Summer 6-8-2012

Suboptimal Nutrient Intake in HIV-Infected Youth and Associations with Serum Lipid Profiles and HIV-Related Factors

Lindsey A. Stricker
Georgia State University

ACCEPTANCE

This thesis, SUBOPTIMAL NUTRIENT INTAKE IN HIV-INFECTED YOUTH AND ASSOCIATIONS WITH SERUM LIPID PROFILES AND HIV-RELATED FACTORS, by Lindsey A. Stricker was prepared under the direction of the Master's Thesis Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree Master of Science in the Byrdine F. Lewis School of Nursing & Health Professions, Georgia State University.

The Master's Thesis Advisory Committee, as representatives of the faculty, certify that this thesis has met all standards of excellence and scholarship as determined by the faculty.

_____
Murugi Ndirangu, PhD
Committee Chair

_____
Anita Nucci, PhD, MPH, RD
Committee Member

_____
Allison C. Ross, MD
Committee Member

_____
Date

AUTHOR'S STATEMENT

In presenting this thesis as a partial fulfillment of the requirements for the advanced degree from Georgia State University, I agree that the library of Georgia State University shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to quote, to copy from, or to publish this thesis may be granted by the professor under whose direction it was written, by the Byrdine F. Lewis School of Nursing & Health Professions director of graduate studies and research, or by me. Such quoting, copying, or publishing must be solely for scholarly purposes and will not involve potential financial gain. It is understood that any copying from or publication of this thesis, which involves potential financial gain will not be allowed without my written permission.

_____

Signature of Author

NOTICE TO BORROWERS

All theses deposited in the Georgia State University library must be used in accordance with the stipulations prescribed by the author in the preceding statement. The author of this thesis is:

Lindsey A. Stricker
2970 Skyland Dr. NE
Atlanta, GA 30341

The director of this thesis is:

Murugi Ndirangu
Division of Nutrition
Byrdine F. Lewis School of Nursing & Health Professions
Georgia State University
Atlanta, Georgia 30303-3083

VITA

Lindsey A. Stricker

EDUCATION:

GEORGIA STATE UNIVERSITY
M.S. HEALTH SCIENCE 2012

UNIVERSITY OF GEORGIA
B.B.A. INTERNATIONAL BUSINESS, FINANCE 2004

PROFESSIONAL EXPERIENCE:

GRADY MEMORIAL HOSPITAL, PIEDMONT HOSPITAL, DAVITA DIALYSIS, SENIOR CONNECTIONS, ETHICA LONG-TERM CARE, DEKALB MEDICAL CENTER FOR OUTPATIENT DIABETES EDUCATION, GEORGIA STATE UNIVERSITY COUNSELING CENTER, EMORY UNIVERSITY'S METABOLIC CAMP, WIC, NATURALLY OCCURRING RETIREMENT COMMUNITY, CHICK-FIL-A, INC.
DIETETIC INTERN 2010-2012

GEORGIA STATE UNIVERSITY STUDENT RECREATION CENTER
NUTRITION EDUCATOR GRADUATE ASSISTANT 2011-2012

EMORY UNIVERSITY HOSPITAL
NUTRITION RESEARCH ASSISTANT 2011-2012

DREW CHARTER SCHOOL
COOKING INSTRUCTOR 2010

RBC BANK
SENIOR RELATIONSHIP BANKER 2008-2010

WACHOVIA BANK
LICENSED FINANCIAL SPECIALIST 2005-2008

WELLS FARGO
ACCOUNT EXECUTIVE 2004-2005

PROFESSIONAL SOCIETIES AND ORGANIZATIONS:

AMERICAN DIETETIC ASSOCIATION, STUDENT MEMBER 2010-2012

GREATER ATLANTA DIETETIC ASSOCIATION,
NATIONAL NUTRITION MONTH COMMITTEE MEMBER 2011-2012

PRESENTATIONS AND PUBLICATIONS:

THE 14TH INTERNATIONAL WORKSHOP ON CO-MORBIDITIES AND ADVERSE DRUG REACTIONS IN HIV POSTER PRESENTATION 2012

ABSTRACT TO BE PUBLISHED IN *ANTIVIRAL THERAPY* SUPPLEMENT*:*
LA Stricker, M Ndurangu, A Nucci, TR Ziegler, V Tangpricha, GA McComsey, JK Frediani, E Millson, L Seaton, AC Ross. Habitual Nutrient Intake in HIV-Infected Youth and Associations with HIV-Related Factors. 2012

GEORGIA ACADEMY OF NUTRITION AND DIETETICS
PROFESSIONAL EXCHANGE & POSTER PRESENTATION 2012

ABSTRACT

Background: Few studies have evaluated habitual nutrient intake among HIV-infected youth in the United States, even though diet may influence immune function and thus HIV-related outcomes. This study sought to determine micro- and macronutrient intake in HIV-infected youth, and investigate the relationships among nutrient intake, demographics, lipid profiles, and HIV-related factors.

Methods: HIV-infected subjects and healthy controls 1-25 years old were prospectively enrolled. Demographics, clinical and laboratory data (including fasting lipids) were collected. Food and nutrient intake was assessed via 24-hr dietary recalls performed one-on-one with a trained investigator every 3 months for one year. Nutrient intake was determined from averaged food recall data using NDS-R software and directed by research nutritionists. Nutrient intake was compared to Dietary Reference Intakes (DRI) and Acceptable Macronutrient Distribution Ranges (AMDR). Analysis utilized non-parametric and parametric tests and Pearson correlations to evaluate associations.

Results*:* Subjects with ≥2 food recalls were analyzed (175 HIV+; 43 controls). Groups were similar in age, race, sex, body mass index (BMI), and kilocalorie intake (HIV+: mean(SD) age=17.4±4.8 years; 95% black; 54% male). Neither group met the DRI for vitamins A, D, E, calcium, magnesium, sodium, and potassium (all $P<0.01$). HIV+ patients did not meet recommendations for pantothenic acid or folate (both $P<0.01$) and had lower %DRI than controls for vitamins A, E, pantothenic acid, magnesium, calcium, folate and potassium ($P\leq0.04$). Micronutrient intake that met recommendations for both groups still had a lower intake in HIV+ (vitamins K, C, thiamin, riboflavin, copper, phosphorus, manganese). Carbohydrate/protein intake were within AMDR for both groups; however, %kilocalories from fat was above normal and higher in HIV+ (both $P=0.02$). Both groups consumed less fiber, and more saturated and trans-fat than recommended; cholesterol intake was normal. In HIV+, BMI was negatively correlated with %DRI for vitamins A, D, E, B6, B12, riboflavin, thiamin, niacin, pantothenic acid, folate, magnesium, iron, zinc, copper, potassium and selenium (all $P<0.05$). Caucasian HIV+ patients had significantly greater vitamin D and calcium %DRI than black HIV+ patients ($p< 0.05$). Mean lipid profiles were within a healthy range for both groups. Mean serum triglycerides were significantly higher and HDL-C lower in HIV+ subjects (both $p<0.01$). Fiber and trans-fat intake were correlated with triglycerides ($r=0.16$;$P=0.04$) and low-density lipoprotein ($r=0.16$;$P=0.04$), respectively. Total fat intake was correlated with triglycerides ($r=-0.17$;$P=0.03$). Mean caloric intake was negatively correlated with current ($r=-0.12$;$P=0.02$) and nadir CD4 counts($r=-0.11$;$P=0.04$). Zinc, riboflavin, and magnesium %DRI were correlated with current CD4 (all $P<0.01$), and vitamin A %DRI with nadir CD4 ($r=0.10$;$P=0.05$). In HIV+ subjects not on ART (N=56), HIV-1 RNA levels were negatively correlated with protein intake ($r=-0.30$;$P=0.05$).

Conclusions: HIV+ youth have inadequate intake of several essential vitamins and minerals compared to the DRIs, and lower habitual dietary intake of a variety of micronutrients compared to HIV- controls. HIV+ youth consumed higher than recommended amounts of dietary fat and lower than recommended amounts of dietary fiber. While mean lipid profiles were normal and intake did not correlate with values, the HIV+ group had a higher prevalence of dyslipidemia, which long-term, may contribute towards a greater risk of cardiovascular disease when combined with poor diet. Intake of some nutrients was associated with HIV-related factors, including CD4 counts. Further investigation is warranted to determine whether nutrient intake data correlate with plasma nutrient concentrations in HIV+ youth and the potential impact of nutritional status on immune function, HIV progression, and CVD risk in this patient population.

SUBOPTIMAL NUTRIENT INTAKE IN HIV-INFECTED YOUTH AND ASSOCIATIONS WITH SERUM LIPID PROFILES AND HIV-RELATED FACTORS

By

Lindsey A. Stricker

A Thesis Submitted to the Graduate Faculty of Georgia State University in Partial Fulfillment of the Requirements for the Degree of

MASTER OF SCIENCE IN HEALTH SCIENCES
BYRDINE F. LEWIS SCHOOL OF NURSING & HEALTH PROFESSIONS
DIVISION OF NUTRITION
GEORGIA STATE UNIVERSITY

Atlanta, Georgia
2012

ACKNOWLEDGEMENTS

I would like to acknowledge and thank the following people:

Benjamin Stricker: For his incredible patience and understanding. He is my hero and #1 supporter and I could not have made it through this process without him.

Dr. Murugi Ndirangu: For encouraging me to take on such an incredible project, and providing guidance along its course.

Dr. Allison Ross: For her knowledge, mentoring, and support throughout this study, and above all, for allowing me to use her data to develop my thesis.

Dr. Anita Nucci: For her guidance through the intricate thesis process.

Dr. Meera Penumetcha: For providing me the research knowledge and ability to complete statistical analysis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ACTSI	Atlanta Clinical & Translational Science Institute
AHA	American Heart Association
AI	Adequate Intake
AIDS	Acquired Immunodeficiency Syndrome
AMDR	Acceptable Macronutrient Distribution Range
AND	Academy of Nutrition and Dietetics
ART	Antiretroviral Therapy/Treatment
BMI	Body Mass Index
CD4	Cells that are targeted by the HIV virus
CDC	Centers for Disease Control and Prevention
CIN	Clinical Interaction Network
CRP	C-Reactive Protein
CVD	Cardiovascular Disease
DRI	Dietary Reference Intake
EAR	Estimated Average Requirements
FFQ	Food Frequency Questionnaire
FMD	Flow Mediated Dilation
HAART	Highly Active Antiretroviral Therapy
HDL-C	Serum High-Density Lipoprotein Cholesterol
HIV	Human Immunodeficiency Virus
HIV+	HIV-infected subjects

HIV-	HIV-negative controls
IDP	Infectious Disease Program
IMT	Intima-Media Thickness
IOM	Institute of Medicine
LDL-C	Serum Low-Density Lipoprotein Cholesterol
NDS-R	Nutrition Data System for Research Software
PI	Protease Inhibitors
RDA	Recommended Dietary Allowance
REACH	Reaching for Excellence in Adolescent Care and Health
REE	Resting Energy Expenditure
TC	Total Serum Cholesterol
TG	Serum Triglycerides
UL	Tolerable Upper Intake Level
WHO	The World Health Organization

CHAPTER I

INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC),[1] approximately 1.2 million people, aged 13 and older, were living with human immunodeficiency virus (HIV) infection in the U.S. at the end of 2008. Almost 43,000 new diagnoses of HIV infection in the U.S. were made in 2009. An estimated 8,460 of those diagnoses were children and youths between the ages of 0 and 24 years.[1] Among all age groups, seven and a half percent of the HIV diagnoses in the U.S. in 2009 occurred in Georgia. The only states with a greater percentage of overall HIV diagnoses were Florida, New York and Texas.[2] New cases of HIV-infection continue to be a problem in the U.S. and even more so in Georgia.

