] sought to determine if lifestyle modification could reduce the incidence of diabetes in overweight people with IGT (n=522). The participants randomized into the treatment group received individualized nutrition counseling aimed at increasing physical activity, promoting weight loss, increasing fiber intake and reducing total fat intake. They found that the incidence rate was reduced 58% ($P<0.001$) in the intervention group [7]. Another large-scale study conducted by Pan *et al.,* [6] sought to determine if lifestyle modifications in diet and exercise could potentially delay and reduce the incidence of diabetes in people with IGT, in order to reduce the overall complications associated with diabetes. The participants (n=110,660) were randomized into 4 study arms: diet, exercise, diet + exercise, or control and found that modifications to diet and/or exercise resulted in a reduction of diabetes incidence ranging between 31-46%. In the Malmo study conducted by Eriksson and Lindgarde [4], glucose tolerance was normalized in >50% of the participants with IGT in the lifestyle intervention. They found that weight loss was correlated with improvements in glucose tolerance ($r=0.19$, $p<0.02$). In addition, the diabetes incidence rate in the intervention group was 10.6% over 5 years compared to 28.6% in the control group [4], demonstrating that lifestyle modification can reduce incidence of diabetes more than two-fold.

In a more recent study by Parker *et al.* [13] conducted a randomized, controlled, clinical nutrition intervention with overweight people with prediabetes. The participants (n=76) with impaired fasting plasma glucose or an HbA1C of 5.7 to 6.4% were recruited to participate in a 12-week nutrition intervention. The participants were randomized into the treatment group (n=41) or the control group (n=35). The intervention consisted of medical nutrition therapy (MNT), which was based on the American Diabetes Association Standards of Medical Care. The control group only received printed educational material related to prediabetes. The intervention was conducted by a registered dietitian and consisted of education that encouraged lifestyle changes to promote weight loss of 5% to 7% of starting weight, regular physical activity of approximately 150 minutes per week and various ways to encourage caloric and dietary fat intake reduction. Self-management training was also provided to the participants in the intervention group regarding individualized goals and enabled the participant to identify certain risk factors related to type 2 diabetes and formulate appropriate weight loss goals [13]. The participants met with the registered dietitian 4 times during the intervention, with the first visit being an assessment visit lasting about 60 minutes, and the following 3 visits lasting ~30-45 minutes each. The encouraged diet consisted of 15-20% of total caloric intake to be from protein sources, 60% to 70% from carbohydrate and fat mainly from monounsaturated fat sources, with <7% saturated fat and low *trans* fat intake. The micronutrient distribution was individually modified according to the participant's needs by the registered dietitian. The participants were encouraged to consume whole grains to increase their fiber intake in accordance with the US Department of Agriculture recommendations for dietary fiber (14 grams fiber/ 1000 kcal). Alcohol was limited to moderate consumption (<1 drink per day for women and <2 drinks per day for men).

After the 12-week intervention, the authors found a significant reduction in HbA1C levels in the treatment group compared to the control group (P=0.01). They also found a significant reduction in Diabetes Risk Scores in the treatment group compared to the control group (P=0.001). They concluded that individualized MNT is effective in reducing diabetes risk in people with prediabetes.

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CHAPTER III: METHODOLOGY

Design

Approval from the Institutional Review Board (IRB) was obtained at Florida International University (FIU) prior to the start of the study (IRB-17-0058-CR01). A 6-month randomized, controlled nutrition intervention was conducted in prediabetic people living with HIV (PLWH). The study participants were recruited from the Miami Adult Studies for HIV (MASH) cohort. MASH cohort participants have previously provided consent to search their study charts for eligibility in additional studies.

To identify the potential participant the eligibility and Inclusion/Exclusion Criteria described below were used, and telephone calls to these participants were made to attend a screening study visits:

Inclusion criteria:

> HIV positive, prediabetic (IGT, IFG or elevated glucose levels according to American Diabetes Association guidelines), 18-65 years of age, receiving stable ART for at least 6 months, undetectable controlled viral load (<50 copies/mL) and English speaking

Exclusion criteria:

> Previous history or treatment of type 2 diabetes, concomitant use of medication known to alter glucose levels such as corticoids, use of weight loss drugs, pregnancy or breastfeeding, and refusal or inability to give informed consent to participate in this study.

Informed consent for the proposed study was administered prior to the screening and those eligible were asked to participate. Upon their consent, the participants were randomized into the treatment group (intervention) or the control group. All participants visited the FIU Research Clinic at Borinquen Health Care Center at baseline for assessment and at the 6-month follow-up as part of the MASH cohort.

The intervention consisted of monthly visits to receive the intervention for those randomized to the intervention group. The intervention was based on the American Diabetes Association (ADA) Standards of medical care in diabetes, consisting of medical nutrition therapy (MNT), nutrition education and nutrition counseling. At baseline, the control group received printed educational material on prediabetes/diabetes, which were based on the ADA Standards of Medical Care.

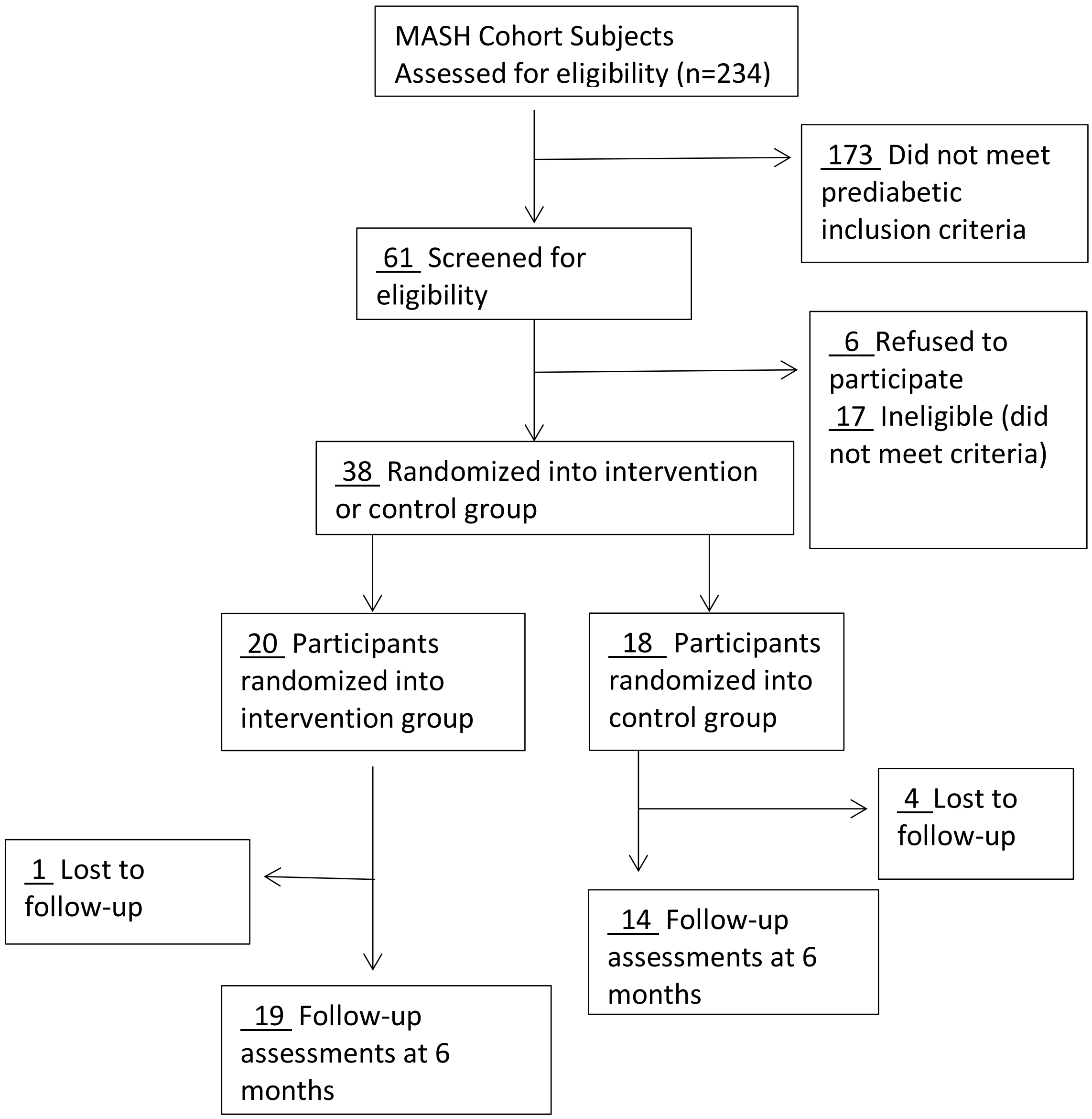
Recruitment

Subjects were recruited from the Miami Adult Studies on HIV (MASH) cohort and consented at the FIU-Borinquen Clinic. Once participants provided informed consent, blood was collected to assess levels of biomarkers of interest (fasting blood glucose, 8OHdG and hs-CRP). The advantage of recruiting from the MASH cohort is that the characteristics and medical history of the participants are known, and most participants received their care at the Borinquen Health Care Center. Detection of any abnormal values during the research study were reported to the participants and to their primary care providers with the participant's permission.

Randomization

After the study participants have been recruited and screened for eligibility, those eligible and willing to participate in the proposed study signed the informed consent form and were randomized into the treatment (intervention) group or the control group. Participants were randomized using a computer random number generator to assign them to the study groups. Even numbers were assigned to the intervention group and odd numbers were assigned to the control.

Figure 1. CONSORT Diagram of Study Cohort



Intervention (Treatment)

Education Sessions

Participants randomized into the intervention group (n=20) attended monthly one-on-one sessions with the investigator under the supervision of a registered dietitian at the FIU-Research Clinic located at the Borinquen Health Care Center in Miami, Florida. The initial assessment visit at baseline lasted approximately 1 hour with the remaining 5 sessions lasting 45 minutes each, for a total of 6 sessions. The sessions were formal education sessions consisting of medical nutrition therapy (MNT) based on the American Diabetes Association Standards of Medical Care.

The sessions consisted of diabetes education, emphasis on lifestyle changes to promote moderate weight loss (5-7% of starting weight), regular physical activity (~150 minutes/week) and strategies to reduce calorie and fat intake. The participants were also encouraged to limit alcohol consumption (women: <1 drink/day and men: <2 drinks/day), and to eat more whole grains, fruits and vegetables.

In order to tailor the nutrition intervention to meet the specific needs of PLWH, the education sessions also included basic education about HIV disease and its treatment (ART). This familiarized the participants with their HIV disease and its implications, the importance of adhering to ART doses, and informed them of the adverse effects of ART on their body and the need to increase intentional care in response. All educational material regarding HIV and nutrition were based on the standards of the American Dietetic Association of nutrition intervention in the care of persons with HIV.

Assessments

Anthropometrics such as height (cm), weight (kg), waist circumference (cm), hip circumference (cm), BMI (kg/m^2) were measured by the investigator and the registered nurse at the Borinquen Health Care Center located in Miami, FL. Blood was drawn at baseline and 6-month follow-up visits to measure fasting blood glucose, 8OHdG and hs-CRP levels.

Table 1. Measures of the Study Collected at Baseline and 6-Month Follow-up

Measurements	
Anthropometrics	Height (cm)
	Weight (kg)
	Waist circumference (cm)
	BMI (kg/m^2)
Metabolic Outcomes	Fasting blood glucose (mg/dl)
	8OHdG (mg/dl)
	hs-CRP (mg/dl)

Blood Draws and Urine Collection

Blood was drawn by a trained phlebotomist/registered nurse at baseline and at the 6-month follow-up at the FIU Research Clinic. The blood was processed at the FIU laboratory located at the Modesto Maidique FIU campus (Miami, FL). The whole blood was separated into sera and plasma, which was then aliquoted and stored in -80^oC freezers until all the samples were collected at the end of the intervention. Enzyme linked immunosorbent assay (ELISA) kits were used to perform the tests to measure biochemical parameters.

Metabolic Parameters

Fasting blood glucose levels were measured to assess the effectiveness of the proposed intervention in improving glycemic control. 8OHdG levels were measured to assess the effectiveness of the nutrition intervention in reducing oxidative stress associated with elevated glucose levels. Hs-CRP was measured to assess the effectiveness of the intervention in reducing inflammation associated with elevated glucose levels.

Data Management

Data from the nutrition intervention were recorded by the investigator into the data management system, REDCap, as well as on de-identified data collection forms. Each assessment form had an assigned ID to link it. In addition, to protect the identity of the participants and any confidential information, participant IDs (PIDs) were assigned to each participant and that number were used on the assessment form itself. No PHI was printed on the assessment forms.