There are a number of nutritional issues affecting HIV-infected individuals. Nutritional issues range depending on medications and disease status. Furthermore, with developments in medications, long-term nutritional implications have become a bigger concern for those infected with HIV. In addition to long-term metabolic abnormalities, more immediate nutrient deficiencies can also impact the disease status of those living with HIV. Fortunately, vigilant dietary intake by these individuals may limit such issues.

Prior to the introduction of highly active antiretroviral therapy (HAART), wasting syndrome and growth impairment were some of the major nutritional implications in children with HIV.[3,4] Since the introduction of HAART, children and adults infected with HIV are living longer,[5,6] and there is less concern about wasting and growth impairment. In contrast, nearly half of the HIV-infected participants in the Reaching for

Excellence in Adolescent Care and Health (REACH) study,[7] a prospective, observational cohort study following adolescents' progression of HIV infection, were either overweight or obese. Furthermore, they found the obesity prevalence among HIV-infected adolescents was higher in the southern region of the United States.

With a decrease in wasting, and increase in survival times and obesity, the concern has shifted toward long-term health problems and chronic diseases associated with HIV infection and HAART medications.[6] Metabolic abnormalities, including dyslipidemia, and the risk of cardiovascular disease (CVD) are of growing concern in the HIV infected population.[8] Studies[8,9] have shown the effectiveness of dietary intervention on decreasing lipid levels in this population; thus, the first step for improving hypercholesterolemia and hypertriglyceridemia in patients with HIV should be consultation with a dietitian.[10] Barrios et al.[11] found that HIV infected individuals that complied with a low-fat diet, had significantly lower lipid levels, especially when taking protease inhibitors (PI). For the general population, the American Heart Association (AHA) recommends total fat intake to be between 25 and 35% of total calories, saturated fat to be less than 7% of total calories, trans fats to be less than 1% of total calories, cholesterol to be less than 300mg per day, and to consume 14g of fiber per 1000 calories consumed per day, to reduce the risk of CVD.[12] CVD is the number one cause of death, amongst the general population, in the United States. Due to the increased CVD risk factors in HIV-infected patients, these recommendations may need a stricter following by the HIV-population. Fat, saturated fat, trans fats, cholesterol and fiber intake are all associated with the risk of developing CVD.

Alternatively, malnourishment is still a concern among some HIV-infected children and adolescents, especially those taking PI.[13] Present treatment guidelines include PI as part of the antiretroviral therapy (ART) regimen for children and adults.[14] Children on PI have been shown to have significantly lower body mass index (BMI) and z scores for weight for age and height for age.[13] Regardless of medication, a higher rate of protein oxidation has been seen in HIV-infected children due to the "inability to down-regulate protein catabolism" in this population.[15] Similarly, HIV infected adults have been shown to have an increased resting energy expenditure (REE) compared to healthy people;[16] however, data on REE in children is not as clear.[6] Johann-Liang and colleagues did not find evidence for an increased REE in children ages 1 to 13 years.[3] On the other hand, Banerjee and colleagues did find that children on HAART had higher REE than those not on HAART, and that weight Z-score was significantly negatively associated with REE.[5]

Furthermore, studies show that nutritional deficiencies, including selenium, vitamin A, calcium, vitamin D, zinc, and glutathione, are not uncommon among children with HIV,[17-19] even with the introduction of HAART.[13] Several studies on adults infected with HIV have found micronutrient deficiencies were associated with decreased immune status, disease progression to AIDS, and increased mortality.[20-27] Assessment of nutritional status can be accomplished using Dietary Reference Intakes (DRIs),[28-29] which are the nutrient reference values derived from years of scientific research that include four reference values: Recommended Dietary Allowance (RDA), Adequate Intake (AI), Tolerable Upper Intake Level (UL), and Estimated Average Requirements (EAR). The RDA is the "average daily dietary nutrient intake level that is sufficient to meet the

nutrient requirements of nearly all (97-98 percent) healthy individuals." For some nutrients, there is not enough research to establish an RDA, therefore those nutrients have an AI, which is considered an adequate amount of intake of the nutrient for healthy individuals. Unfortunately, in those infected with HIV, the RDA may not meet their needs, as research[30] has suggested that there is a greater utilization of nutrients, possibly due to increased oxidative stress.

Several studies[5,31] have shown that nutrition counseling and support improved the health of children and adults with HIV, emphasizing the importance of dietary intake among the HIV-infected population. Given the aforementioned nutritional implications affecting HIV-infected individuals and that dietary intake is an important environmental factor contributing to the health of those infected with HIV,[6,32] it is important to understand the current dietary intake of this population. HIV-infected children and adolescents are at an even higher nutritional risk due to growth and development demands,[33] and few studies have thoroughly described the micro- and macro-nutrient intake of this population. Micronutrients play an important role in immune function, and studies show that lower micronutrient intakes are associated with mortality and the progression of HIV,[16] as assessed by biomarkers such as viral load and CD4+ cell count.[23] CD4 are immune cells that are targeted and inactivated by the HIV-virus, and thus decrease in HIV-infected individuals.[16] However, research shows micronutrient supplements have also had adverse effects on individuals infected with HIV. Therefore, The World Health Organization[16] (WHO) suggests that an adequate diet is the best method for meeting micronutrient needs in HIV-infected individuals. Thus, determining deficiencies in micronutrient intake among children and adolescents infected with HIV

will provide valuable information for patient care, as will assessing associations between intake and HIV-related factors. Furthermore, given the increased risk factors of CVD in the HIV-infected population, the question remains, do HIV-infected children and youth follow a heart healthy diet, and does the dietary intake of unhealthy fats and limited fiber affect nutritional markers of CVD, such as lipid levels, in this population? Therefore, the objectives of this thesis research are (1) to determine the micro- and macronutrient intakes of HIV-infected children and youths, (2) to compare the nutrient intakes to the DRI and to the healthy controls, (3) to determine if nutrient intake is associated with HIV-related values (CD4+ counts, viral loads), (4) to compare nutrient intake to the American Heart Association's recommendations for a heart healthy diet, and (5) to assess the associations between dietary intake of nutrients (fat, saturated fat, trans fat, cholesterol and fiber) and serum lipid levels.

CHAPTER II

REVIEW OF LITERATURE

Micronutrient Needs in HIV-Infected Individuals

Micronutrients are important for maintaining the body's functions and immune system, and deficiencies have been associated with disease advancement and mortality in HIV-infected individuals.[20-27]A U.S. study[21] following HIV-infected men over an 8-year period, found that increased intake of thiamin, riboflavin, niacin, and vitamin B-6 were associated with longer survival. A 3.5 year study[22] following 125 HIV-infected, drug-using men and women revealed plasma vitamin A, B-12, zinc and selenium deficiencies were significantly associated with mortality. However, after controlling for CD4+ cell counts less than 200/mm^3, only selenium deficiency was significantly associated with increased mortality. Vitamin B-6 and E did not show any association with mortality. In a study of 400 HIV-infected Kenyan women,[23] inadequate serum beta-carotene was significantly associated with the immune response and HIV progression biomarkers such as viral load, CD4+ cell count and C-reactive protein (CRP). Increased CRP and viral loads were the strongest predictors of inadequate serum beta-carotene. However, the direction of the association was not established. Fortunately, Baum and colleagues[24] conducted a longer, 18-month study on 90 HIV-infected men to determine nutritional and immune status over time and better understand causality. A significant drop in CD4+ cell count occurred after serum vitamin A and B-12 became deficient. Additionally, they found that when serum vitamin A, B-12 and zinc reached sufficient levels, CD4+ cell counts were increased and disease progression abated. On the other hand, in the

multicenter AIDS Cohort Study that followed 310 men semiannually for over 10 years, Tang and colleagues[25] found that vitamin A was not associated with progression to AIDS, nor was vitamin A or E associated with a decline in CD4+ cell count to less than 200/mm^3. However, when vitamin E levels were studied in quartiles, "median AIDS free time" in the highest quartile of vitamin E intake was 1.5 years greater than in the lower quartiles and the adjusted risk of progression to AIDS was 34% lower in the highest quartile of intake compared to the lowest quartile. In an additional study[26] following the same cohort of men, deficiency in serum B-12 preceded disease progression to AIDS after adjusting for CD4+ cell count. Median time to first AIDS diagnosis was extended 4 years in those with adequate B-12 concentrations compared to those who were B-12 deficient, and there was an 87% increased risk of progression to AIDS in the serum B-12 deficient group. No association was found between B-6 and folate concentrations and progression to AIDS. Further analysis [27] of dietary intake from the AIDS Cohort Study revealed decreased risk of progression to AIDS with the highest intake levels of vitamins C, thiamin, and niacin. Alternatively, increased zinc intake was associated with an increased progression to AIDS. The highest and lowest intakes of vitamin A were associated with a higher progression to AIDS.

Likewise, micronutrient deficiencies are common in individuals infected by HIV. Studies[20] have shown both insufficient dietary intake and inadequate serum levels of some micronutrients in this population. For instance, Baum and colleagues [24], found HIV-infected men were more likely to have serum deficiencies in vitamin B-6, B-12, A, E and zinc than the non-infected control group. In addition, sufficient dietary intake of micronutrients above the RDA has been seen in HIV-infected individuals, but with

inadequate serum concentrations of those micronutrients, suggesting that HIV-infected people have increased needs above the RDA for certain micronutrients.[30,34]

In summary, several studies have demonstrated an association between poorer health outcomes and micronutrient deficiencies in HIV-infected adults. Inferior outcomes were associated with both serum micronutrient deficiencies and dietary intake deficiencies. Research reveals an association between decreased immune status and inadequate vitamin A, B-12, and zinc; increased mortality and inadequate selenium, thiamin, niacin, riboflavin and B-6; and progression to AIDS and inadequate vitamins C, E, thiamin, niacin and B-12. Some researchers[35] believe that part of the contributory role of these vitamins and minerals to the slowing of HIV progression are related to their antioxidant effects and ability to reduce oxidative stress. Oxidative stress is considered as an important factor in the pathogenesis of the HIV disease. Overall, research suggests that sufficient micronutrient status may contribute to improved immune status and survival.