Statistical Analyses

The analyses on the outcomes of this study were conducted with intent-to-treat analyses. The effectiveness of the nutrition intervention in reducing glycemic parameters was assessed by a significant reduction in fasting blood glucose in the treatment group as compared with the group that will not receive intervention. The effectiveness of the intervention was also assessed by the reduction in oxidative stress and inflammation biomarkers, 8OHdG and hs-CRP levels.

Data were tested for normality (Shapiro-Wilk test); means/standard deviations were used to describe normally distributed data and frequencies/proportions were used to describe non-normally distributed data. Parametric tests were used to analyze normally distributed data (paired t-test, independent student t-test, etc.); categorical data were presented as frequencies and proportions and analyzed with McNemar, Fisher Exact test and Mann Whitney U-test. Significance was set at $p \leq 0.05$ and all statistical tests were performed using Statistical Package for Social Science (SPSS) version 23.

CHAPTER IV: Effectiveness of a 6-Month Nutrition Intervention Targeting Prediabetes in People Living with HIV (PLWH) and Prediabetes

Introduction

People living with HIV (PLWH) are known to have higher risk for co-morbidities, such as prediabetes/diabetes and cardiovascular disease, at earlier ages compared with their non-infected counterparts [1-2]. Their increased risk may be due to a myriad of factors including, but not limited to HIV infection and the chronic use of antiretroviral therapy (ART) [3-6]. The incidence of prediabetes in PLWH is reported in the literature to be 2-3 times higher than the general non-HIV infected population and is expected to rise if effective interventions are not implemented [7-9].

Prediabetes is a transient state of hyperglycemia which is known to increase the risk of developing diabetes, with an annual conversion rate of 5-10%, if left unaddressed [10-11]. The American Diabetes Association (ADA) and the World Health Organization (WHO) have similar but slightly different diagnostic criteria for prediabetes. According to the ADA's guidelines, prediabetes is diagnosed with fasting blood glucose levels between 100 mg/dl to 125 mg/dl (fasting for ≥8 hours), hemoglobin A1C (HbA1C) values 5.7-6.4% and/or 2-hour plasma glucose of 140-199 mg/dl after a 75 gram of oral glucose tolerance test [10]. The WHO has a difference fasting blood glucose range of 110-125 mg/dl, similar 2-hr oral glucose tolerance test range to ADA guidelines, but no diagnostic range for HbA1C [10].

People with prediabetes are a target population for the implementation of effective interventions to stop and/or reverse to normal glucose levels [11-15]. In a study conducted by Eriksson and Lindgarde [17], reported that glucose tolerance was normalized in >50% of the participants with impaired glucose tolerance (IGT) with effective lifestyle modifications. Prior research has shown the effectiveness of implementing lifestyle changes in reducing overall diabetes risk/incidence by 58% in people with prediabetes, thus supporting the importance of implementing interventions in this particular population [13-14] [16].

Nutrition Interventions for Prediabetes

The Diabetes Prevention Program was a large scale 27-center intervention randomized clinical study (*n=1079*) conducted to determine the effectiveness of a lifestyle intervention to lower diabetes risk and/or prevent diabetes incidence in people with prediabetes [13]. The intervention was multifaceted, consisting of a variety of ways to reduce diabetes risk including weight loss, physical activity and behavior change techniques. The researchers utilized individual case managers or "lifestyle coaches" to implement the 16-session core curriculum that taught participants certain beneficial lifestyle changes. They found that certain lifestyle changes aimed at weight loss and increasing physical activity decreased the incidence of type 2 diabetes by 58% [13].

Another study conducted by Tuomilhto et al. [16] assessed the effectiveness of lifestyle modifications in reducing diabetes risk among overweight people with prediabetes (*n=522*). The participants that were randomized into the treatment group received nutrition counseling to increase physical activity, increase fiber intake and reduce dietary fat intake, and for overweight participants promote weight loss. Similarly, to Diabetes Prevention Program, they found that the incidence rate was also reduced by 58% ($p<0.001$) in the intervention group [16]. Moreover, Pan et. al. [18] conducted a randomized controlled clinical study (N=110,660) to determine if lifestyle changes in diet and exercise could delay and/or reduce diabetes incidence in people with impaired glucose tolerance. They found that changes in diet and/or increasing exercise frequency reduced diabetes incidence by 31-46%.

Oxidative Stress

Hyperglycemia, or elevated blood glucose levels, which is characteristic of prediabetes is known to increase the production of reactive oxygen species, i.e. oxidative stress [19] [24]. Therefore, prediabetes has been associated with elevated levels of oxidative stress [19-24], with studies suggesting that hyperglycemia-induced oxidative stress may be responsible for the damage of pancreatic Islet beta cells, thus increasing diabetes risk [20]. It is reported that although beta cell death can be mediated by various etiological factors such as glucotoxicity, lipotoxicity, and pro-inflammatory mediators, hyperglycemia was determined to be the biggest contributor [20]. Chronic exposure to hyperglycemia has been shown to initiate beta cell death in cell cultures, as well as animal models; these effects have been observed in autopsy examinations of humans [20].

In an effort to minimize beta cell destruction and delay/prevent diabetes incidence in people with prediabetes, glycemic monitoring and control may help prevent development of diabetes, especially in PLWH, who already are exposed to elevated levels of oxidative stress related to HIV infection and/or the chronic use of ART [25-26]. Kwak et al. [27] demonstrated the effectiveness of a 4-week dietary intervention in significantly reducing blood glucose and oxidative stress in people with prediabetes or newly diagnosed type 2 diabetes; however, this has not been assessed in PLWH with prediabetes.

Inflammation

In PLWH elevated levels of inflammation are frequent, despite sustained ART mediated viral suppression [28][31]. Although inflammation and immune activation normally decline during consistent ART treatment, they tend to remain elevated in many PLWH and predict mortality and/or co-morbidities, including diabetes and cardiovascular disease [28]. An Analysis of the FRAM Study Cohort revealed that PLWH have elevated inflammatory marker, C-reactive protein (CRP). In FRAM, levels of CRP >3mg/L had 2.7 folds higher adjusted odds of mortality than those with CRP levels of <1mg/L [29].

On the other hand, prediabetes and hyperglycemia are also associated with elevated inflammation levels [30], independent of HIV status. The increased levels of inflammation in PLWH may increase risk for diabetes, as systemic inflammation has been associated with incident diabetes [32]. Moreover, it is expected that prediabetic PLWH will have an even higher risk for developing diabetes, including inflammation related to HIV infection along with inflammation related to hyperglycemia.

Significance

Numerous studies have shown the effectiveness of lifestyle modifications in lowering diabetes risk in people with prediabetes [13] [16-18]; however, research on the effectiveness of lifestyle modifications in lowering diabetes risk in prediabetic PLWH has been scarce. Therefore, we conducted a randomized controlled clinical trial of a 6-

month nutrition intervention in prediabetic PLWH to assess the effectiveness of lifestyle modifications in lowering blood glucose, oxidative stress and inflammation.

Methods

Approval from the Institutional Review Board was obtained at Florida International University (IRB-17-0058-CR01). A 6-month randomized, controlled nutrition intervention was conducted in prediabetic people living with HIV (PLWH). The study participants were recruited from the Miami Adult Studies for HIV (MASH) cohort. MASH cohort participants provided consent to review their medical documentation for eligibility. Inclusion/exclusion criteria were used to identify participants who were eligible and telephone calls to these participants were made to attend a screening study visit. After their consent, the participants were randomized into the treatment group (intervention) or the control group. All participants visited the FIU Research Clinic at Borinquen Health Care Center at baseline for assessment and at the 6-month follow-up as part of the MASH cohort.

Participants were determined to be "prediabetic" based on the American Diabetes Association (ADA) diagnostic criteria of fasting blood glucose values of 100 mg/dl to 125 mg/dl (fasting for ≥8 hours) or hemoglobin A1C (HbA1C) values 5.7-6.4% [10]. Inclusion criteria included HIV seropositive, prediabetic, 18-65 years of age, receiving stable ART for at least 6 months, undetectable HIV viral load (<50 copies /ml) and English speaking. Exclusion criteria included any previous history of type 2 diabetes, concomitant use of glucose altering medication (corticosteroids, etc.), use of weight loss drugs, pregnancy or breastfeeding and/or refusal or inability to give informed consent to participate in the study.

Participants (N=38) were randomized into either the intervention group (n=20) or the control group (n=18). Participants randomized into the intervention group received individualized sessions composed of medical nutrition therapy (MNT), nutrition education and nutrition counseling, which are all based on the American Diabetes Association (ADA) Standards of Medical Care in Diabetes [33]. The first session lasted approximately 1 hour, and each subsequent visit lasted approximately 45 minutes, for a total of 6 visits. The intervention utilized a developed curriculum that was specifically tailored to PLWH which provided structure to the intervention; however, each session was individualized and catered to each participant's nutritional needs at the time of the session. The participants randomized into the control group received at baseline educational material on prediabetes/diabetes, which is consistent with the ADA Standards of Medical Care in Diabetes [33].

The educational portion of the intervention included the following topics: 1) HIV, ART and prediabetes—how are they all interrelated?; 2) Understanding BMI and the importance of maintaining normal body weight; 3) Dietary intake and the importance of fruits and vegetables; 4) Energy expenditure and the importance of physical activity; 5) Dietary fat and ways to avoid excessive eating; and 6) Alcohol and its effect on the body.

The overall goal of the intervention was to encourage fruits and vegetables intake, reduce simple carbohydrate intake and promote physical activity, both of which tends to be inadequate in this low-income population. Fasting blood was drawn at baseline and at the 6-month follow up visit by a trained phlebotomist/registered nurse to measure the levels of biomarkers of interest. Whole blood was separated and processed into plasma and aliquoted to be stored at -80^{o}C freezers and were batch analyzed. Samples were sent to LabCorp to obtain levels of FBG and CRP, and enzyme linked immunosorbent assay (ELISA) kit from G-Biosciences was used to measure changes in 8OHdG.

Parametric tests (Independent student t-test, paired t-test, etc.) were used to determine significant difference between means if the data was normally distributed; non-parametric tests (Mann-Whitney U-Test, etc.) were used to determine significant difference if the data are not-normally distributed. All statistical analyses were conducted on Statistical Package for the Social Sciences (SPSS) Version 23.0 and p-values ≤0.05 were considered significant difference.

Results

Participants (N=38) that were recruited in the study had a mean age of ~57 years old, 58% were male and the mean annual income was about $13,325.03/year (Table 1). The average number of years since the participant was diagnosed with HIV infection was 20. The average BMI was 30 kg/m^2, which is considered to be obese class I. The average waist circumference was 40 inches, hip circumference is 42 inches and waist-to-hip ratio (WHR) is 0.95. The mean fasting blood glucose (FBG) was 108 mg/dl, which falls within the American Diabetes Association (ADA) prediabetic guidelines of 100-125 mg/dl. The mean inflammatory marker, high sensitivity C-reactive protein (hs-CRP), was 7.73 mg/dl (normal is <3 mg/dl).

There were no significant differences between the two study arms at baseline for age, income, BMI, waist circumference, hip circumference, waist-hip circumference (WHR), fasting blood glucose or 8OHdG. Significant differences were found in the number of years having HIV infection between the intervention group (mean= 16 years) and the control group (mean=24 years) and levels of hs-CRP with intervention group having a mean of 2.5 mg/dl and the control group with mean of 6.3 mg/dl.

Table 1. Comparison of Baseline Characteristics Between Intervention and Control Group Participants

Baseline Characteristic	**Intervention Group Mean ± SD (n=20)**	**Control Group Mean ±SD (n=18)**	**Comparison between groups (P-Value)**
Sex: *Female* *Male* *Transgender*	 7 13 0	 8 9 1	 0.516
Age (years)	56±6	58±9	0.317
Income ($/year)	13072±8578	13605±14323	0.889
Years of HIV Infection	16.3±7	24.8±8	0.001**
BMI (kg/m^2)	29.4±6	30.7±6	0.473
Waist Circumference (inches) *Female* *Male*	 39.6±6* 39.9±4	 40.6±5* 39.2±5	0.914
Hip Circumference (inches) *Female* *Male*	 44.5±6 41.1±4	 43.8±5 41.1±4	0.959
Waist-to-hip ratio (WHR) *Female* *Male*	 0.91±0.05* 0.96±0.06*	 0.93±0.06* 0.96±0.05*	0.931
Fasting Blood Glucose (mg/dl)	107.80±6.26	108.33±8.56	0.79
High-sensitivity C-Reactive Protein (mg/dl)	2.5±2.6	6.30±5.30	0.03**
8-hydroxydeoxyguanosine (mg/dl)	127.23±65.40	90.04±58.66	0.21

*risk of metabolic complications is substantially increased
**significant differences observed; significant set at $p \leq 0.05$.