Macronutrient Needs in HIV-Infected Individuals

The World Health Organization[16] suggests asymptomatic HIV-infected individuals increase calorie intake by 10% and those fighting infection increase calorie intake by 20-30% because of increased energy expenditure. Furthermore, HIV-infected children losing weight need to increase their calorie intake by 50-100%. However, recommendations on the macronutrient composition for HIV-infected individuals are the same as the recommendations for non-infected persons, without a greater need for protein.[4,16,31,36] The Institute of Medicine (IOM)[37] recommends an Acceptable Macronutrient Distribution Range (AMDR) of 10 to 35% of energy from protein, 45 to

65% of energy from carbohydrates, and 20 to 35% of energy from fat, in adults. The AMDR for children and youths between the ages of 4 and 18 is between 25 and 35% of energy from fat and between 10 and 30% of energy from protein. Carbohydrate recommendations are the same for children and youths. With the advent of ART and the increased risk of CVD in these patients, some researchers have suggested a decreased fat intake.[33] Miller and colleagues[38] suggest that HIV-infected children with any "metabolic dysfunction" keep fat intake at less than 30% of calories and saturated fat at less than 10% of calories. The Academy of Nutrition and Dietetics (AND) also emphasizes a diet with less than 7% of calories from saturated fat, less than 1% of calories from trans fatty acids, and less than 200 mg of cholesterol each day for HIV-infected individuals with hyperlipidemia.[36]

Macronutrient needs vary in individuals infected with HIV and may also vary based on disease complications. Energy needs are increased for the HIV-infected individual, and are even greater with infection or if there has been weight loss. The recommendation on the macronutrient breakdown of protein, carbohydrate and fat does not differ for the HIV-infected individual; however, research has suggested limiting fat intake and the AND has suggested limiting trans fat, saturated fat and cholesterol intake in HIV-infected individuals with hyperlipidemia

Micronutrient Deficiencies and Needs of HIV-Infected Youths

Increased micronutrient needs may explain malnourishment and nutritional deficiencies among HIV-infected children. Studies[19,30] have shown that HIV infection may cause micronutrient deficiencies in children. Steenkamp and colleagues[19] showed that the nutrients with the greatest prevalence of deficiency in an analysis of serum levels

were vitamin A, vitamin D, zinc, and glutathione, which are all important in immune regulation. In this study of children not receiving HAART, they found that children with abnormally low levels of zinc and vitamin A had significantly lower CD4+ cell counts and higher viral loads. They did not find any correlations between deficient nutrient intake and growth impairment. Furthermore, Stephensen et al.[30] concluded from the REACH study, that vitamin C and vitamin E intake in HIV-infected youths must be increased due to the greater utilization of these vitamins as a result of increased oxidative stress with HIV-infection. Plasma ascorbate levels were marginally lower in subjects with HIV, but intake of vitamin C was sufficient, suggesting "chronic immune activation" lowers plasma ascorbate levels. The positive association found between vitamin E intake and plasma alpha-tocopherol in HIV-negative subjects was not seen in HIV-positive subjects, suggesting an increased need for vitamin E among youths with HIV. Therefore, these studies[19,30] have concluded that nutrition support along with nutrient-dense foods and supplements are critical for the treatment of children with HIV.

Earlier studies[4, 18] show conflicting results on micronutrient deficiencies. Henderson and colleagues[4] saw no differences in serum plasma micronutrients between HIV-infected and non-HIV infected individuals, but suggested that there still may be an increased need for micronutrients in HIV-infected children. Furthermore, they found no greater micronutrient deficiencies in HIV infected children with growth retardation. Fawzi[18] suggests that overall, deficiencies of biochemical micronutrients are more common among children infected with HIV than those uninfected.

Similar to adults infected with HIV, HIV-infected children also face micronutrient deficiencies that compromise immune and nutritional status. While research is more

limited on children, so far it reveals deficiencies in vitamins A, D, C, E and zinc. Deficiencies in vitamins A and zinc have been associated with poorer immune status. Furthermore, the chronic disease status of HIV-infected youths may result in increased nutrients needs beyond the recommended intakes.

Current Studies Assessing Nutrient Intake of HIV-Infected Youths

While several studies have described the intake of HIV infected adults,[21,39,40] few have thoroughly described the nutritional intake of youths with HIV in the United States. Of those that have studied dietary intake in children, very few[3] have found a decreased energy or macronutrient intake in HIV-infected children and adolescents;[4,6,13,32] however, deficient micronutrient intakes were uncovered.

Henderson and colleagues[4] assessed dietary intake through 24-hour recalls in 38 children ages 2 to 11 years old. The study only described the intake of energy, protein, zinc, selenium and vitamin A. Energy intake of the HIV infected children was approximately 100% of the RDA, and protein intake was over 200% of the RDA. Only zinc intake was low at less than 65% of the RDA. Zinc deficiency is related to changes in immune function, which is a concern for this population. They found no significant difference in intakes between HIV-positive and HIV-negative groups.

In one of the oldest studies[41] looking at dietary intake of HIV-infected children, Zuin and associates used 3-day food diaries to assess intakes of 33 HIV-infected children compared to 16 HIV-negative children. The analysis only considered energy, protein, calcium, phosphorus and iron intake. All HIV infected children had protein intake greater than the RDA. There were no significant differences in energy and nutrient intakes between the HIV-infected children and the controls. Although, they did find that

those patients that were "symptomatic" had slightly decreased energy and nutrient intakes, and they were also more at risk for acute complications, which led to an even greater reduction of energy and protein intake.

In one of the REACH studies[42], which spanned the U.S., the Block Food Frequency Questionnaire (FFQ) was administered to 264 HIV-infected and 127 non-infected youths between the ages of 12 and 18 years of age. Energy, vitamin A, C, E, iron, and zinc intake were assessed. No significant differences in nutrient intakes were found between HIV-positive and HIV-negative youths. When compared to the Estimated Average Requirements (EAR), 13-38% of the study population had inadequate intakes of vitamins A, E and zinc. Moreover, there were no significant differences in intakes when comparing patients by CD4+ cell counts. Another REACH study[7] assessed "diet quality" using a modified Healthy Eating Index (HEI), which assessed total fat, saturated fat, cholesterol, sodium, and the 5 Food Guide Pyramid food groups. Poorer-quality diets were seen in HIV-positive youths that had higher intakes of fat, saturated fat and cholesterol compared to the non-infected controls.

In an HIV-infected cohort (n=126) aged 3-20 years old, Sharma et al.[32] collected an average of 5, 24-hour recalls per subject between 1995 and 2004. They found that the dietary intake of the HIV infected children were similar to healthy children, and calorie intake was 161% of estimated energy requirements (EER) in males and 140% of EER in females. Fat, protein and carbohydrate intake were all within the AMDR. Though, saturated fat intake was high at 12.6% and 12.7% of kilocalories for males and females, respectively. Protein intake at the beginning of the study was 400% of the RDA, but slightly decreased as nutrition education was provided every 3 months.

In a group of HIV-infected 4-17 year olds from Brazil, Tremeschin and colleagues[13] used an adapted semi-quantitative FFQ to assess dietary intake. They found no difference in macronutrient and energy intakes between the HIV-positive and HIV-negative groups, but they did see excessive dietary fat intake (38.5% of kilocalories) amongst both groups. The authors concluded that the diet of this population must be monitored due to the high lipid consumption and the risk of CVD in this group.

Few studies have thoroughly assessed micro- and macro-nutrient intakes of youths with HIV. Deficient intakes were found for vitamins A, E and zinc, but none were seen for the macronutrients. In contrast, excess intake of protein, fat, saturated fat and cholesterol among HIV-infected youths was common.

HIV, Dyslipidemia, and Cardiovascular Disease Risk

Several studies[38,43] emphasize a growing concern for an increased risk of CVD due to lipid abnormalities, lipodystrophy, and vascular structural changes in children infected with HIV. Lipid abnormalities, or dyslipidemia, among HIV-infected individuals include one or more of the following: increased fasting total cholesterol (TC) greater than 200mg/dl, serum triglycerides (TG) greater than 140mg/dl, or low-density lipoprotein (LDL-C) greater than 130mg/dl, or decreased high-density lipoprotein (HDL-C) less than 40mg/dl.[13,38,43,44] These characteristics of high blood cholesterol are more specifically called hyperlipidemia because the levels are elevated. Lipodystrophy is loosely defined as fat redistribution in which there is an accumulation of visceral fat around the stomach and back of the neck, and a wasting of fat in the extremities and face.[38] Changes in the vascular structure, or damage to the arterial walls, have been characterized by thickening of the right and left common carotid arteries and a decreased

brachial artery flow mediated dilation, a measure of arterial function, in those infected with HIV.[43] Chronic infection and inflammation in HIV-infected individuals seems to increase atherosclerotic processes, which creates critical risk factors for CVD.

In a study[10] looking at the effect of ART drugs on lipid changes, it was found that 10% of children on ART might require hyperlipidemia intervention due to the increased risk of inflammation from HIV infection. In a cohort of 94 children ages 1 through 18 that had taken PI for at least 2 years, 62% had dyslipidemia.[44] Miller and colleagues[38] believe that an alteration in diet can positively affect HIV patients with "metabolic dysfunction." They suggested that well-balanced diets, high in fiber, micronutrients and antioxidants might offset nutrient deficiencies. Furthermore, they advise these patients to keep dietary fat at <30% of kilocalories and saturated fat at <10% of kilocalories.

In Brazil, Tremeschin and colleagues,[13] studied 4 groups of 4-17 year olds that were either HIV-positive on nucleoside or non-nucleoside reverse transcriptase inhibitors (NRTI, NNRTI), PI for more than 2 months, PI for less than 2 months, or were healthy HIV-negative children. They found no statistical differences in hyperlipidemia between any of the groups, suggesting that the HAART regimen alone does not increase dyslipidemia. On the other hand, they found that triglycerides were higher in those taking PI. Both groups had excessive dietary lipid intake, which along with the increased concern for CVD risk in children with HIV, suggests that the diet in this population needs to be monitored.

Common carotid intima-media thickness (IMT), or the arterial wall thickness of those arteries that supply the head and neck with blood, is a marker for atherosclerosis in children at risk for CVD.[45] A few studies examined IMT, along with other risk factors

for CVD, in HIV-infected youths to determine their risk for CVD. Several risk factors for CVD were studied in 83 HIV-infected children in London.[43] Triglyceride, non-HDL cholesterol, and apoB levels were all significantly higher in HIV-infected children when compared to the control group. HDL cholesterol levels were significantly lower in the HIV group. Furthermore, they found that children treated with ART had higher total cholesterol than children not treated with ART. This study also looked at vasculature in the groups and determined that the average of the right and left common carotid artery's IMT was significantly higher in the HIV infected children compared to the non-infected. Those children on PI had significantly higher IMT than those not treated with PI. Moreover, flow mediated dilation (FMD) of the brachial artery was lower in HIV infected children compared to controls; meaning that the HIV infected children had increased arterial stiffness. PI patients had significantly lower FMD than non-PI patients. The authors concluded that vascular changes are occurring at young ages in the HIV infected population, supporting the concern for the increased risk of atherosclerosis and CVD among these patients. A study by Vigano and colleagues[45] in young adults and adolescents with HIV supported these results. They found that the common carotid IMT was higher, after controlling for confounders, in the HIV-infected group than in the controls that were matched for age, gender and BMI. IMT was higher among those patients on ART.

Shah et al.[40] looked at the role of diet in dyslipidemia in 51 HIV-infected adults using 3-day food records to assess macronutrient intake. Despite, the population being adults, this study is worth noting due to the correlations made between diet and lipid levels. They found increased protein and animal protein were positively correlated with

increased total cholesterol, triglycerides, and non-HDL cholesterol. Trans fats were positively correlated with triglyceride levels. Moreover, soluble fiber intake, which was low, was negatively correlated with total cholesterol, triglycerides, and non-HDL cholesterol. They did not find any associations between lipid levels and omega-3 fatty acids, cholesterol, and saturated fat intake. Of the 51 subjects, all with exposure to PI therapy, 50% had either high or very high triglycerides, 50% had either borderline-high total cholesterol or high total cholesterol, and 86% of men and 68% of women had LDL > 130 mg/dL.

Studies have also assessed the acute myocardial infarction (AMI) rates among HIV-infected adults to determine outcomes of CVD risk factors. Triant and colleagues[46] looked at 3,851 HIV-infected patients and 1,044,589 non-HIV patients at Boston hospitals between 1996 and 2004. The amount of AMI events was two times greater in the HIV-infected patients compared to the controls. This study also found that the HIV-patients had significantly higher rates of hypertension, diabetes and dyslipidemia. Unfortunately, there are insufficient studies to determine the adverse outcomes of the markers of CVD risk in children.[38]

Several studies have revealed that HIV-infected individuals have many increased risk factors for atherosclerosis and CVD. Dyslipidemia, increased arterial stiffness, thickening of the arteries, and increased AMI events have commonly been seen in HIV research. Research has also suggested that a well-balanced diet with proper micro- and macro-nutrient intake may help improve these risk factors in the HIV-population.

Literature Review Summary

Research has revealed a number of nutritional issues affecting HIV-infected individuals. Micronutrients play an important role in immune function, and studies show that lower micronutrient intakes and serum levels are associated with disease advancement and mortality in HIV-infected individuals. While energy needs are increased for the HIV-infected individual, there is not a need for a different macronutrient composition of protein, carbohydrate or fat. However, research has suggested limiting fat intake, trans fat, saturated fat and cholesterol intake in HIV-infected individuals with hyperlipidemia. Hyperlipidemia is common among HIV-infected individuals and several studies have revealed many increased risk factors for atherosclerosis and CVD. Dyslipidemia, increased arterial stiffness, thickening of the arteries, and increased AMI events were more commonly seen in HIV-infected individuals than in those not infected. Children with HIV also face micronutrient deficiencies that compromise immune and nutritional status, and research suggests that the chronic disease status of HIV-infected youth may result in increased nutrients needs beyond the recommended intakes. Unfortunately, few studies have thoroughly assessed micro- and macro-nutrient intakes of youth with HIV. The few studies that have assessed intakes, found energy and macronutrient deficiencies were uncommon. In contrast, excess intake of protein, fat, saturated fat and cholesterol was common among HIV-infected youths.

Research suggests that sufficient micronutrient status may contribute to improved immune status and survival and that a well-balanced diet with the proper macronutrient intake may help improve CVD risk factors in the HIV-population. Additionally, The World Health Organization[16] suggests that an adequate diet is the best method for

meeting micronutrient needs in HIV-infected individuals as opposed to taking supplements. Therefore, determining deficiencies in micronutrient intake among children and adolescents infected with HIV will provide valuable information regarding the nutrition counseling that may be needed to provide these youths with healthier and longer lives. Furthermore, given the research showing HIV-infected individual's increased risk factors of CVD, it is important to know whether HIV-infected children and youths follow a heart healthy diet, and if the intake of nutrients such as fats and fiber influence nutritional markers of CVD, such as lipid levels. Only one study was found which looked at associations between dietary intakes and lipid profiles.

CHAPTER III

METHODS AND PROCEDURES

Participants

HIV-Infected

200 documented HIV-infected children, adolescents and young adults (ages 1-25) enrolled in the Infectious Disease Program (IDP) at the Ponce de Leon HIV Clinic of the Grady Health System in Atlanta, Georgia were recruited for the original study titled, "Vitamin D and cardiovascular biomarkers in HIV-infected children and young adults".

Inclusion criteria

All individuals, 1-25 years of age, with documented HIV-1 infection (positive HIV-1 antibody test, confirmed by western blot), who obtain their medical care at the IDP (Ponce Center) were eligible for the study.

Exclusion criteria

Patients who had scheduled "sick visit" appointments, or were found to be acutely ill during their regular visits, were not eligible at that visit, and were re-evaluated at their next routine or follow-up visit for enrollment in the study. "Acutely ill" was defined as having an oral or axillary temperature >100.4°F, significant upper or lower respiratory tract symptoms, acute otitis media, pharyngitis, or other notable signs or symptoms consistent with acute illness or opportunistic infection that would likely interfere with inflammatory marker measurements. Once resolution of signs and symptoms had been shown for at least one month, the patient was again eligible for the study. Stable or well-controlled chronic infectious or inflammatory conditions were not exclusionary, but were

noted in the data collection forms for accurate data analysis. Children under 1 year of age were ineligible due to an immature immune system and inability to interpret inflammatory marker levels at this age.

Recruitment of HIV-infected subjects

Subjects were recruited in several ways, including (1) recruitment mailing; (2) phone call prior to scheduled appointment; (3) approached by study staff during routine medical appointment; and (4) case manager/physician referrals. A flyer was mailed to all potentially eligible patients at the IDP at one time with a general description of the study and a copy of the informed consent. These patients had regular appointments scheduled at the IDP within the upcoming 3 months (as soon as within 1 week or as long as 3 months from the time of the flyer mailing). Study staff also called patients a few days before their scheduled appointments to tell them about the study and ask them to arrive at their appointments after at least 8 hours of fasting if interested in learning more about the study for potential participation. Patients/families were approached during their routine visits by study staff, and if interested and eligible, were consented and enrolled into the study. Case managers and patient physicians were also made aware of the study by a general flyer, and told patients about the study. If patients were interested, they were referred to the study staff. In all cases, subjects were given ample time to review the consent forms and ask questions.

Controls

A small median age-matched control group (n=50) with similar proportions of sex and race was recruited and enrolled for comparison to the HIV-infected group. The control group had similar study procedures to that of the HIV-infected group except that

HIV-related laboratory and clinical information were not collected. Controls were recruited from the clinic, as either uninfected patients who received their regular health care at the clinic, or were uninfected siblings or relatives of the HIV-infected patients, or from physician referrals.

Inclusion criteria

Healthy uninfected children and young adults, 1-25 years of age, were included.

Exclusion criteria

Individuals with current or recent infectious or inflammatory illness, known chronic disease, hypertension, or receiving any prescription medication known to affect inflammatory or endothelial activation markers were excluded. Individuals were excluded if they were at high-risk of having or acquiring HIV by either (1) engaging in sexual activity with a known HIV partner currently or previously without no intercurrent negative HIV test, (2) sharing needles for drug injection currently or previously without no intercurrent negative HIV test; (3) have had another sexually transmitted disease without acquiring HIV testing; or (4) the investigator or subject feels that he/she may be infected and has not had a negative HIV test. Subjects 13 years of age or older were screened for HIV before enrollment with the OraQuick Advance Rapid HIV test.

Recruitment of controls

Healthy volunteers were recruited in several ways, including (1) case manager/physician referrals of uninfected patients who receive their routine medical care at the IDP or of relatives of the HIV-infected patients seen at the IDP; (2) uninfected patients seen at the IDP for their routine medical care and/or their guardians were approached by study staff during their medical appointments; (3) HIV infected patients

and/or guardians were told during their regular appointments and in the recruitment mailing that we are looking for uninfected healthy volunteers so they can refer their healthy friends or relatives. Volunteers were given copies of the informed consent forms and verbal information about the study. Interested volunteers returned to the clinic for a scheduled research visit. In all cases, volunteers were given ample time to review the consent forms and ask questions.

All Participants

Consent and confidentiality

Study staff fully explained all assessments to the patient and/or legal caregiver, and asked for their written consent to participate. All parents or legal guardians and subjects ≥18 years of age provided written informed consent to participate in the study, and those subjects 17 years of age signed the written consent along with their parent or legal guardian. Subjects ages 6-10 years gave verbal assent and those 11-16 years gave written assent. Details about the study, including its benefits and potential risks were explained to the patients or their parent/guardian.

All information regarding the patient remained confidential to the extent allowed by law. Unique numeric subject numbers were used for data entry.

Compensation

Subjects received $50 after completion of all study procedures to compensate for time and transportation costs (with the exception of the follow-up 24-hour food consumption recalls). If a subject had to return to the clinic for a separate fasting blood draw, the subject received $50 at the time of their return.

Data Collection

Data collection began May of 2010 and was completed in January of 2012. Clinical measurements collected include weight, height, standardized waist and hip measurements (based on procedure recommendations from the Metabolic Study Group of the AIDS Clinical Trials Group), alcohol intake, smoking habits, physical activity level, family history of CVD, CD4 counts, HIV-1 RNA (viral load) and fasting lipoprotein profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides). Information was also collected on medication use, demographics, and medical conditions. Extensive medical chart evaluations were conducted to collect detailed information on past and current medical diagnoses, ART use and history (including calculation of cumulative exposure to each class of antiretrovirals), CD4 cell count nadir, current ART and non-ART medication use, HIV stage based on CDC classification system, calculation of HIV duration in months, and methods of HIV acquisition (vertical or behavioral). Relevant medical information on the control group was collected through interview.

Laboratory Assessments

Subjects fasted for ≥8 hours prior to blood sampling. Plasma was extracted and stored at -80° C until analysis without prior thawing.

Future measurements

Extra plasma was obtained and stored for measurements of additional micronutrient levels and inflammatory/endothelial activation markers for future, related studies. Stored samples were labeled with subject number only. Subject study numbers matched to name were stored in a separate location on a password-protected computer.

Dietary intake

Each subject or guardian completed an age-appropriate, semi-quantitative, Block Food Frequency Questionnaire (FFQ), and a total of four, 24-hour food consumption recalls. One, 24-hour recall was obtained for each season of the year, for each subject, to total four recalls per subject. Food intake over the last 24 hours was reported by the subject and amounts were entered into Nutrition Data System for Research (NDS-R), available through the Clinical Interaction Network (CIN) of the Atlanta Clinical & Translational Science Institute (ACTSI), which is a dietary analysis program designed for the collection and analysis of 24-hour dietary recalls. NDS-R provided a detailed analysis of macro- and micro-nutrient intake in units per day. The 24-hour food consumption recalls were either obtained by telephone or on subsequent routine visits to the clinic, by trained investigators.