Analyses shown in Table 2 revealed significant differences within the intervention group for BMI (*p=0.03*), fasting blood glucose (*p=0.03*) and 8OHdG (*p=0.04*) between the baseline and 6-month assessment; no significant differences were observed in the control group. No significant differences were observed for waist circumference, hip circumference, waist-to-hip circumference or CRP levels in either the intervention group or the control group. Moreover, no significant difference was observed between the two study arms at the 6-month follow-up for any of the parameters. However, significant difference was observed for BMI change (~1 unit reduction) for the participants in the intervention group compared to the BMI change of the participants in the control group (*p=0.05).* No significant difference was observed for the remaining parameter changes (Table 2).

Table 2. Comparison of Changes in Parameters Between Intervention and Control Groups from Baseline to 6-Months

Parameter	**Intervention Group (mean±SD)**		**Pre/ Post Test (p-value)**	**Control Group (mean±SD)**		**Pre/ Post Test (p-value)**	**Parameter Changes Comparison (p- value)**
	Baseline (n=20)	**6-Month (n=19)**		**Baseline (n=18)**	**6-Month (n=14)**		
BMI (kg/m^2)	29.4±6	28.8±6	0.03*	30.7±6	31.6±6	0.10	0.05**
Waist (in)	39.9±4	39.2±5	0.16	40.1±5	41.4±5	0.13	0.08
Hip (in)	42.3±5	42.3±4	0.74	42.4±5	43.29±5	0.11	0.52
WHR	0.94±0.1	0.93±0.1	0.56	0.95±0.1	0.96±0.1	0.11	0.22
FBG (mg/dl)	108.4±6	96.2±18.2	0.03*	109.9±9	99.2±23	0.11	0.86
CRP (mg/dl)	2.5±2.6	4.1±4	0.40	6.3±5	4.3±4	0.12	0.56
8OHdG (mg/dl)	127.23± 65.4	100.9± 53.74	0.04*	90.04±58.6	87.24±49	0.43	0.16

*significant differences observed within intervention group; significance set at p≤ 0.05
**significant difference observed between study arms; significance set at p≤ 0.05

After the 6-month nutrition intervention, there was a significant reduction in fasting blood glucose (FBG) levels within the intervention group at the 6-month follow-up when compared to their baseline values; however, this was not observed in the control group, although marginally significant. As can be seen, although not significant, there was still an improvement in the fasting blood glucose levels in the control group after the 6-months, and this may be due to the initial visit where all participants were notified that their blood glucose levels are above normal and were eligible to participate in a randomized, controlled trial of an intervention. When the participants were made aware of their prediabetic state at baseline during recruitment, they were more likely to make changes at that point. They were also given educational material at baseline, which provided additional information, promoting lifestyle changes. No significant difference was observed when comparing the FBG values between the study groups at the 6-month follow-up or comparing the changes in FBG between the 2 study groups.

We also observed a significant reduction in the body mass index (BMI) within the intervention group after the 6-month intervention, which is favorable. However, no significant difference in BMI was observed in the control group participants. It is also worth noting that the participants in the intervention group lost a significant amount of weight, with an average drop in 1 unit of mean BMI; however, the participants in the control group had the exact opposite experience, where they had gained weight after the 6-months, resulting in a 1-unit increase in mean BMI. There was no significant difference in the BMI between the 2 study groups after the 6-month follow up.

Significant difference was also observed for BMI change for the participants in the intervention group compared to the BMI change of the participants in the control group. With the mean BMI change in the intervention group being negative and the mean

BMI change in the control group being positive, it is evident that the participants in the intervention group were consistently losing weight, while the participants in the control group were gaining weight.

Although there was no significant difference within the groups after the 6-month intervention in regard to waist and hip circumferences, it is notable to mention that the waist and hip circumference in the control group actually increased by 1 inch (each anthropometric parameter), while the waist and hip circumference in the intervention group remained the same after the 6-month intervention. Moreover, although not significant, the waist-to-hip ratio (WHR) also decreased in the intervention group by 1 unit, while the WHR in the control group increased by one unit, thus further increasing risk for other metabolic conditions such as diabetes and cardiovascular disease. These findings suggest that nutrition interventions may be effective in halting the adverse effects of bodily dysmorphia associated with HIV infection and chronic use of ART treatment.

In relation to inflammation, no significant differences were observed within or between the study groups in C-reactive protein (CRP) levels. Lastly, a significant reduction was observed in oxidative stress biomarker, 8-hydroxy deoxyguanosine (8OHdG) levels within the intervention group; however, no significant difference was observed within the control group. This finding suggests that nutrition interventions are effective in lowering oxidative stress in prediabetic PLWH by promoting lifestyle changes, thus lowering risk for metabolic complications such as incident diabetes and cardiovascular disease. No significant difference was observed between the study arms at the 6-month follow-up, which may be due to the small sample size ($N=38$).

Discussion

The increased risk for prediabetes/diabetes in PLWH is well documented in the literature [7-9] and while numerous studies have previously shown the effectiveness of nutrition/lifestyle interventions in lowering diabetes risk among people with prediabetes [13][16][17], research is lacking for PLWH. However, studies such as this one, are now emerging, demonstrating the effectiveness of interventions in promoting positive outcomes and lowering diabetes risk in prediabetic PLWH.

A recent mixed-methods study by Duncan et al. [34] conducted a 6-month diet and physical activity intervention for prediabetic PLWH (N=28) to assess its effectiveness and acceptability to reduce diabetes risk in PLWH. They provided individualized advice monthly to assist the participants in meeting 10 diet and physical activity goal, including but not limited to weight loss, fruit and vegetable intake and physical activity. assessed diabetes risk based on pre-post glucose and insulin responses to 3-hour meal tolerance test. They found that glucose, insulin, waist circumference, systolic blood pressure and triglycerides were significantly reduced after the 6-month intervention [34]. They concluded that their 6-month intervention was effective in mitigating the increased risk of type 2 diabetes associated with HIV infection.

The results of the study conducted by Duncan et. al. [34] supports the results of this current intervention study, demonstrating the effectiveness of lifestyle changes in lowering diabetes risk in prediabetic PLWH. They found that the fasting blood glucose of the participants (N=28) had an average of 0.5 mmol/l (~9 mg/dl) reduction after the 6-month intervention (paired t-test; p-value=0.003). This finding is consistent with the average fasting blood glucose reduction of ~12 mg/dl observed in the intervention group after the 6-month intervention.

Along with significant reduction in fasting blood glucose for the intervention group, there were significant reductions in BMI and 8OHdG levels within the intervention group after the 6-month intervention. Moreover, while participants in the control group were gaining weight after the 6-month duration with a unit increase in BMI, waist and hip circumferences and WHR, these same anthropometric parameters (BMI, waist/hip circumference, WHR) of the participants in the intervention group either remained relatively the same (waist/hip circumferences) or improved (BMI, WHR); this suggests that the intervention was effective in reducing and/or reversing the progressive adverse effects associated with prediabetes in PLWH.

The positive outcomes from this intervention study and the study by Duncan et al. [34] demonstrated the effectiveness of lifestyle modifications in lowering diabetes risk by significantly lowering blood glucose levels, BMI, oxidative stress, insulin, waist/hip circumference, systolic blood pressure and triglyceride levels in prediabetic PLWH. There are no other known intervention studies that were conducted in this unique population. Large scale studies with longer duration of follow-up visits are needed in this high-risk population to determine if they are effective in subsequently lowering diabetes incidence and overall prevalence in prediabetic PLWH.

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CHAPTER V: Effectiveness of a 6-Month Nutrition Intervention in Behavioral Change in People Living with HIV (PLWH)

Introduction

The prevalence of prediabetes in people living with HIV (PLWH) is 2 to 3 times higher than the general population [1-3]. The increased risk for prediabetes in this specific population is multifactorial, including but not limited to HIV infection, chronic use of antiretroviral therapy (ART), and aging due to the success of the ART treatment [4-7]. As diabetes/prediabetes are known to be delayed with healthy-eating and lifestyle habits, it is important to develop effective behavioral interventions to promote healthy changes to balance the higher risk for prediabetes in PLWH.

Many PLWH tend to be low income and of lower socio-economic status, with greater prevalence of HIV infection occurring at the lower end of income and socioeconomic status [8]. The additional factors of low income and socio-economic status may contribute to the difficulty in implementing effective nutrition interventions in this unique population. Therefore, the purpose of this study was to test a modified nutritional intervention that promotes adequate behavioral changes to prevent or ameliorate the risks of prediabetes in this unique population of low-income prediabetic PLWH.

Several behavioral-change frameworks have been proven effective in creating positive behavioral change, including but not limited to Health Belief Model [9-10] and Transtheoretical Model [11-12]. The Health Belief Model was developed to help understand and explain health-related behavior based on perceived barriers, benefits, self-efficacy and threat. Based on these parameters, an individual's behavior may be effectively altered if any of these domains are properly addressed [8-10]. Narayan *et al*. [13] assert that based on the Health Belief Model, people need to perceive both risk of disease and potential benefit of implementing a behavior change. As people with prediabetes have increased risk of developing diabetes, they are perfect candidates for implementing an intervention based on the Health Belief Model, creating clear connections between increased risk and potential benefit of health promoting behaviors [13].

Moreover, the Transtheoretical Model is an integrative behavior change model that assesses an individual's readiness to make certain positive changes and is composed of constructs such as *stages of change* and *self-efficacy* [11-14]. The Transtheoretical Model proposes that in order for effective behavior change, an individual must progress through the 5 *stages of changes*: *precontemplation, contemplation, preparation, action* and *maintenance* [14].

A randomized controlled pilot study, Avoiding Diabetes Thru Action Plan Targeting (ADAPT) conducted by Kolb et al. [15] utilized the Transtheoretical Model to assess the readiness and *stage of change* of people with prediabetes in implementing health behavior changes. They found that the study participants were already aware of their increased risk of developing diabetes and after the intervention, demonstrated increased levels of *self-efficacy* to make behavioral changes to lower their diabetes risk [15].

Although numerous studies incorporating proven behavioral change models have been conducted in the general population, research utilizing behavioral change models and assessing the different constructs is limited in PLWH, a unique population group with high risk for diabetes. The objective of this randomized, controlled clinical trial is to assess the effectiveness of a 6-month lifestyle/nutrition intervention in guiding low income prediabetic PLWH through the *stages of change* and promoting *self-efficacy*, as measured by domains and instruments of the Health Belief Model and the Transtheoretical (Stages of Change) Model.

Methods

Approval from the Florida International University (FIU) Institutional Review Board (IRB) was obtained (IRB-17-0058-CR01). A 6-month randomized, controlled nutrition intervention was conducted in prediabetic people living with HIV (PLWH). The study participants were recruited from the Miami Adult Studies for HIV (MASH) cohort. MASH cohort participants provided consent to review their medical documentation for eligibility and to participate in the study procedures, which was explained to them in detail. Inclusion/exclusion criteria were used to identify participants who were eligible, and telephone calls to these participants were made to attend a screening study visit. Participants were randomized into the treatment group (intervention) or the control group. All participants visited the FIU Research Clinic at the Borinquen Health Care Centers at baseline for assessment and at the 6-month follow-up as part of the MASH cohort. Those randomized into the intervention group were seen monthly for 6 months. During the recruitment process, five potential participants were not eligible and excluded from the study because they were previously initiated on metformin, which is becoming the standard of care for this population.

Participants were determined to be “prediabetic” based on the American Diabetes Association (ADA) diagnostic criteria of fasting blood glucose of 100 mg/dl to 125 mg/dl (fasting for ≥8 hours) or hemoglobin A1C (HbA1C) values 5.7-6.4% [16]. Inclusion criteria were: HIV seropositive, prediabetic, 18-65 years of age, receiving stable ART for at least 6 months, undetectable HIV viral load (<50 copies /ml) and English speaking. Exclusion criteria included any previous history of type 2 diabetes, concomitant use of glucose altering medication (corticosteroids, etc.), use of weight loss drugs, pregnancy or breastfeeding and/or refusal or inability to give informed consent to participate in the study.