Research Design

The design of the current study was cross-sectional and exploratory, intending to fully describe the nutrient intake of HIV-infected youth. The study protocol was approved by Emory University's Institutional Review Board (IRB FWA# 00005792; registration #s 569 & 570). This study analyzed the aforementioned data that was previously collected for the original study that examined vitamin D's role in cardiovascular health among 200 HIV-infected patients and 50 controls, ages 1-25. The original study specifically looked at inflammatory cytokines and endothelial activation markers, and the Block FFQ was used to assess vitamin D status.

The current study assessed nutrient intakes, using the 24-hour recalls that were collected and analyzed in NDS-R, and compared intakes to the DRIs, AMDRs, and the

recommendations by the American Heart Association for the prevention of CVD. The study used the same sample population as the original study including all subjects that completed at least two, 24-hour recalls. Subjects with less than two, 24-hour recalls collected were excluded. Also excluded were 24-hour recalls that were obvious outliers and the subjects were suspected of over- or under-reporting dietary intake for that specific recall (less than 500 kilocalories or greater than 5000 kilocalories in one 24-hour period). The recalls included in analysis were collected every 3 months for one year to capture seasonal changes in dietary intake, as well as day-to-day variation in diet. The micro- and macronutrient intakes of the 24-hour recalls were compared to the DRIs and AMDR given the age of the child or adolescent on the day of intake. DRI varies depending on age and gender. Percent of DRI was then determined based on the youth's IOM life stage group (age and gender) on the date of intake. The percent of DRI for each intake date was then averaged for each individual subject. The average micro- and macronutrient intake and percent DRI was the basis for all dietary analysis of this study. The IOM recommends using at least two, 24-hour recalls on nonconsecutive days to assess usual intake.[47]

Intake of all micro- and macronutrients were assessed to see if the participants were meeting the RDA, AI, or AMDR for each individual nutrient. The IOM[47] recommends comparing micronutrient intake to the Estimated Average Requirement (EAR) for the general population. However, the World Health Organization recommends that children and adults with HIV meet at least the Recommended Dietary Allowance (RDA);[16] therefore, intake of micronutrients were compared to the RDA. For those nutrients without an RDA, intake was compared to the Adequate Intake (AI). The mean

composition of macronutrient intake was compared to the AMDR.

The study population was separated into two groups: HIV-infected youth (HIV+) and HIV-negative controls (HIV-) with similar demographics. Calorie, BMI, waist-to-hip ratios, lipid profiles, and macro- and micronutrient intake were compared between the groups. Nutrient intake was also compared between race and gender. Furthermore, fat, fiber, trans fatty acids, saturated fatty acids, and cholesterol intake was compared to the recommendations of the American Heart Association. Fasting lipid levels, including total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides, were individually compared between groups and against standards of 200mg/dL, 130mg/dL, 40mg/dL, and 140mg/dL, respectively. Associations between nutrient intake and BMI, CD4+ counts, viral loads, and lipid profiles were analyzed.

Statistical analysis

Sample Size and Power Considerations: Table 1 provides power calculations for correlation.[48] Approximately **153** HIV-infected children provides 80% statistical power to a correlation coefficient of 0.20.

Table 1. Sample Size and Power to Determine the Effect of Diet (i.e., Saturated Fat, Trans Fat, Cholesterol, and Fiber) on Lipid Levels ($\alpha_1 = 0.05$)

Outcome	Power	Sample Size	Correlation Coefficient, r
Hyperlipidemia			
	.80	617	0.10
	.80	**153**	**0.20**
	.80	68	0.30
	.80	37	0.40
	.80	22	0.50

Descriptive statistics, such as mean ± SD, were used to describe micronutrient and macronutrient intake, as well as age, BMI, and lipid levels for both the HIV+ and HIV-

groups. Frequencies tables were used to describe gender, race, ART use, and deficient nutrient intakes. All variables were checked for normality. If variables were not normally distributed, log transformations were performed and normality was again assessed. If the variables were not normally distributed after log transformations, non-parametric tests were used for analysis. The subject's average intake was compared to the DRI using one-sample t-tests, comparing the % DRI of the deficient micronutrient intakes to a test value of 1.0 or 100% DRI. For between-group comparisons of nutrients, BMI, age, waist measurements, and lipids, normally distributed variables were compared using independent t-tests, and non-normally distributed variables were compared using Mann-Whitney U tests. Lipid levels (total cholesterol, LDL, HDL, and triglycerides) were compared to healthy standards using one-sample t-tests. One-way ANOVA and Bonferroni post-hoc comparisons were used to determine differences between race in nutrient intakes. Pearson's correlation coefficient (parametric) or Kendall's Tau (non-parametric) looked at the associations between nutrient intake and age, BMI, lipid levels and HIV-related factors. Additional regression analysis was not performed on correlations, as only weak associations were found. A P value < 0.05 was considered significant. SPSS 18.0 was used to analyze the data.

CHAPTER IV

RESULTS

A total of 674 24-hour recalls were analyzed. 558 recalls were analyzed for the HIV+ group and 113 recalls were analyzed for the control group. The HIV+ group had 75 subjects with 4 recalls (43% of subjects), 58 subjects with 3 recalls (33% of subjects), and 42 subjects with 2 recalls (24% of subjects). On average, there were 3.2 recalls per subject in the HIV+ group. The control group had 7 subjects with 4 recalls (16% of subjects), 13 subjects with 3 recalls (30% of subjects), 23 subjects with 2 recalls (53% of subjects). On average there were 2.6 recalls per subject in the control group.

Study Population

Upon excluding all subjects with less than two 24-hour recalls, 175 HIV-infected subjects and 43 healthy controls were included in the analysis. Subject characteristics are summarized in Table 1. Antiretroviral (ART) medication use is summarized in Figures 1 and 2, and perinatal infection frequencies are given in Figure 3.

Age was not normally distributed and could not be log transformed. Mann-Whitney U test showed that there was no significant difference between groups for age (P=0.688). The range of age for HIV-infected was 1.46 to 24.41 years. The age range for the controls was 5.5 years to 26.39 years.

Chi-squared tests were used to determine if there was a significant difference between groups for race and gender, as these are categorical variables. There was no significant difference in race (P=0.183) or gender (P=0.804) between the HIV+ group and the control group.

BMI was not normally distributed. Upon log transformation, BMI was normally distributed and an independent t-test showed that there was no significant difference in mean BMI between groups (P=0.716).

Waist-to-hip ratios were normally distributed and independent t-tests revealed no difference between the groups (P=0.124).

Table 1. Subject Characteristics

Mean ± SD or no. (%)		**HIV+ (n=175)**	**Controls (n=43)**	**P-value**
Age (Years)		17.44 ± 4.79	17.26 ± 6.14	0.688
Race	Black	166 (94.9%)	39 (90.7%)	0.183
	White	6 (3.4%)	4 (9.3%)	0.183
	Latino	3 (1.7%)	0 (0%)	0.183
Gender	Male	94 (53.7%)	24 (55.8%)	0.804
	Female	81 (46.3%)	19 (44.2%)	0.804
Body Mass Index (kg/m^2)		22.53 ± 5.72	22.16 ±5.17	0.813
Waist-to-Hip Ratio		0.85 ± 0.08	0.83 ±0.07	0.124

Figure 1.

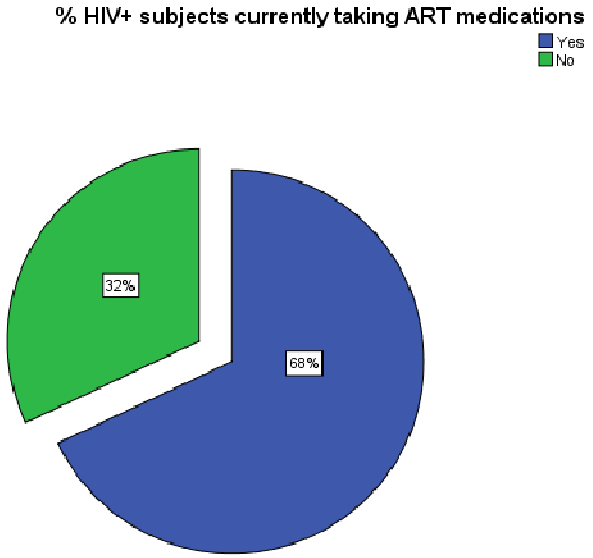


Figure 2.

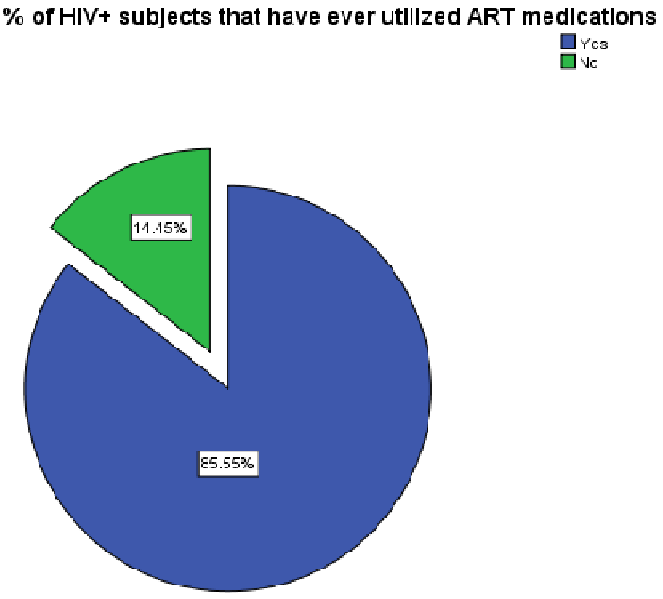
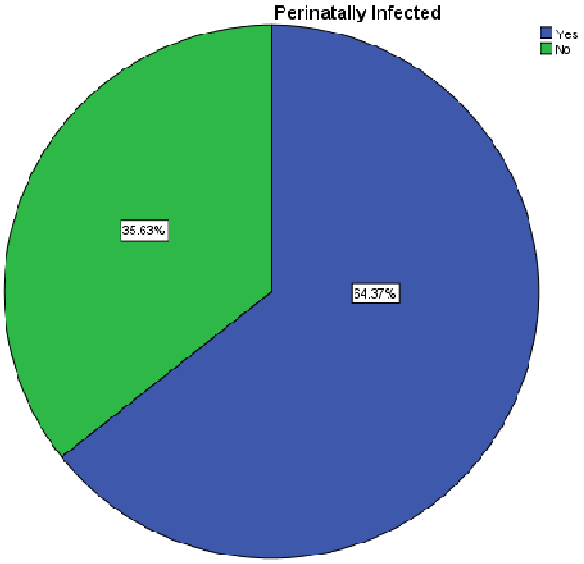


Figure 3.