Participants (N=38) were randomized into either the intervention group (n=20) or the control group (n=18). Participants randomized into the intervention group received individualized sessions that comprised medical nutrition therapy (MNT), nutrition education and nutrition counseling, which are all based on the American Diabetes Association (ADA) Standards of medical care in diabetes [16]. The first session lasted approximately 1 hour, and each subsequent visit lasted approximately 45 minutes, for a total of 6 visits. The intervention utilized a curriculum that was specifically tailored to PLWH which provided structure to the intervention; however, each session was individualized and catered to each participant's nutritional needs at the time of the session. The participants randomized into the control group received educational materials on prediabetes/diabetes, also based on the ADA Standards of medical care in diabetes only at the baseline visit [16].

The educational portion of the intervention included the following topics: 1) HIV, ART and prediabetes- how are they all interrelated?; 2) Understanding BMI and the importance of maintaining normal body weight; 3) Dietary intake and the importance of fruits and vegetables; 4) Energy expenditure and the importance of physical activity; 5) Dietary fat and ways to avoid excessive intake; and 6) Alcohol and its effect on the body. The overall goal of the intervention was to encourage fruits and vegetables intake, reduce simple carbohydrate intake and promote physical activity, all of which may decrease the risks associated with prediabetes.

Validated questionnaires were administered at baseline and at the 6-month follow-up visit in an interview style method. The questionnaires that were administered to the participants in both groups included the *Stage of Change Assessment Tool* [17-19], *Nutrition Knowledge Assessment Tool* [20], and *Self-Efficacy Assessment Tool* [20-21]. Each assessment tool has been well validated, but tailored specifically to PLWH to be more applicable to this unique population of interest.

As this particular population is low-income with an average annual income of $13,325.03 ± $11,495 / year, most participants could not afford to obtain gym memberships or have easy access to a safe and conducive environment to partake in outdoor activities. To account for this, the intervention was focused particularly on increasing daily physical activity with normal day-to-day functions, such as cleaning the house, taking stairs instead of the elevator, walking to and from the grocery store, etc.

The *Stage of Change Assessment Tool* is based on the Transtheoretical Model [14] [22], which as aforementioned, is a proven behavior change model that proposes effective behavior change progresses through a series of stages. The *Stage of Change Assessment Tool* evaluates the participant's stage of change according to their willingness to make positive changes in their behavior in relation to physical activity, fruits and vegetable intake, fiber intake, fat consumption and usual alcohol consumption. Based on the participant's answers, they were categorized into the *1) Precontemplation, 2) Contemplation, 3) Preparation, 4) Action* and the *5) Maintenance Stage.*

First, the participants' diets were assessed using the guidelines described in the United States Department of Health and Human Services (USDHHS) 2000 Dietary

Guidelines for Americans [18] for each of the assessment components. The *Stage of Change* at which each participant was initially assigned was based on their answers to a series of questions in a *Stage of Change Assessment Flow Chart* (Figure 1).

Table 1. Overview of Dietary Guidelines based on the Dietary Guidelines for Americans-2000

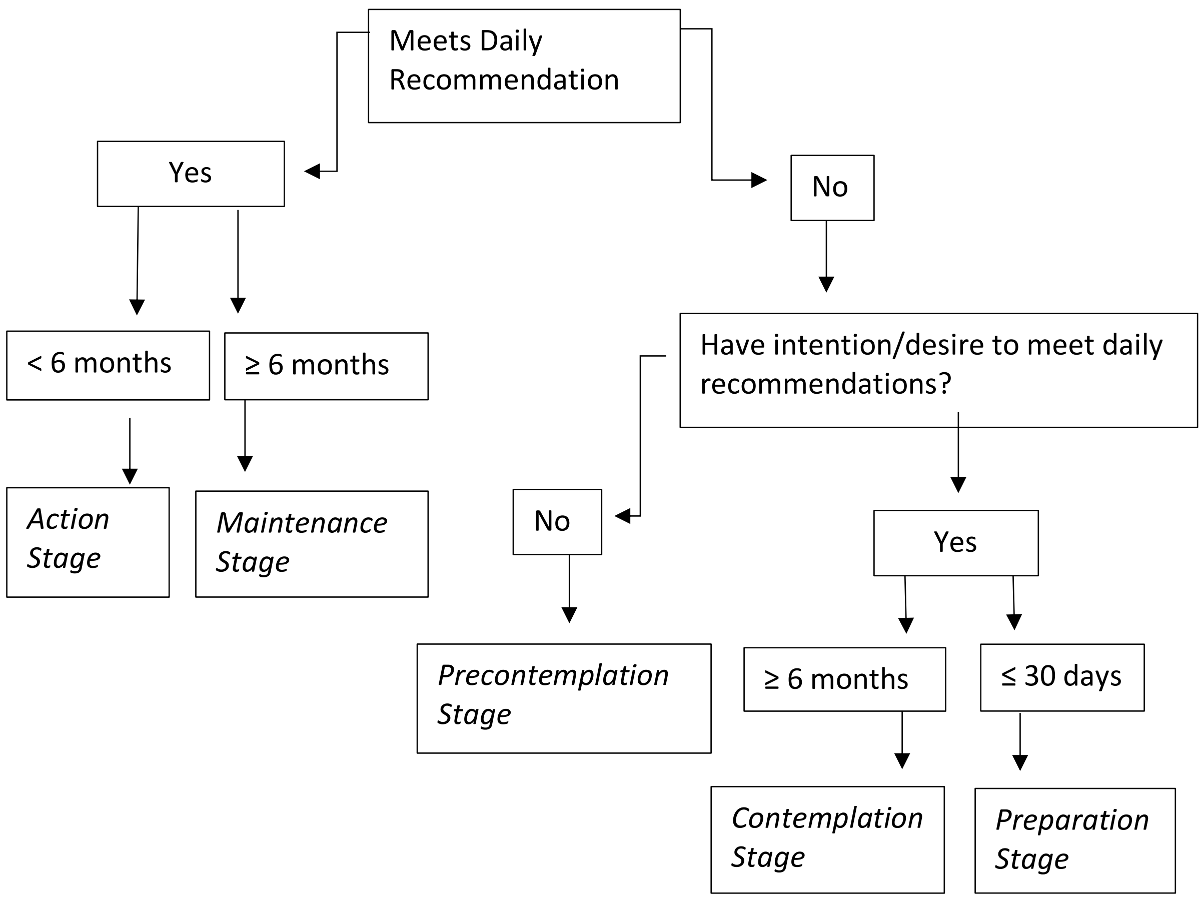
Behavior	**Guideline/Recommendation**
Physical Activity	≥ 30 minutes of *purposeful physical activity* regularly, preferably daily
Fruit and Vegetable Intake	≥ 2 servings of fruits and ≥ 3 servings of vegetables per day
Dietary Fiber Intake	≥ 6 servings of grain products, with ≥ 3 being whole grains
Dietary Fat Intake	< 30% of energy intake from total fat
Alcohol Consumption	≤ 1 alcoholic beverage per day (women) ≤ 2 alcoholic beverages per day (men)

If the participants were not currently meeting the guidelines (Table 1), they were asked if they have any desire to make changes to meet the recommended guidelines. If they were not interested and expressed no desire to make any changes, they were categorized in the *Precontemplation Stage of Change*. If they expressed that they desire to make changes, they were asked if they were willing to make changes in the near future (within 30 days) and those were assigned to the *Preparation Stage of Change,* or if those changes were considered in the far future (>6 months), they were categorized as being in the *Contemplation Stage of Change (*>6 months).

If the participants were currently meeting the guidelines, they were asked if they had met the guidelines for at least 6 months, which would put them in the *Maintenance Stage of Change*. If they have been meeting the guidelines for less than 6 months, then they would be categorized in the *Action Stage of Change.*

The Nutrition Knowledge Assessment Tool is a true/false and multiple-choice questionnaire with a total of 25 questions. The questionnaire contained a broad spectrum of questions about health and nutrition, including the selection of the correct MyPlate illustration [23] with the appropriate proportions of the different food groups, good sources of fiber and basic understanding of the role of food/nutrition in lowering disease risk. In addition, based on the Health Belief Model, it contained questions to assess the participants awareness of the role of nutrition and physical activity in health promotion and disease prevention. Visual aids were used to assess the process of assessing nutrition knowledge.

Figure 1. Flowchart of *Stage of Change* Assessment



Lastly, the *Self-Efficacy Assessment Tool* was used to assess the *self-efficacy* and confidence of the participants in making certain changes in their lives to promote positive health outcomes. The questionnaire was slightly modified to be more applicable to this particular population group. Such modifications included questions about fast food consumption, which is common in this low-income population and excluded numerous questions about gym memberships and attendance, which is not very common in this particular low-income study population.

Areas related to self-efficacy in the questionnaire included confidence in meeting guidelines for fruits and vegetable consumption, physical activity, and meeting health goals despite being sad or depressed. Participants can answer the 25-unit questionnaire in a range between 0-3 (0 being least confident and 3 being very confident) in terms of their confidence for making decisions regarding their health and lifestyle choices, with a maximum score of 75.

Data were tested for normality (Shapiro-Wilk test); means/standard deviations were used to describe normally distributed data and frequencies/proportions were used to present categorical data. Parametric tests were used to analyze normally distributed data (paired t-test, independent student t-test, etc.) and categorical data were presented as frequencies and proportions and analyzed with McNemar, Fisher Exact test and Mann Whitney U-test. Significance was set at $p \leq 0.05$ and all statistical tests were performed using Statistical Package for Social Science (SPSS) version 23.

Results

To analyze changes in the *stage of change* of the participants in both the intervention and control groups, the 5 *stages of change* were separated into two groups: a) stages of inaction and b) stages of action. The stages of inaction included the Precontemplation, Contemplation and Preparation *stages of change*; the stages of action included the Action and Maintenance *stages of change*. The frequencies of each *stage of change* being reported in each study group for baseline and 6-month visits are shown in Table 2.

McNemar's test was used to assess significant changes in the frequencies of the *stages of change* in the participants within the study groups. No significant differences were observed in the reported *stages of change* at baseline between the intervention and control groups. However, significant differences were observed for physical activity, fruit/vegetable intake and fiber intake when comparing the 6-month values of the intervention group to the control group. Moreover, significant difference was observed for fruits/vegetable intake in the intervention group when comparing the pre/post frequencies (*p=0.011*). No significant differences in frequency changes for pre/post values were observed in the control group (Table 2).

Table 2. Frequency of Stages of Change at Baseline and 6- Month and Comparison in Parameter Changes of Participants in Intervention and Control Groups

Stages of Change	Physical Activity	Fruits and Vegetable	Fiber	Fat	Alcohol
	Baseline / 6- Month				
	Intervention Group (n=20 / n=19)				
Precontemplation	1 / 0	1 / 0	3 / 1	1 / 1	3 / 1
Contemplation	1 / 0	1 / 0	0 / 0	0 / 0	1 / 1
Preparation	3 / 1	11 / 5	6 / 3	7 / 4	2 / 1
Action	4 / 1	3 / 3	5 / 3	3 / 3	1 / 1
Maintenance	11 / 17	4 / 11	6 / 12	9 / 11	13 / 15
McNemar Test Pre/Post Comparison (p-value)	0.110	0.011*	0.063	0.227	0.250
	Control group (n=18 / n=14)				
Precontemplation	3 / 2	2 / 3	0 / 2	1 / 3	1 / 1
Contemplation	0 / 0	0 / 1	0 / 1	0 / 1	0 / 0
Preparation	6 / 4	9 / 7	8 / 5	9 / 4	3 / 1
Action	2 / 0	2 / 0	1 / 0	1 / 1	2 / 2
Maintenance	7 / 8	5 / 3	9 / 6	7 / 5	12 / 10
McNemar Test Pre/Post Comparison (p-value)	0.344	0.188	0.313	0.500	0.500
Fisher's Exact Test Comparison					
Baseline	**0.184**	**0.535**	**0.615**	**0.258**	**0.360**
6-Month	**0.007***	**0.002***	**0.033***	**0.074**	**0.649**

*significant differences observed; significance set at p≤ 0.05; one-sided p-values presented

Table 3. Comparison of Nutrition Knowledge and Self-Efficacy at Baseline, 6-Month and Changes in Intervention and Control Groups

Parameter	Intervention (Mean±SD)		Pre/ Post (P-value)	Control (Mean±SD)		Pre/ Post (P-value)	Comparison Between Groups (P-value)		Parameter Changes Comparison (P-value)
	Base-line	6-Month		Base-line	6-Month		Base-line	6-Month	
Nutrition knowledge score (0-25)	17.74 ± 2.3	20.47± 2.5	0.001*	17.64± 2.5	17.64± 2.7	0.99	0.60	0.003*	0.006*
Nutrition knowledge (%)	70.95 ± 9.0	81.89± 9.8	0.001*	70.57± 10.1	67.21± 16.1	0.29	0.60	0.003*	0.002*
Self-efficacy (0-75)	63.32 ± 10.21	67.37± 6.3	0.000*	59.50± 9.2	61.43± 5.2	0.36	0.49	0.007*	0.014*
Self-efficacy percentage (%)	83.95 ± 13.8	89.79± 8.5	0.000*	79.36± 12.3	82.07± 6.8	0.33	0.55	0.009*	0.014*

*significant differences observed; significance set at $p \leq 0.05$

After the 6-month nutrition intervention, significant differences were observed in multiple parameters including physical activity, fruit and vegetable intake, fiber intake, nutrition knowledge, and self-efficacy. No significant differences were seen in fat intake and alcohol consumption between the two study groups at the 6-month follow-up. However, as shown in Table 2, significant difference was observed in fruit/vegetables intake and marginal significance in fiber intake when comparing pre/post values in the intervention group. Table 3 shows significant differences in nutrition knowledge within the intervention group, when the baseline values were compared to those after 6 months of the intervention. No significant differences were observed in any of the parameters within the control group when comparing the pre/post values (see Tables 2-3).

Discussion

<u>Progression of *Stages of Change*</u>

The results and analyses from this randomized, controlled clinical trial, based on the Health Belief Model and the Transtheoretical Model demonstrate that a 6-month nutrition/lifestyle intervention is effective in progressing PLWH through the different *stages of change*. Many of the participants in both study groups started at baseline around *Preparation* and *Action Stages of Change*; however, the participants in the intervention group continued to consistently progress towards *Action Stage of Change* while the participants in the control group remained the same or even regressed towards the *Contemplation Stage of Change*, as is the case with Fruit and Vegetable Intake.

Significant differences were observed between the two study groups at the 6-month follow-up in the following parameters: physical activity, fruit and vegetable intake, fiber intake, nutrition knowledge and self-efficacy. In addition, significant difference was observed in the pre/post intervention values for fruits and vegetable intake within the intervention group.

In regard to physical activity, due to the fact that this population is low-income with an average annual income of \$13,325.03 ± \$11,495 / year, the intervention was focused particularly on increasing daily physical activity with normal day-to-day functions, such as cleaning the house, taking stairs instead of the elevator, walking to and from the grocery store, etc. Those that had access to a safe park nearby were encouraged to take advantage and partake in some physical activity. Participants were more receptive to being more intentional and increasing physical activity through day-to-day functions than increasing physical activity through an exercise and structured programs. This intervention demonstrated the effectiveness of progressing low-income prediabetic

PLWH through the *stages of change* in increasing daily physical activity while the participants in the control group did not significantly progress through the *stages of change*.

One theme that was common among the participants in the study population at baseline was the awareness of not eating enough fruits and vegetables and the desire to increase consumption. Although participants in both study groups expressed awareness of not meeting guidelines and the desire to increase consumption of fruits and vegetables, the participants in the intervention group were actually successful in increasing consumption. This may be due to the subsequent visits that provided additional accountability and motivation. As fruit and vegetable consumption were notably low in this study population, one of the first and simple way to increase regular consumption among the participants was to encourage the increase in consumption of at least 1 fruit per day, of which seemed very feasible to the participants. Once the participant reported success in consuming 1 additional fruit per day for at least a month, they were then encouraged to increase consumption of a vegetable that they liked. This process continued until the participant reached guidelines, of which then they were encouraged to maintain that practice. By taking small and feasible steps towards the goal, the participant did not feel overwhelmed but empowered, especially when they were excited to report their success the following visit.

Although the participants were more willing to increase intake of fruits and vegetables, they were less inclined to change from refined grains to whole grains to increase fiber intake. This may be due to the unfamiliarity of whole grains in this particular population. To increase fruit and vegetable intake, the participants were encouraged to increase intake of their favorite fruits and vegetables, of which they are already familiar with. While the participants were less likely to change to whole grains, they were not as reluctant in consuming more legumes to increase fiber intake, as beans seem to be a part of their cultural cuisine (i.e. Latin, African American). This may explain why a significant difference in fiber intake was observed in the intervention group but not in the control group after the 6-month nutrition intervention.

In regard to fat intake, participants have reported the desire to reduce fat intake from sources such as fast food and fried food; however, they have also shared that they didn't want to remove some of their favorite sources of fatty foods. It is evident that fried foods, especially fried chicken is very common and may be a source of comfort in this population. Moreover, many participants have shared that they don't have access to fully functional kitchens with a fridge/freezer or oven to cook foods. This limits their ability to cook healthy meals at home and tend to resort to buying fast food or ready-prepared foods at grocery stores. This may be the reason why no significant differences in progression of stage of change was observed in either study group for fat intake.

Lastly, most of the participants have reported not exceeding the daily recommendations for alcohol consumption with most participants reporting meeting alcohol consumption guidelines in both groups (Table 2); however, there were a select few (*n=4*) that were exceeding recommendations and clearly expressed no desire to change. It is worthy to note that a few of the homeless participants were staying at shelters and were required to remain sober during their stay. They also mentioned that they would continue to exceed alcohol recommendations if they were able to (have access to stable living conditions, access to alcohol, etc.). It is evident that progressing through *stages of change* in alcohol consumption was the most difficult decision compared to other behaviors for this specific population who live in poverty, with the stresses accompanying their living conditions and with a chronic disease that, until the advent of antiretrovirals, was a death sentence.

Nutrition Knowledge and *Self-Efficacy*

The participants in the intervention group significantly improved their Nutrition Knowledge and *Self-Efficacy* scores from the respective assessment tools. One of the major findings from the *Nutrition Knowledge Assessment* was not necessarily the knowledge of the different components of healthy foods (fiber content, difference between trans-fat, saturated fat, etc.) but rather being able to differentiate healthy foods from unhealthy foods. Moreover, the *Nutrition Knowledge Assessment Tool* was able to assess the participants' understanding of the impact of nutrition and physical activity on overall health and prevention of disease. Based on the Health Belief Model, the link between food intake/ lifestyle choices and health/disease was established and measured in the *Nutrition Knowledge Assessment Tool.*

The 6-month nutrition intervention demonstrated to be effective in establishing the connection between nutrition and health with significant improvement in the *Nutrition Knowledge Assessment Scores* in the intervention group compared to the control group. Furthermore, significant improvement in *self-efficacy* was observed in the intervention group compared to the control group. This demonstrates that along with improvement in nutrition knowledge and understanding the link between nutrition and health, based on the Health Belief Model, the participants in the intervention group expressed greater confidence in making changes to promote positive health outcomes compared to the control group.

Conclusions

Behavior change models including but not limited to Health Belief Model and the Transtheoretical Model have been shown to be effective in creating health-promoting changes in people with prediabetes [8-15]; however, research demonstrating their effectiveness in PLWH until this study, has been limited. This randomized, controlled clinical trial conducted in low-income prediabetic PLWH has shown the effectiveness of a 6-month nutrition/lifestyle intervention based on the Health Belief Model and the Transtheoretical Model in creating the connection between nutrition/lifestyle changes and health risk along with advancing the participants through the *stages of change*.

Although the intervention helped improve the participants' nutrition knowledge as assessed through the *Nutrition Knowledge Assessment Tool,* the greater impact of the intervention was to establish the link between healthy habits and disease risk. In addition, in lieu of educating PLWH of the different nutrition components of food (i.e. content of fiber, trans fat, saturated fat, etc.), more attention should be focused on assisting PLWH on identifying and differentiating a healthy food from a not-so-healthy food item. The ability to know that a grilled option is healthier than a fried food option is more beneficial than knowing why (complicated nutrient components). In short, it is important to communicate the information at the client's level of comprehension or perceived importance. In this case, the more complex the information, the less effective in promoting change. Moreover, solidifying the connection between lifestyle habits (i.e. regular physical activity, increasing intake of fruits and vegetables, reducing intake of not-so-healthy alternatives such as pastries, fried foods, etc.) and health/disease risk has been very effective in promoting healthy lifestyle changes. In addition, as healthy lifestyle habits are promoted, it is important to note that the more these lifestyle habits are incorporated, it creates a double effect of displacing a poor habit with a good habit. For example, when a participant is encouraged and chooses to eat a fruit in the morning, this also discourages and possibly prevents the consumption of a not-so-healthy alternative.

The 6-month intervention was also effective in advancing the participants through the *stages of change* based on the Transtheoretical Model, while the participants in the control group either remained where they started at baseline or even regressed, in terms with their readiness for change. Along with the consistent nutrition education the participants in the intervention group were receiving, they were also being held accountable for their habits once a month, which was effective in promoting behavior change. The fact that the participants had an external third party, the nutritionist, to report on their health and habits, creates an external motivation for change that reaffirms and guide the internalized reasons for change.

While the 6-month lifestyle intervention was able to effectively change behavior in the short-term, more research is needed to confirm if the effects are maintained after the intervention is completed. Although the educational material of the intervention is not expected to change overtime, the participants are most in need of consistent follow-up visits to be reminded of the education provided and to create accountability. In view of the results of this study, frequent visits every three months with a registered dietitian or another healthcare professional are recommended to maintain or increase motivation among prediabetic PLWH to achieve long-lasting results of health promoting habits.

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CHAPTER VI: Effectiveness of 6-Month Nutrition/Lifestyle Intervention by Compliant Compared to Non-Compliant Participants

Introduction

Nutrition and lifestyle interventions have been shown to be effective in lowering diabetes risk among people with prediabetes [1-6]. Latest guidelines published from the American Diabetes Association in a consensus report about nutrition therapy for adults with diabetes/prediabetes state that strong evidence supports the effectiveness of nutrition interventions in the medical management of diabetes/prediabetes [7]. However, research in lowering diabetes risk in people living with HIV (PLWH) is limited. PLWH is a high-risk population, with prediabetes prevalence rates 2-3 times higher than in the general population [8-10]. Their increased risk for prediabetes/diabetes is multifactorial, including, but not limited, to HIV infection, chronic use of antiretroviral therapy (ART), and the aging process related to the success of ART treatment [11-14].

The implementation of an intervention can be costly, requiring resources including, but not limited to, hiring staff, providing educational materials and overhead expenses. It is important to assess the acceptance and effectiveness of the intervention before implementing it on a large-scale. Moreover, other factors such as drug and alcohol problems and low income/socio-economic status, which are common in PLWH, may affect compliance.

Therefore, a 6-month nutrition/lifestyle intervention was piloted in low-income PLWH with prediabetes to lower diabetes risk and delay onset of diabetes. The objective was to assess the association of compliance with monthly lifestyle/nutrition intervention sessions with biological markers and behavioral scores based on: Heath Belief Model and the Transtheoretical Model.

Methods

Approval from the Florida International University (FIU) Institutional Review Board (IRB) was obtained (IRB-17-0058-CR01). A 6-month randomized, controlled nutrition intervention was conducted in low-income prediabetic people living with HIV (PLWH). The study participants were recruited from the Miami Adult Studies for HIV (MASH) cohort. MASH cohort participants provided consent to review their medical documentation for eligibility and to participate in the study procedures.

Inclusion/exclusion criteria were used to identify eligible participants, and telephone calls to these participants were made to attend a screening study visit. Participants were randomized into two groups: intervention or the control. All participants visited the FIU Research Clinic at the Borinquen Health Care Centers at baseline for assessment and at the 6-month follow-up as part of the MASH cohort. Those randomized into the intervention group were seen monthly for 6 months.

Participants were determined to have prediabetes based on the American Diabetes Association (ADA) diagnostic criteria of fasting blood glucose of 100-125 mg/dl (fasting for ≥8 hours) or hemoglobin A1C (HbA1C) values 5.7-6.4% [15]. Inclusion criteria were: HIV seropositive, having prediabetes, 18-65 years of age, receiving stable ART for at least 6 months, undetectable HIV viral load (<50 copies /ml) and English speaking. Exclusion criteria included any previous history of type 2 diabetes, concomitant use of glucose-altering medication (diabetes medication, corticosteroids, etc.), use of weight loss drugs, pregnancy or breastfeeding and/or refusal or inability to give informed consent to participate in the study.