Dietary Intake of HIV-infected Subjects and Controls

Energy intake is summarized in Table 2. Total calorie (energy) intake from the four 24-hour recalls, over the course of the study, was averaged for each subject. Energy intake was normally distributed; therefore, an independent t-test was used to calculate any difference in means between the HIV+ and HIV- group. There was no significant difference between groups in mean energy intake.

Table 2. Energy Intake

Mean ± SD	HIV+	HIV-	P-value
Energy (kcal)	1953.9 ± 610.87	1990 ± 540.8	0.723
Median Energy	1859 kcal	1997 kcal	

Micronutrient intake

A summary of the mean percent of DRI intake for the nutrients analyzed is presented in Table 3. For the nutrients analyzed, the DRIs recommended by the IOM are given in Table 4 for a reference. For the HIV-infected group, mean micronutrient intake was less than 100% of the DRI for vitamin A (77.61% ± 120), vitamin D (27% ± 21.25), vitamin E (54.05% ± 33.67), pantothenic acid (87.47%± 38.24), folate (96.81%± 48.27), calcium (57.57% ± 27.22), magnesium (63.72% ± 30.4), and potassium (39.49% ± 14.09). Mean intake of sodium (236.27% ± 83.08) was greater than the recommended DRI. For the HIV+ subjects, all variables were significantly different than the 100% DRI with P-values <0.001.

For the controls, micronutrient intake was less than 100% of the DRI for vitamin A (96.83%± 74.98)**,** vitamin D (35.96% ± 31.75), vitamin E (64.57% ±27.92), calcium (69.45% ± 30.68), magnesium (80.21%± 40.35), and potassium (44.95% ± 12.70), and greater than the recommended DRI for sodium (247.15% ± 74.3). All micronutrients

consumed suboptimally were significantly different than the 100% DRI with P-values<0.001. Median nutrient intake can be found in Table 4.

Macronutrient Intake

Mean percent calories from carbohydrate, fat, and protein fell within the acceptable macronutrient distribution range (AMDR) for the control group. Mean percent calories from carbohydrate and protein fell within the AMDR for the HIV+ group. Mean fat intake significantly exceeded the AMDR for HIV-infected subjects (36.02% ± 5.67, P=0.018) only. See Figure 4.

Table 3. Mean % DRI (RDA or AI) ± SD

	HIV-Infected (N=175)		**Controls (N=43)**	
	Mean Intake that Met DRI	Mean Intake That Did Not Meet DRI	Mean Intake That Met DRI	Mean Intake That Did Not Meet DRI
MICRONUTRIENTS				
Vitamin A		77.61%± 120		96.83%± 74.98
Vitamin D		27%± 21.25		35.96%± 31.75
Vitamin E		54.05%± 33.67		64.57%±27.92
Vitamin K *	115.04%± 120.9		152.68%± 146.03	
Vitamin C	127.8%± 109.39		170.35%± 110.79	
Thiamin	145.3%± 53.57		170.75%± 79.8	
Riboflavin	154.47%± 69.34		196.42%± 101.36	
Niacin	259.71%± 84.18		285.43%± 90.29	
Pantothenic Acid *		87.47%± 38.24	106.06%± 54.79	
B-6	142.99%± 58.77		162.19%± 64.81	
Folate		96.81%± 48.27	114.10%± 54.36	
B-12	208.35%±327.76		225.29%±177.97	
Calcium		57.57%± 27.22		69.45%± 30.68
Phosphorus	117.12%± 53.53		137.1%± 58.62	
Magnesium		63.72%±		80.21%± 40.35

		30.4		
Manganese *	114.84%± 53.57		132.97%± 48.87	
Iron	126.63%± 69.72		131.21%± 66.78	
Zinc	108.33%± 46.89		111.72%± 41.63	
Copper	133.67%± 174		151.89%± 95.56	
Selenium	206.61%± 77.5		228.41%± 85.83	
Sodium *		236.27%± 83.08		247.15%± 74.3
Potassium *		39.49%± 14.09		44.95%± 12.70
MACRONUTRIENTS				
	Intake Within AMDR	**Intake Exceeds AMDR**	**Intake Within AMDR**	**Intake Exceeds AMDR**
Mean % kcal from FAT		36.02%± 5.67	33.8%± 5.07	
Mean % kcal from CHO	48.16%± 7.02		51.03%± 5.57	
Mean % kcal from PRO	15.65%± 3.55		14.87%± 2.6	
AMERICAN HEART ASSOCIATIONS RECOMMENDATIONS				
	Met	**Did not meet**	**Met**	**Did not meet**
Mean % kcal from saturated fat (% of 7% recommendation)		11.55% ± 2.3 (165.01%± 32.8)		11.12%± 2.18(158.8%± 31.1)
Mean % kcal from TRANS- fat (% of 1% recommendation)		1.45%± 0.55 (145.10%)		1.15%± 0.57 (115%)
Cholesterol (% of 300mg)	84.97%± 45.03		87.67%± 43.56	
Fiber (% of recommended intake (14g/1000kcal))		43.3% ± 13.7		48.81%± 15.67
*** Denotes micronutrient with adequate intake (AI) instead of an RDA**				

Table 4. DRIs of Nutrients Analyzed: Recommended Dietary Allowances, Adequate Intakes, and Acceptable Macronutrient Distribution Ranges[37]								
	Children		Males			Females		
Nutrients	1-3y	4-8y	9-13y	14-18y	19-30y	9-13y	14-18y	19-30y
MICRONUTRIENTS								
Vitamin A (µg/d)	300	400	600	900	900	600	700	700
Vitamin D (µg/d)	15	15	15	15	15	15	15	15
Vitamin E (mg/d)	6	7	11	15	15	11	15	15
Vitamin K* (µg/d)	30	55	60	75	120	60	75	90
Vitamin C (mg/d)	15	25	45	75	90	45	65	75
Thiamin (mg/d)	0.5	0.6	0.9	1.2	1.2	0.9	1.0	1.1
Riboflavin (mg/d)	0.5	0.6	0.9	1.3	1.3	0.9	1.0	1.1
Niacin (mg/d)	6	8	12	16	16	12	14	14
Pantothenic Acid * (mg/d)	2	3	4	5	5	4	5	5
B-6 (mg/d)	0.5	0.6	1.0	1.3	1.3	1.0	1.2	1.3
Folate (µg/d)	150	200	300	400	400	300	400	400
B-12 (µg/d)	0.9	1.2	1.8	2.4	2.4	1.8	2.4	2.4
Calcium (mg/d)	700	1000	1300	1300	1000	1300	1300	1000
Phosphorus (mg/d)	460	500	1250	1250	700	1250	1250	700
Magnesium (mg/d)	80	130	240	410	400	240	360	310
Manganese * (mg/d)	1.2	1.5	1.9	2.2	2.3	1.6	1.6	1.8
Iron (mg/d)	7	10	8	11	8	8	15	18
Zinc (mg/d)	3	5	8	11	11	8	9	8
Copper (µg/d)	340	440	700	890	900	700	890	900
Selenium (µg/d)	20	30	40	55	55	40	55	55
Sodium * (g/d)	1.0	1.2	1.5	1.5	1.5	1.5	1.5	1.5
Potassium * (g/d)	3.0	3.8	4.5	4.7	4.7	4.5	4.7	4.7
MACRONUTRIENTS: Acceptable Macronutrient Range (% of kilocalories)								

Fat	30-40	25-35	20-35	25-35	20-35
Carbohydrate	45-65				
Protein	5-20	10-30	10-35	10-30	10-35
*** Denotes micronutrient with adequate intake (AI) instead of an RDA**					

Table 5. Dietary Median Intake for the HIV+ and Control Groups

	HIV+			Controls		
	Percentiles			Percentiles		
	25	Median	75	25	Median	75
MICRONUTRIENTS (% DRI)						
PercentDRI_A	*37.41%*	*58.61%*	*81.43%*	*54.07%*	*77.22%*	*110.99%*
PercentDRI_D	*12.41%*	*21.44%*	*36.36%*	*16.69%*	*27.46%*	*46.98%*
PercentDRI_E	*33.40%*	*45.00%*	*65.19%*	*43.21%*	*63.15%*	*78.32%*
PercentDRI_K	*48.59%*	*74.61%*	*129.76%*	*62.09%*	*96.47%*	*148.06%*
PercentDRI_C	*53.58%*	*97.50%*	*182.03%*	*93.01%*	*136.27%*	*211.44%*
PercentDRI_Thiamin	*107.69%*	*139.33%*	*179.13%*	*118.77%*	*151.64%*	*198.23%*
PercentDRI_Riboflavin	*112.21%*	*138.08%*	*179.73%*	*122.88%*	*154.99%*	*230.33%*
PercentDRI_Niacin	*200.73%*	*252.31%*	*314.30%*	*232.28%*	*272.68%*	*339.92%*
PercentDRI_Pantothenic Acid	*62.20%*	*79.59%*	*103.09%*	*72.55%*	*95.16%*	*111.00%*
PercentDRI_B6	*105.08%*	*130.00%*	*173.48%*	*116.81%*	*154.29%*	*190.04%*
PercentDRI_Folate	*66.88%*	*88.33%*	*114.61%*	*71.98%*	*103.34%*	*138.04%*
PercentDRI_B12	*97.93%*	*155.46%*	*213.56%*	*129.72%*	*174.83%*	*296.38%*
PercentDRI_Calcium	*40.15%*	*53.44%*	*67.88%*	*52.79%*	*57.58%*	*73.84%*
PercentDRI_Phosphorus	*80.86%*	*107.88%*	*143.16%*	*89.51%*	*119.82%*	*167.97%*
PercentDRI_Magnesium	*43.05%*	*55.81%*	*73.34%*	*48.00%*	*68.81%*	*102.31%*
PercentDRI_Manganese	*80.07%*	*104.96%*	*130.88%*	*89.45%*	*124.25%*	*166.39%*
PercentDRI_Iron	*72.87%*	*115.70%*	*162.75%*	*68.96%*	*124.14%*	*164.18%*
PercentDRI_Zinc	*75.93%*	*100.49%*	*129.35%*	*77.93%*	*102.80%*	*137.48%*
PercentDRI_Copper	*82.56%*	*107.89%*	*140.83%*	*98.16%*	*133.67%*	*177.16%*
PercentDRI_Selenium	*149.26%*	*199.33%*	*251.20%*	*163.85%*	*222.59%*	*276.05%*
PercentAI_Sodium	*178.12%*	*219.26%*	*285.18%*	*196.06%*	*239.12%*	*282.98%*
PercentDRI_Potassium	*29.62%*	*37.11%*	*47.14%*	*35.66%*	*45.66%*	*54.03%*
MACRONUTRIENTS (% of kcals)						
Percent_KCal_from_CHO	*43.51*	*48.09*	*53.56*	*47.72*	*51.98*	*53.85*
Percent_KCals_from_PRO	*13.48*	*15.02*	*17.89*	*13.09*	*14.66*	*16.20*

Percent_KCals_from_SFA	***9.99***	***11.34***	***12.84***	***10.13***	***10.91***	***12.20***
Percent_KCals_from_Fat	***32.24***	***35.93***	***39.79***	***31.57***	***33.87***	***36.60***
Percent_KCalsfrom TransFat	***1.03%***	***1.35%***	***1.77%***	***0.81%***	***0.97%***	***1.36%***
OTHER (% of recommendation)						
PercentDRI_Cholesterol	***52.78%***	***74.70%***	***111.91%***	***62.57%***	***79.36%***	***107.26%***
Percent_Recommended_Fiber	***34.33%***	***41.06%***	***49.24%***	***35.97%***	***46.39%***	***58.76%***

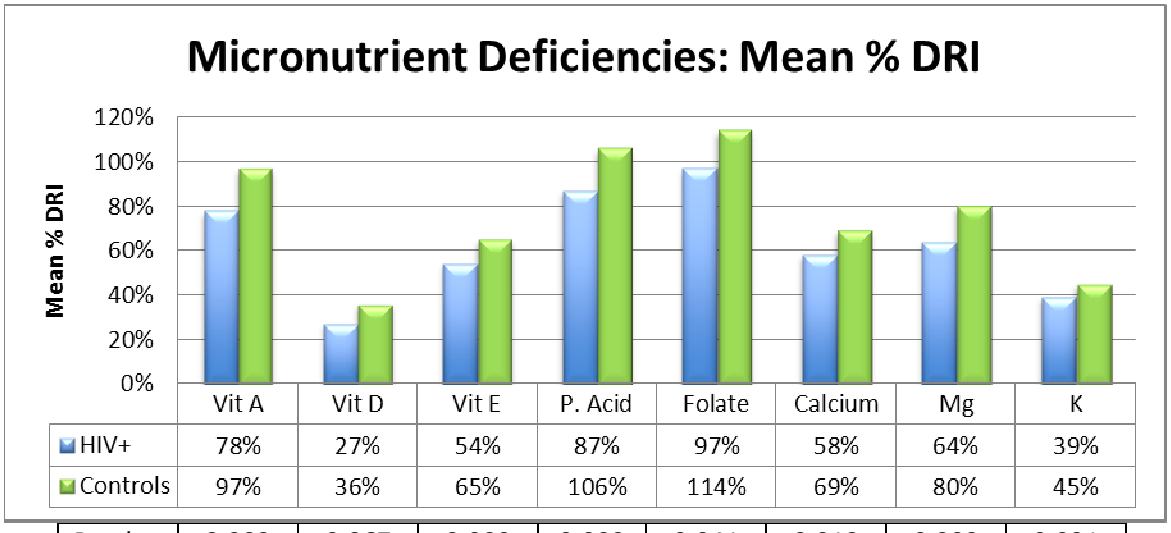
Table 6. Frequencies of Subjects with Suboptimal Nutrient Intake		
	Controls (n=43)	HIV+ (n=175)
Fiber	43 (100%)	174 (99.4%)
Vitamin A	29 (67.4%)	144 (82.3%)
Vitamin D	41 (95.3%)	173 (98.9%)
Vitamin E	40 (93.0%)	163 (93.1%)
Calcium	37 (86%)	162 (92.6%)
Magnesium	32 (74.4%)	152 (86.9%)
Potassium	43 (100%)	175 (100%)
Pantothenic Acid	27 (62.7%)	127 (72.6%)
Folate	20 (46.5%)	107 (61.1%)
Prevalence of excess nutrient intake above the recommended intake		
Sodium	43 (100%)	174 (99.4%)
Saturated Fat	42 (97.7%)	174 (99.4%)
Trans Fat	18 (41.9%)	140 (80.0%)

Intake Differences Between Groups

Comparisons between groups of nutrient intakes were done using independent t-tests of the mean percent DRIs. Cholesterol, vitamin A, D, E, K, C, thiamin, riboflavin, pantothenic acid, B-12, copper, and percent of recommended trans fats were log transformed to approach Normality. The HIV+ group had a significantly lower mean percent DRI for fiber (-5.5%, P=0.023), folate (-17.3%, P=0.041), calcium (-11.9%, P=0.013), vitamin A (-19.2%, P=0.003), vitamin E (-10.5%, P=0.009), vitamin K (-37.6%, P=0.038), vitamin C (-42.6%, P=0.003), thiamin (-25.45%, P=0.029), riboflavin

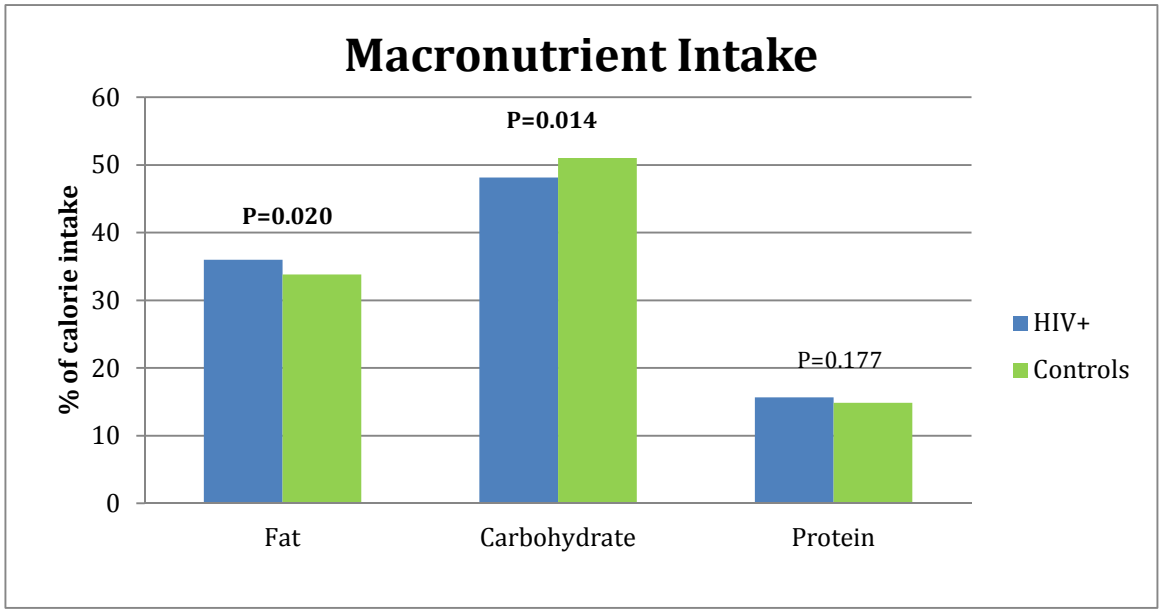
(-42%, P=0.002), pantothenic acid (-18.6%, P=0.009), copper (-18.2%, P=0.048), phosphorus (-20%, P=0.033), magnesium (-16.5%, P=0.003), manganese (-18.1%, P=0.044), potassium (-5.5%, P=0.021). The HIV+ group had significantly higher % calories from fat (8.1%, P=0.020) and % calories from trans fat (0.3%, P<0.001), and significantly lower % calories from carbohydrate (-2.9%, P=0.014). See Figure 5 and 6. Figure 4 summarizes the suboptimal micronutrient intake of the HIV+ group, and the differences from the control group.

Figure 4. HIV+ Micronutrient Intake Deficiencies: Differences Between Groups in Mean % DRI intake.



	Vit A	Vit D	Vit E	P. Acid	Folate	Calcium	Mg	K
HIV+	78%	27%	54%	87%	97%	58%	64%	39%
Controls	97%	36%	65%	106%	114%	69%	80%	45%
P-value	0.003	0.067	0.009	0.009	0.041	0.013	0.003	0.021

Figure 5. Differences Between Groups in Macronutrient Distribution.



Comparisons to The American Heart Association Recommendations

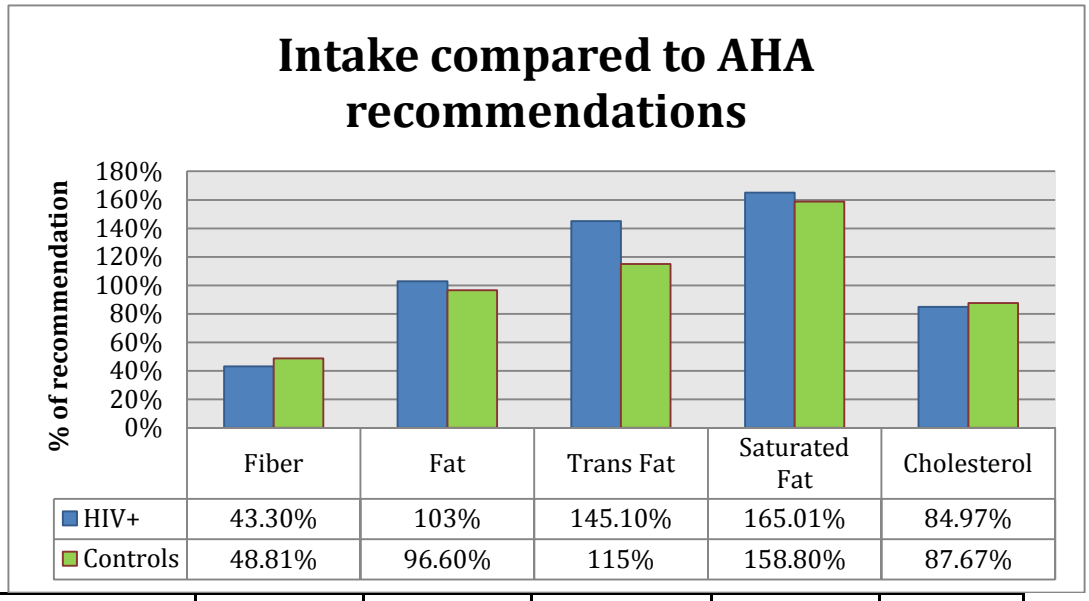
The intake of the HIV+ and the control group were compared to the AHA recommendations using independent t-tests for fiber and one-sample t-test for fat, saturated fat, trans fat, and cholesterol. See Figure 6.

The control group had significantly less fiber intake than the AHA recommendation of 14g per 1000 kilocalories (mean difference=-14.56g, P<0.001), significantly more saturated fat intake than the AHA 7% recommendation (mean difference=4.12%, P<0.001), and significantly more trans fat intake than the AHA 1% recommendation (mean difference=0.15%, P<0.001). Fat intake for the controls fell within the recommended range, but not significantly (-1.2%, P=0.128). Cholesterol intake was less than the recommended intake, but not significantly (-36.98g, P=0.070).