Participants (N=38) were randomized using a computer program into either the intervention group (n=20) or the control group (n=18). Participants randomized in the intervention group received individualized sessions that consisted of medical nutrition therapy (MNT), nutrition education and nutrition counseling, which were all based on the American Diabetes Association (ADA) Standards of medical care in diabetes [15]. The first session lasted approximately 1 hour, and the subsequent 5 visits lasted about 45 minutes, for a total of 6 visits. The intervention utilized a curriculum that was specifically tailored to PLWH which provided structure to the intervention; however, each session was individualized and catered to each participant's nutritional needs at the time of the session. The participants randomized into the control group received educational materials on prediabetes/diabetes, also based on the ADA Standards of medical care in diabetes only at the baseline visit [15].

Blood (<2 tablespoons) was drawn at baseline and the 6-month follow-up visit to measure associated biological markers such as fasting blood glucose, oxidative stress and inflammatory markers. Validated questionnaires were used to assess *stages of change* based on the Transtheoretical Model and other behavioral parameters including nutrition knowledge, understanding of link between perceived risk and benefit, and *self-efficacy* based on the Health Belief Model. Participants randomized into the intervention group were considered compliant with the intervention if they attended at least 4 of the 6 scheduled visits. We chose the cut-off of 4 visits out of a total of 6 visits to be considered compliant because it would have covered more than half (~67%) of the intervention and demonstrated the participants' diligence in attending the sessions.

Data were tested for normality (Shapiro-Wilk test); means/standard deviations were used to describe normally distributed data and frequencies/proportions were used to present categorical data. Parametric tests were used to analyze normally distributed data (paired t-test, independent student t-test, etc.) and categorical data were presented as frequencies and proportions and analyzed with McNemar, Fisher Exact test and Mann Whitney U-test. Significance was set at $p \leq 0.05$ and all statistical tests were performed using Statistical Package for Social Science (SPSS) version 23.

Results

The majority of the participants in the intervention group (n=20) were compliant (75%), with only 5 participants attending ≤3 visits during the intervention (Table 1). As can be seen in Table 1, thirteen of the fifteen compliant participants (87%) completed all 6 of the intervention sessions, demonstrating a high acceptability of the intervention among PLWH. After the intervention was completed, each participant was asked to fill out evaluations and most of the participants expressed satisfaction in learning more about nutrition and their health risk, increasing awareness and providing empowerment when making daily decisions.

Table 1. Compliance of Participants Attending Intervention Sessions

Number of sessions completed	Number of Participants
0	0
1	0
2	4
3	1
4	1
5	1
6	13

When comparing the biological markers of fasting blood glucose, oxidative stress and inflammation, no significant differences were observed at baseline between compliant and non-compliant participants; however, a significant difference was observed when comparing the pre/post values for fasting blood glucose in the compliant participants. No significant differences were observed for any of the pre/post values in the non-compliant participants (Table 2).

Table 2. Comparison of Biological Markers Between Compliant Participants and Non-Compliant Participants

Biomarker	**Compliant (n≥4 visits) Mean ± SD *(n=15)***		**Pre/ Post (p-value)**	**Non-compliant (n≤3 visits) Mean ± SD *(n=5)***		**Pre/ Post (p-value)**	**Baseline Comparison (P-Value)**	**6-Month Comparison (P-Value)**
	Base line	**6-Month**		**Base line**	**6-Month**			
Fasting Blood Glucose (mg/dl)	108.5± 6.3	95.6± 19.7	0.04*	108.8± 4.0	97.8± 16.0	0.14	0.32	0.37
C-Reactive Protein (mg/dl)	3.3± 2.9	4.4± 4.2	0.11	1.9± 1.6	3.28± 4.5	0.11	0.14	0.44
8-hydroxy Deoxy Guanosine (mg/dl)	127.6± 70.1	102.5±58.2	0.10	126.3± 55.7	96.6± 44.3	0.24	0.21	0.33

*statistically significant difference; significance set at p≤0.05; one-sided p-values presented

When comparing the behavioral parameters based on the Transtheoretical Model and the Health Belief Model between compliant participants and non-compliant participants in the intervention study group, significant difference was observed for *self-efficacy* at the 6-month follow up visit (Table 4). When assessing the pre/post values of the compliant participants, significant differences were observed for fruits and vegetables intake, fiber intake, nutrition knowledge and *self-efficacy* (Tables 3 and 4). Although a significant difference was observed for *self-efficacy* in the non-compliant participants, a closer look reveals that participants actually decreased *self-efficacy* scores while the compliant participants increased *self-efficacy* scores after the 6-month intervention.

Table 3. Comparison of Behavioral Parameters Between Compliant Participants and Non-Compliant Participants

Stages of Change	**Physical Activity**	**Fruits and Vegetable**	**Fiber**	**Fat**	**Alcohol**
	Baseline / 6- Month				
	Compliant Group (n≥4 visits) (n=15 / n=15)				
Precontemplation	1 / 0	1 / 0	2 / 0	1 / 1	3 / 1
Contemplation	0 / 0	1 / 0	0 / 0	0 / 0	0 / 1
Preparation	3 / 0	8 / 3	6 / 2	4 / 2	2 / 1
Action	3 / 0	2 / 3	4 / 3	2 / 3	0 / 1
Maintenance	8 / 15	3 / 9	3 / 10	8 / 9	10 / 11
McNemar Test Pre/Post Comparison (p-value)	0.063	0.020*	0.016*	0.344	0.250
	Non-Compliant Group (n≤3 visits) (n=5 / n=4)				
Precontemplation	0 / 0	0 / 0	1 / 1	0 / 0	0 / 0
Contemplation	1 / 0	0 / 0	0 / 0	0 / 0	1 / 0
Preparation	0 / 1	3 / 2	0 / 1	3 / 2	0 / 0
Action	1 / 1	1 / 0	1 / 0	1 / 0	1 / 0
Maintenance	3 / 2	1 / 2	3 / 2	1 / 2	3 / 4
McNemar Test Pre/Post Comparison (p-value)	0.500	0.500	0.500	0.500	0.500
Fisher's Exact Test Comparison					
Baseline	**0.634**	**0.594**	**0.221**	**0.296**	**0.517**
6-Month	**0.106**	**0.136**	**0.089**	**0.136**	**0.235**

*significant differences observed; significance set at p≤ 0.05; one-sided p-values presented

Table 4. Comparison of Nutrition Knowledge and Self-Efficacy Parameters Between Compliant and Non-Compliant Participants at Baseline and 6-Month

	Compliant Group (n≥4 visits)	**Pre/ Post test (p-value)**	**Non-Compliant Group (n≤3 visits)**	**Pre/ Post test (p-value)**	**Baseline Comparison between study groups (p-Value)**	**6-Month Comparison between study groups (p-Value)**
	Mean ± SD		**Mean ± SD**			

	Baseline (n=15)	6-Month (n=15)		Baseline (n=5)	6-Month (n=4)			
Nutrition Know-ledge	17.3± 2.3	20.7± 2.7	0.001*	18.2± 2.6	19.8± 1.0	0.604	0.379	0.511
Self-efficacy	61.7± 10.6	68.9± 6.1	0.024*	67.4± 7.1	61.5± 2.7	0.049*	0.204	0.043*

*significant differences observed; significance set at p≤ 0.05; two-sided p-values presented

Discussion

The results of this study demonstrate greater effectiveness of the 6-month nutrition/lifestyle intervention in compliant participants who attended ≥4 sessions in fruit and vegetable intake, fiber intake, nutrition knowledge and self-efficacy compared to non-compliant participants, who attended ≤ 3 intervention sessions. There was a significant improvement in fasting blood glucose observed in compliant participants' pre/post values. No significant improvements were observed for any of the biomarkers in the non-compliant participants.

These results demonstrate that an intervention is more effective when the participants are committed and attend the sessions. Developing an intervention with high acceptance among the participants is crucial for the success of the intervention. A study by Kristensen et al. [16] conducted a randomized nutrition intervention investigating the inverse relationship between whole grain intake and weight gain; after the 12-week intervention, they found that non-compliance with the intervention confounded the study results.

With ~75% compliance among the participants in this current study, attending at least 4 sessions of the total 6 sessions provided, this intervention proved to have high acceptance among PLWH with prediabetes. Moreover, more than 86% of the compliant participants attended all 6 sessions, further demonstrating the intervention's high acceptability among this study population. A randomized, controlled study conducted by Dietrich et al. [17] assessed compliance of nutrition interventions and found a high compliance (87-90%) among the participants in both study groups, further supporting high acceptability of nutrition interventions among participants.

During the recruitment process, 89% of eligible participants agreed to participate in the intervention study, particularly due to the non-invasive nature of the intervention and their initial desire to lower their diabetes/health risk. However, there were several who were not interested in participating in the study due to their non-concern with their health and were only interested in monetary compensation and other motives. Non-compliant participants also exhibited similar behavior with marked alcohol usage and excessive concern for monetary compensation and other motivations to participate in intervention, rather than concern for their health.

On the other hand, although the participants were informed that group placement is random, many of the participants that were randomized into the control group were hopeful about being placed in the intervention group and expressed enthusiasm about making lifestyle change. When the participants in the control group were made aware of their elevated glucose levels and increased risk for diabetes, and were provided with educational material based on the American Diabetes Association (ADA) Standards of medical care, they may have made lifestyle changes on their own and implemented the education that was provided at baseline as part of the study. The participants that were randomized into the intervention group were provided additional resources to promote healthier outcomes; however, non-compliance during the intervention is likely to extend into non-compliance in their lifestyle habits.

Conclusions

The results of this study demonstrate that the success of an intervention is not only dependent on its implementation but also the acceptability, motivation and compliance of the intervention by the participants. Based on the Health Belief Model, when the PLWH with prediabetes were made aware of their increased risk for diabetes and other co-morbidities, most of them expressed concern and desire to make lifestyle changes to lower their risk.

Moreover, apart from their initial desire to make change, the high compliance rate of the participants demonstrated the participants' sustained desire for lifestyle change. This suggests that large scale interventions will be successful in PLWH with prediabetes to lower diabetes risk and improve overall lifestyle habits, as high acceptability, initial motivation and compliance was observed despite certain barriers such as low income/socio-economic status. Further research is needed to assess the long-term effects of nutrition interventions in PLWH after the intervention is completed.

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CHAPTER VII: SUMMARY AND CONCLUSIONS

Biomarker and Anthropometric Measures

The results of this randomized, controlled clinical trial reveal the effectiveness of a 6-month nutrition/lifestyle intervention in lowering diabetes risk and promoting healthy habits. The participants randomized in the intervention group experienced significant reductions in their BMI, fasting blood glucose levels and oxidative stress after the 6-month intervention. In addition, although they did not experience reductions in waist or hip circumferences, they maintained the same average measurements, with slight improvement in average waist-to-hip ratio in the intervention group.

On the other hand, the participants randomized into the control group had an increase in BMI, waist, hip circumferences, and WHR after the 6-months follow-up. These results demonstrate that the 6-month nutrition intervention was effective in delaying the onset of diabetes and other co-morbidities in PLWH by improving common risk factors such as fasting blood glucose, body composition and oxidative stress.

The results from this randomized intervention study is supported by the results of another study conducted by Duncan et al. in the same population. After a 6-month diet and physical activity intervention, they found that glucose, insulin, waist circumference, systolic blood pressure and triglycerides were significantly reduced in PLWH and prediabetes (*N=28).* They concluded that a 6-month nutrition/lifestyle intervention is effective in lowering the increased risk for diabetes in PLWH, a high disease risk and unique population.

Behavioral Parameters

In addition, the results of this randomized, controlled clinical trial demonstrated the effectiveness of a 6-month nutrition/lifestyle intervention in advancing PLWH through the *stages of change* based on the Transtheoretical Model. The *stages of change* that the participants in the intervention group significantly advanced through included improvement in physical activity, fruits and vegetable intake and fiber intake. No significant improvements were observed in the control group for any of the *stage of change* parameters.

Moreover, the participants randomized into the intervention group also demonstrated significant improvements in nutrition knowledge and self-efficacy after the 6-month nutrition/lifestyle intervention. However, no significant improvements were observed for the participants in the control group. Furthermore, compliance and acceptability were also observed in this current intervention with significant differences in multiple parameters including fasting blood glucose, fruit/vegetable intake, fiber intake, nutrition knowledge and *self-efficacy* in compliant participants compared to non-compliant participants in the intervention. These observations demonstrate the importance of high acceptability and compliance for the success of a nutrition/lifestyle intervention.

This randomized, controlled clinical trial of a 6-month nutrition intervention proved to have high acceptability and compliance among prediabetic PLWH, which contributed to its effectiveness in significantly improving variables such as fasting blood glucose and oxidative stress, as well as advancing the participants through the *stages of change,* improving nutrition knowledge and *self-efficacy*.

CHAPTER VIII: FUTURE RESEARCH

This randomized, controlled clinical trial demonstrated the effectiveness of a 6-month nutrition/lifestyle intervention in lowering diabetes risk and promoting healthy lifestyle habits in PLWH and prediabetes. The favorable results of this pilot study suggest that large scale nutrition/lifestyle interventions may be implemented to delay the onset of diabetes and lower disease risk in a high-risk population such as prediabetic PLWH.

Although significant improvements were observed in multiple biological markers and behavioral parameters after the 6-month intervention, further research is needed to assess the long-term effects of the intervention, at least 6 months after the completion of the intervention.

APPENDIX:

NUTRITION EDUCATION BROCHURES

NUTRITION EDUCATION SESSION BROCHURE 1

Title:

HIV, Antiretroviral Therapy and Prediabetes- How are they all related and how does it affect me?

Antiretroviral therapy controls HIV infection however it increases risk for diabetes.

- Some HIV treatments may increase blood glucose levels and lead to diabetes.
- If you have 1 or more of the diabetes risk factors listed, you are more likely to develop diabetes.
- If high glucose levels develop, the HIV treatment may be changed to keep blood glucose at normal levels.

What can be done to lower risk in people with HIV and prediabetes?

- ❖ You can lower your risk of diabetes by losing excess weight and by being active most days of the week

Diabetes Basics:

- ❖ Food is broken down by the body into sugar

↓

- ❖ Pancreas releases insulin

↓

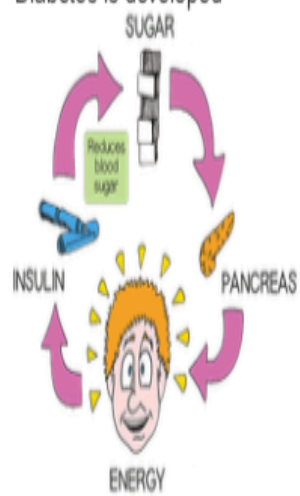
- ❖ Insulin brings sugar into cells

↓

- ❖ If insulin is not working, too much sugar is in bloodstream

↓

- ❖ Diabetes is developed

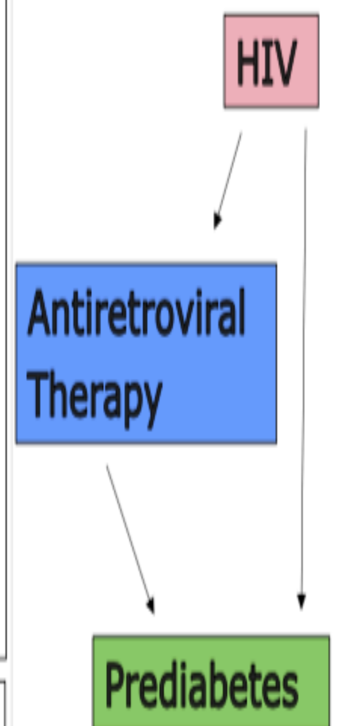


Please contact FIU-Borinquen Research Clinic: 786-615-6196

Attn: Alicia Sneij

HIV, Antiretroviral Therapy and Prediabetes

How are they all related and how does it affect me?



What is HIV?

- HIV is a virus that causes HIV infection.
- HIV is spread through contact with the blood, semen, pre-seminal fluid, rectal fluids, vaginal fluids, or breast milk of a person infected with HIV.

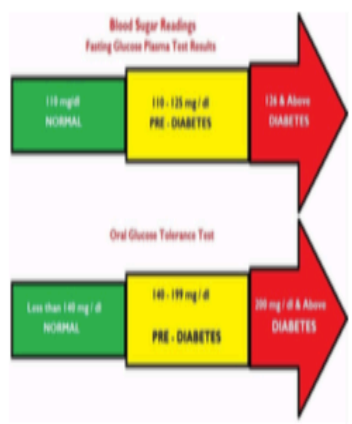
What is antiretroviral therapy (ART)?

- Antiretroviral therapy (ART) is medicine used to treat HIV infection.
- ART can't cure HIV infection, but it can help people infected with HIV live longer, healthier lives.
- ART can also reduce the risk of transmission of HIV.

Diabetes can be delayed or prevented in people with prediabetes through effective lifestyle programs.

What is prediabetes?

- Prediabetes is a condition where blood glucose (sugar) is higher than normal, but has not reached diabetic values.
- Diabetes is a serious disease that can cause heart attack, stroke, blindness, kidney failure, or loss of feet or legs.



Risk Factors for Diabetes

<u>You are at higher risk for type 2 diabetes if:</u>

- >45 years of age
- Family history of diabetes
- Being overweight (**BMI ≥ 25**)
- Physically inactive
- Low HDL cholesterol or high triglycerides
- High blood pressure
- Certain racial and ethnic groups (e.g., African Americans, Hispanic/Latino Americans, Asian Americans, Pacific Islanders, and American Indians)
- Have had gestational diabetes, or have had a baby weighing 9 pounds or more at birth
- Have a history of **prediabetes**

NUTRITION EDUCATION SESSION BROCHURE 2

Title:

Understanding BMI and the Importance of Maintaining Normal Body Weight-

What is BMI and How Does it Affect Prediabetes Risk?

How to attain and maintain ideal BMI

An exercise plan can help you maintain a healthy BMI.

What is the Waist-to-Hip Ratio (WHR)?

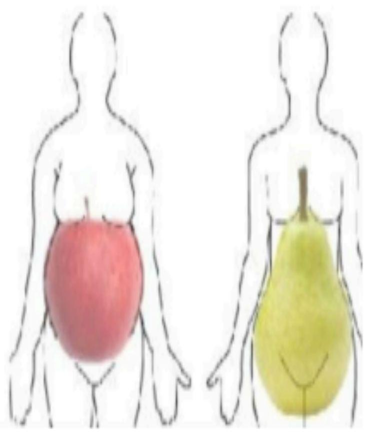
- The waist-to-hip ratio is a comparison of the waist circumference to the hip circumference.

- Pear shaped obesity → less health risks than apple-shaped obesity

What is the difference between apple-shaped and pear-shaped obesity?

→ **Apple-shaped obesity is where more fat is accumulated around the waist.**

→ **Pear-shaped obesity is where more fat is accumulated around the hips.**



- Apple-shaped obesity increases risk for diseases such as diabetes more than pear-shaped obesity.

Please contact FIU-Borinquen Research Clinic: 786-615-6196
Attn: Alicia Snelj

Understanding BMI and the importance of maintaining normal body weight

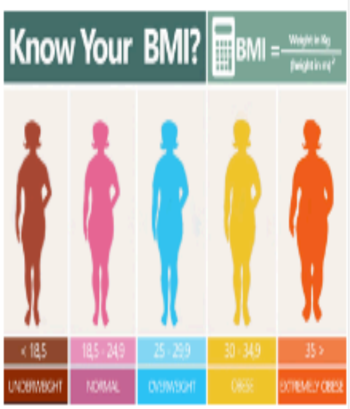
What is BMI and how does it affect prediabetes risk?

What is Body Mass Index (BMI)?

- BMI is used to determine whether a person is underweight, overweight, obese or a healthy weight for their height.
- BMI values are age-independent and the same for both sexes.

What is the normal range for BMI?

- < 18.5: underweight
- 18.5-24.9: normal weight
- 25-29.9: overweight
- 30-39.9: obese
- >40: extremely obese



$$\text{BMI} = \frac{(\text{weight in kilograms})}{\text{height in meters}^2}$$

Benefits of maintaining a healthy weight

- Fewer joint and muscle pains
- Increased energy
- Improved regulation of bodily fluids and blood pressure
- Reduced burden on the heart and circulatory system
- Improved sleep patterns
- Reductions in blood triglycerides, blood glucose, and risk of developing type 2 diabetes
- Reduced risk for heart disease and certain cancers.

What is waist circumference?

- Waist circumference is the distance around the waist.
- It is a common measure that is used to check for fat around the stomach.
- Having extra body fat around the stomach (>35in for women and >40in for men) increases risk of heart disease and diabetes.

What is hip circumference?

- Hip circumference measurements are taken at the widest portion of the buttocks.

NUTRITION EDUCATION SESSION BROCHURE 3

Title:

Dietary Intake and the Importance of Fruits and Vegetables – Why Fruits and Vegetables Should Compose of Half of our Diet.

A good rule is to fill half your plate with fruits and vegetables

Be mindful that fruit juice does not have the same fiber content as whole fruit.

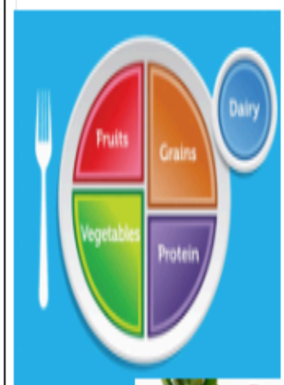
How can we attain the daily recommendations for fruit and vegetable?

- Start small
  - Eat just a little bit more fruits and vegetables than where you started
- Bring fruits and vegetables to your house to make them readily available for consumption
- Eat a variety of fruits/vegetables
  - Provides a wide range of good nutrients
  - Selection should look like the rainbow
- Eat them as snacks
- Frozen vegetables are healthy, inexpensive and easy to prepare

For more information, please contact FIU-Borinquen Research Clinic:
786-615-6196
Attn: Alicia Sneij

Dietary Intake and the Importance of Fruits and Vegetables

Why fruits and vegetables should compose half our diet



What are Fruits and Vegetables?

- A fruit is the part of a plant that develops from a flower and tends to be sweet (orange, apple, peach, etc.)

- Vegetables are the other parts of the plant, such as the root, leaves and stems (celery, broccoli, onions etc.)

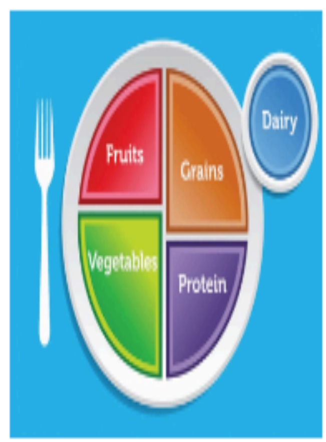
Fruits and vegetables naturally provide all the important components the body needs to remain healthy and to keep functioning optimally.

- **Why are they beneficial for our health?**
  - Nutritious
    - Packed with essential vitamins and minerals
    - Antioxidants to help prevent cancer and other diseases
    - Provides good calories for the body
  - Low fat content
    - Good healthy fats (sources: avocados, nuts, seeds etc.)
    - Helps weight loss and maintain healthy BMI
  - Rich in fiber
    - Helps to feel full longer
    - Helps to clean digestive track
    - Helps keep one regular with normal bowel movements

What is MyPlate and how is it relevant?

- MyPlate is an illustration useful to show the 5 food groups that are necessary to build a healthy diet:
  - *Fruits*
  - *Vegetables*
  - *Grains*
  - *Protein*
  - *Dairy*
- Uses the familiar image of a plate to help choose the right foods to eat

Proportions of food groups on your plate should look like this:



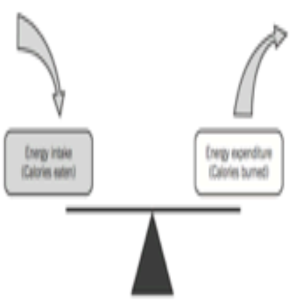
NUTRITION EDUCATION SESSION BROCHURE 4

Title:

Energy Expenditure and the Importance of Physical Activity- What is Energy Balance and How Does it Affect Me?

How do we maintain proper energy balance?

- Proper energy balance is achieved when the energy intake (calories eaten) equals the energy expenditure (calories burned).



NEUTRAL ENERGY BALANCE

ENERGY IN = ENERGY OUT

Why is it important to maintain proper energy balance?

- The excess calories that were eaten and not burned will be converted to fat.
- Fat is energy that is saved for later use.

What is physical activity?

- Physical activity is any form of body movement that works your muscles and requires more energy than resting.
- Physical activity includes walking, running, dancing, swimming, yoga, gardening etc.
    - Exercise is a type of physical activity that is planned and structured.
        - Weight lifting
        - Aerobics class
        - Sports
- What kinds of physical activity are feasible to do?
    - Walking to the store
    - Going up the stairs
    - Cleaning the house

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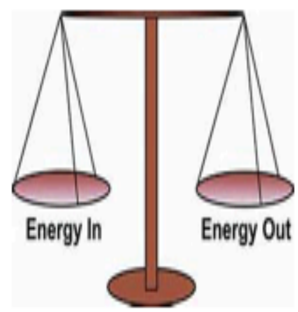
Energy Expenditure and the Importance of Physical Activity

What is Energy Balance and how does it affect me?

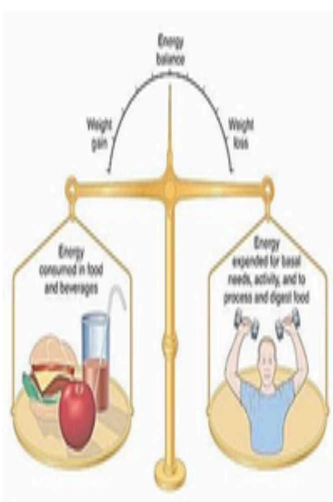


What are calories and where do we get them from?

- Calories is another word for ENERGY.
- Food provides us with calories in order for our bodies to function.

What is energy balance?

- Energy balance is calories consumed through food and drink (ENERGY IN) compared to the calories that is burned through physical activity and exercise (ENERGY OUT).



Weight Management Goal:

ENERGY IN = ENERGY OUT

- **How do we gain weight?**
  - When calories that are being consumed (ENERGY IN) is higher than the calories being burned (ENERGY OUT), the excess calories are stored as fat.

POSITIVE ENERGY BALANCE

(Energy In > Energy Out= Fat Production)

- **How do we lose weight?**
  - When calories that are being consumed (ENERGY IN) is lower that the calories being burned (ENERGY OUT), weight is lost.

NEGATIVE ENERGY BALANCE

(Energy In < Energy Out= Fat Reduction)

NUTRITION EDUCATION SESSION BROCHURE 5

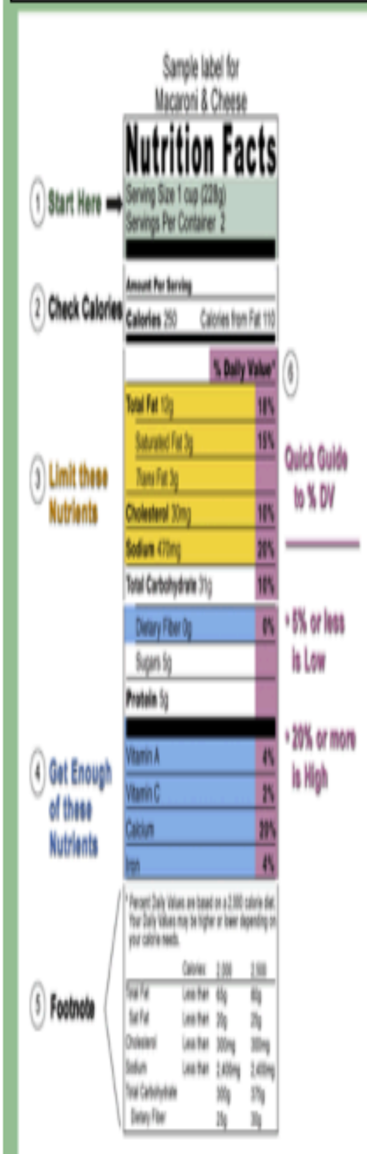
Title:

Dietary Fat and Ways to Avoid Excessive Intake- Why and How to Limit Dietary Fat Consumption

How can we avoid excessive dietary fat intake?

- Identify low fat options at fast food restaurants
  - Salads
  - Grilled versus fried (chicken, fish, shrimp etc.)
  - Limit/avoid French fries
- Learn to read a nutrition label to find fat content:
  (see sample nutrition label on back)
  1. Start at the top to find the serving size and the number of servings in the container
  2. Check to see how many calories are in each serving. All nutrition information on the nutrition label is for 1 serving of the food product.
  3. Check to see how much fat, cholesterol and sodium is in the food item. The goal is to limit these components.
  4. Check to see how much fiber, vitamins and minerals are in the food item- the goal is to get enough of these nutrients.

How to Read a Nutrition Label



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Attn: Alicia Snelj

Dietary Fat and Ways to Avoid Excessive Intake

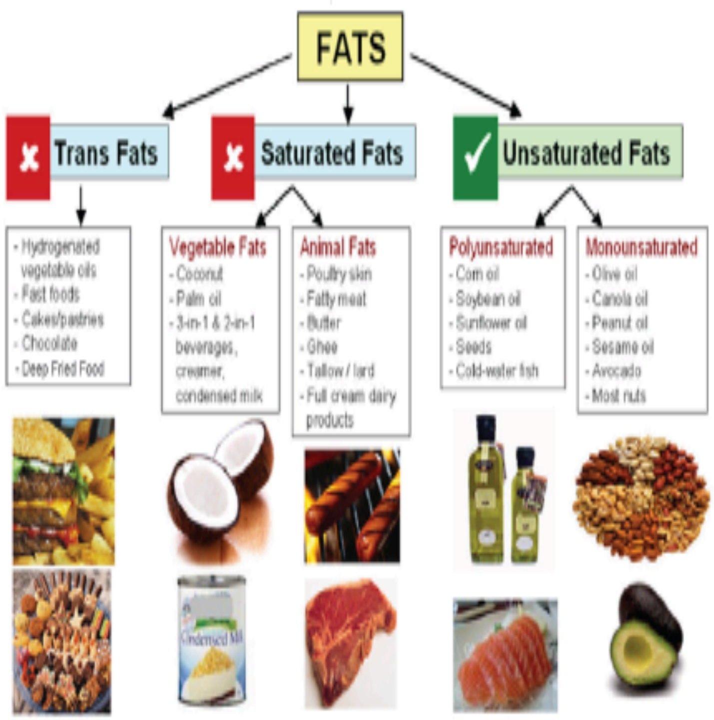
Why and How to Limit Dietary Fat Consumption

- **What is dietary fat?**
  - Dietary fat is fat found in the foods that we eat.
  - Fat is a type of nutrient.
  - Dietary fat can be categorized as:
    - *Trans fat* ✗
    - *Saturated fat* ✗
    - *Unsaturated fat* ✓ (healthy fat)
      - Monounsaturated
      - Polyunsaturated
      - Omega-3 fatty acids

*Trans fat and saturated fats should be **avoided** but unsaturated fats are good fats and are **encouraged**.*

What are major sources of dietary fat?

- *Trans fat*: found in foods which contain hydrogenated oils
  - Stick margarine
  - Commercial snack foods (crackers, cookies etc.)
  - Baked goods
  - Commercially fried foods



- Saturated fat: found in meat and other animal products
  - Butter
  - Shortening
  - Lard
  - Cheese
  - Milk (except skim or non-fat)

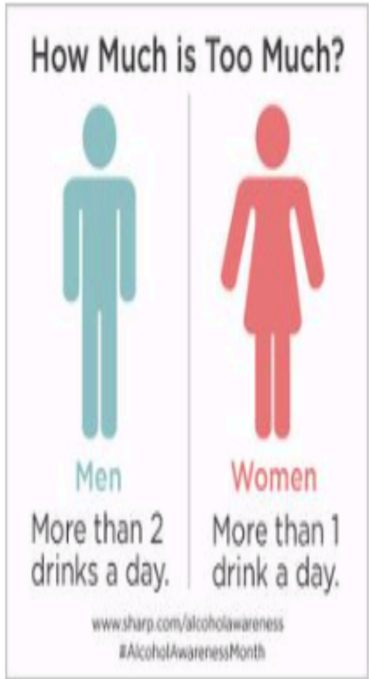
- Unsaturated fat: Plant food and fish; known to be neutral or even beneficial to heart health.
  - *Monounsaturated fat*: avocados and olive, peanut and canola oils.
  - *Polyunsaturated fat*: found mostly in vegetable oils
  - *Omega-3 fatty acids*: type of polyunsaturated fat found in oily fish like tuna and salmon

NUTRITION EDUCATION SESSION BROCHURE 6

Title:

Alcohol and its Effect on the Body- Why and How to Limit Alcohol Consumption While Living with HIV

- **How does alcohol consumption affect blood glucose?**
  - Alcohol consumption can interfere with blood sugar as well as the hormones needed to maintain healthy blood sugar levels.
  - Over time, excessive alcohol consumption can reduce the overall effectiveness of insulin → This results in high blood sugar levels.
  - Many people with alcohol liver disease also have either glucose intolerance (prediabetes) or diabetes.



- **Drinking alcohol while prediabetic and HIV infected:**
  - Due to the increased risk for diabetes associated with HIV treatment and excessive alcohol consumption, it is suggested that *people with prediabetes and HIV should limit and/or avoid alcohol consumption.*
  - When drinking, be sure to drink plenty of water and eat before and while you drink alcohol.
    - This helps your body slow down how quickly the alcohol is absorbed, stay hydrated and avoid negative effects.

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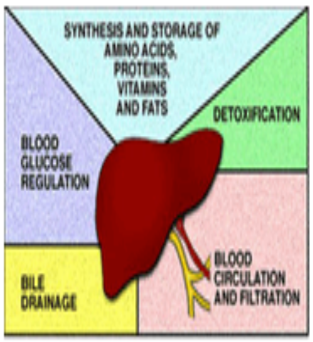
Alcohol and its Effect on the Body

Why and How to Limit Alcohol Consumption While Living with HIV

- **What is alcohol?**
  - Alcohol is a component that is found in beer, wine and spirits which has varying effects on the body.

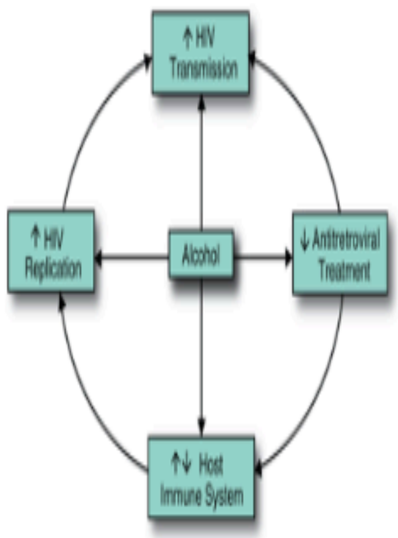


LIVER FUNCTIONS

- **How is it processed?**
  - Alcohol (ethanol or ethyl alcohol) is <u>mainly processed in the liver</u>; however, the stomach, brain and pancreas are also involved in metabolizing alcohol in the body.

<u>Alcohol intake recommendation</u>:
- *≤1 drink/day (women)*
- *≤2 drinks/day (men)*

- **How does it interfere with antiretroviral therapy (ART)?**
  - Alcohol intake lowers effectiveness of antiretroviral therapy (ART).
    - Lowers adherence to ART regimen



- **How does it relate to HIV and prediabetes?**
  - Alcohol intake increases HIV progression
  - Alcohol intake increases risk for prediabetes

- **What is the recommended alcohol intake?**
  - < 1 drink/day (women)
  - < 2 drinks/day (men)

VITA

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PUBLICATIONS AND PRESENTATIONS

Sneij A, Campa A, Baum MK. Review of Randomized Controlled Trials of Nutritional Supplementation in People Living with HIV. Journal of Nutrition and Dietary Supplements. 2016;8*:*21-39.

Sneij A, Campa A, Baum M. Lower Plasma Zinc Levels in HIV Patients with Hyperglycemia. Journal of AIDS and Clinical Research*.* 2016; 7(2):1-9.

Sneij-Perez A, Campa A, Seminario L, Martinez S, Huffman F, Trepka M, George F, Baum M. Preliminary Results on the Effectiveness of a Nutrition Intervention in Lowering Diabetes Risk in Prediabetic People Living with HIV (PLWH) in MASH Cohort (OR36-06-19). Current Developments in Nutrition. 2019;3(1):1148.

Sneij-Perez A, Seminario L, Huffman F, Trepka, MJ, George F, Sales-Martinez S, Campa A, Baum M. Preliminary Results on the Effectiveness of a Nutrition Intervention in Lowering Diabetes Risk in Prediabetic People Living with HIV (PLWH) in MASH Cohort. American Society for Nutrition (ASN) Nutrition 2018 Annual Conference. Baltimore, MD. June 8-11, 2019. *Oral Presentation*

Sneij-Perez A, Tamargo J, Seminario L, Huffman F, George F, Trepka MJ, Sales-Martinez S, Campa A, Baum M. Lowered Fasting Blood Glucose (FBG) in a Prediabetic Individual with HIV Despite Struggle with Weight Control Management- CASE STUDY. American Society for Nutrition (ASN) Nutrition 2018 Annual Conference. Baltimore, MD. June 8-11, 2019. *Oral Presentation*