The HIV+ group had significantly less fiber intake than the AHA recommendation (mean difference= -15.7g, P<0.001). Fiber was log transformed to

approach normality. Mean percent calories from saturated fat was significantly higher than the 7% recommendation (mean difference=4.55%, P<0.001). Mean percent calories from fat was significantly higher than the 35% upper range recommendation (mean difference 1.02%, P=0.018). Mean percent calories from trans fats was significantly greater than the AHA recommendation of 1% (mean difference=0.45%, P<0.001). Cholesterol intake was significantly within the recommended intake of 300mg (mean=254.9mg, P<0.001).

Figure 6. Differences Between Mean % Intake of AHA recommendation.



P-value b/w groups	**0.023**	**0.020**	**<0.001**	0.263	0.638	
P-value from recommendation	**<0.001**	**0.018**	**<0.001**	**<0.001**	**<0.001***	HIV+
	<0.001	0.128*	**<0.001**	**<0.001**	0.070*	Control

*Met AHA recommended intake

Nutrient Intake and Correlations with Subject Characteristics and HIV-factors

Nutrient intake and associations with HIV + subject characteristics

Nonparametric correlations (Kendall's tau) were performed to find associations between BMI and nutrient intakes, as well as age and nutrient intakes, in the HIV+ group. As would be expected, calorie intake was positively associated with age (r=0.152, P=0.003). BMI is negatively correlated with percent DRI of vitamin A (r=-0.135, P=0.008), vitamin D (r=-0.108, P=0.034), vitamin E (r=-0.179, P<0.001), riboflavin (r=-0.201, P<0.001), thiamin (r=-0.184, P<0.001), niacin (r=-0.162, P=0.002), pantothenic acid (r=-0.146, P=0.004), vitamin B6 (r=-0.173, P=0.001), folate (r=-0.190, P<0.001), vitamin B12 (r=-0.129,P=0.012), magnesium (r=-0.229, P<0.001), iron (r=-0.122, P=0.017), zinc (r=-0.179, P<0.001), copper (r=-0.210, P<0.001), potassium (r=-0.110, P=0.032), and selenium (r=-0.163, P=0.001). There was a positive correlation between age and intake of phosphorus (r=0.253, P<0.001), sodium (r=0.113, P=0.027), and fat (r=0.122, P=0.017).

Nutrient intake differences between genders, in the HIV+ group, were compared using independent t-tests. For the suboptimal micronutrient intake, Vitamins A, D, E, pantothenic acid, folate, and magnesium were log transformed to approach Normality. Potassium and calcium did not need to be log transformed. Females had significantly lower mean % DRI for folate (-0.184%, P=0.004), pantothenic acid (-0.182%, P=0.000), vitamin D (-0.09%, P=0.002), calcium (-0.17%, P<0.001), potassium (-0.085%, P<0.001), and calories (-387 kcal, P<0.001).

To determine significant differences in mean suboptimal nutrient intakes between races in the HIV+ group, one-way ANOVA and Bonferroni post-hoc comparisons were

performed for each nutrient. Caucasians had significantly greater mean % DRI of vitamin D intake than African Americans (26.2%, P=0.027). Latinos had significantly lower mean percent fat intake from calories compared to blacks (-10.8%, P=0.003) and Caucasians (-10.1%, P=0.031). Mean percent DRI for calcium intake was significantly lower in African American than in Caucasians (-31.2%, P=0.017).

Nutrient intake and CD4+ count correlations

To determine if nutrient intake was associated with CD4+ counts, correlations were performed. The current, nadir, and change in CD4+ counts were not normally distributed and could not be log transformed; therefore, Kendall's Tau nonparametric correlations were performed.

Amongst all HIV+ subjects, calorie intake was negatively correlated with the current CD4+ (r=-.116, P=0.024) and nadir CD4+ (r=-0.105, P=0.041). The percent of DRI of vitamin A was positively associated with nadir CD4+ count (r=0.102, P=0.047). The percent DRI zinc was positively associated with current CD4+ count (r=0.128, P=0.013), as was the percent DRI of riboflavin (r=0.120, P=0.019), and the percent DRI of magnesium (r=0.141, P=0.006).

When looking at only those on ART, riboflavin intake was positively associated with CD4 nadir (r=0.129, P=0.033), as was B12 intake (r=0.122, P=0.044). Current CD4+ was positively associated with magnesium (r=0.140, P=0.020) and zinc intake (r=0.188, P=0.050).

When looking at those not on ART, there were no significant correlations with CD4+ counts.

For subjects on ART for greater than 6 months that have a viral load less than 1000, there were no significant associations between nutrient intakes and CD4+ change. CD4+ nadir was positively associated with B12 intake (r=0.144, P=0.036) in these specific subjects, as it was in all subjects on ART. Current CD4+ was positively associated with magnesium intake (r=0.148, P=0.030). Calorie intake was negatively associated with both current CD4+ (r=-0.153, P=0.025) and nadir CD4+ (r=-0.136, P=0.049). No other significant correlations were found.

Nutrient intake and viral load correlations in subjects not on ART

In subjects not on ART, viral load was only significantly negatively correlated with protein intake (r=-0.296, P=0.046).

Lipid Profiles

When comparing fasting lipid levels to the healthy standards (TC <200mg/dL, LDL-C < 130mg/dL, HDL-C > 40mg/dL and triglycerides < 140mg/dL), both the control and HIV-infected groups were significantly within the healthy range. Triglycerides and LDL-C were log transformed to normality for the control group. Triglycerides were log transformed to normality for the HIV+ group.

Table 7. Fasting Lipid Levels Compared to Healthy Standards

One-Sample T-test				
	Standard (mg/dL)	**Mean Difference**	**Sig.**	**95% CI**
HIV-Infected				
TC	200	-44.905	0.000	-50.81, -39.00
LDL	130	-35.450	0.000	-39.40, -31.50
HDL	40	3.988	0.001	1.59, 6.39
TG	140	-56.018	0.000	-64.15, -47.89
Controls				
TC	200	-49.326	0.000	-59.01, -39.64
LDL	130	-41.140	0.000	-51.00, -33.28

HDL	40	11.163	0.000	7.16, 15.17
TG	140	-81.442	0.000	-88.75, -74.13

Table 8. Prevalence of Dyslipidemia: Subjects with High TC, LDL-C, TG, or Low HDL-C		
No. (%)	Controls	HIV+
TC	4 (3%)	21 (11.8%)
LDL-C	4 (3%)	14 (7.9%)
HDL-C	7 (5.3%)	78 (43.8%)
TG	1 (0.8%)	16 (9%)

There were no significant differences between groups for TC and LDL-C. See Table 9. HDL-C and triglycerides were not normally distributed and were log transformed to create a normal distribution. Independent t-tests of the log transformations revealed significant differences between the HIV-infected and the control groups. HDL-C was significantly lower in the HIV-infected group (-7.163mg/dL, P=0.001). Triglycerides were significantly higher in the HIV-infected group (25.795mg/dL, P=0.001). Differences within the HIV-infected group between those taking ART and those not taking ART are in Table 10.

Table 9. Mean Lipid Profiles in Fasting State.

Mean ± SD	**HIV+ (n=175)**	**Controls (n=43)**	**P-value**
Total Cholesterol (mg/dL)	155.29 ±38.929	150.67 ± 31.471	0.473
LDL-Cholesterol (mg/dL)	94.66 ± 26.217	87.86 ± 28.779	0.138
HDL-Cholesterol (mg/dL)	44.1 ± 15.923	51.16 ± 13.009	0.001
Triglycerides (mg/dL)	84.35 ± 53.8	58.56 ± 23.757	0.001

Table 10. Differences in Mean Serum Lipids Between HIV-infected on ART vs. Not on ART

	ART	Mean	Std. Deviation	P-value
TC	Currently taking ART	163.4959	38.90568	**0.000**
	Not currently taking ART	134.1702	30.33746	
LDL-C	Currently taking ART	98.6885	25.01672	**0.001**

	Not currently taking ART	84.4167	26.66325	
HDL-C	Currently taking ART	47.1148	16.80132	**0.000**
	Not currently taking ART	36.0833	9.78673	
TG	Currently taking ART	88.6311	58.77316	0.160
	Not currently taking ART	73.4792	36.69598	

Nutrient Intake and Lipid Profile Correlations

Pearson's correlation coefficient was used to calculate the strength and significance of correlations between the nutrients focused on by the AHA (fat, saturated fat, trans fat, cholesterol and fiber) and serum lipid measures (TC, LDL-C, HDL-C, TG). Variables were independent and any non-normal variables were log-transformed to approach Normality.

The HIV-positive group results are in table 11. There was a positive correlation between fiber intake and serum triglycerides (r=0.157, P=0.041) and trans fat intake and serum LDL-C (r=0.158, P=0.040). There was a negative correlation between total fat intake and serum triglycerides (r=-0.170, P=0.027).

The control group results are in table 12. There was a positive correlation between cholesterol intake and serum triglyceride levels (r=0.315, P=0.040).

Table 11. HIV+: Correlations Between Nutrient Intake and Lipid Profiles

	Correlation	TC	LDL-C	HDL-C	Triglycerides
Fiber (% of rec)	**r**	0.097	0.001	0.116	**0.157**
	P-value	0.210	0.987	0.131	**0.041**
Cholesterol (avg mg)	**r**	-0.019	0.066	-0.068	-0.080
	P-value	0.805	0.391	0.378	0.303
% kcal from Fat	**r**	0.033	0.067	0.060	**-0.170**
	P-value	0.672	0.383	0.438	**0.027**
% kcal from SF	**r**	-0.038	-0.007	-0.030	-0.100
	P-value	0.623	0.923	0.702	0.193
% kcal from Trans Fat	**r**	0.115	**0.158**	-0.090	0.119
	P-value	0.136	**0.040**	0.245	0.122

Table 12. Controls: Correlations Between Nutrient Intake and Lipid Profiles

	Correlation	TC	LDL-C	HDL-C	Triglycerides
Fiber (% of rec)	**r**	-0.117	-0.205	0.148	0.001
	P-value	0.455	0.187	0.344	0.993
Cholesterol (avg mg)	**r**	0.077	0.080	-0.064	**0.315**
	P-value	0.623	0.608	0.685	**0.040**
% kcal from Fat	**r**	0.079	0.114	-0.078	-0.049
	p-value	0.616	0.468	0.619	0.753
% kcal from SF	**r**	0.101	0.152	-0.153	0.163
	P-value	0.520	0.332	0.326	0.296
% kcal from Trans Fat	**r**	-0.014	0.009	0.033	-0.144
	P-value	0.931	0.954	0.833	0.356

CHAPTER V

DISCUSSION AND CONCLUSION

Suboptimal Micro- and Macronutrient Intake in HIV-infected Subjects

Micronutrients

Diet was analyzed using at least two, nonconsecutive, 24-hour food recalls, which is recommended by the IOM when analyzing dietary intake.[47] This study showed the intake of 61%-100% of the HIV-infected youth did not meet dietary guidelines for vitamins A, D, E, pantothenic acid, folate, calcium, magnesium, potassium, and sodium. Mean intake for these nutrients was significantly lower, or in the case of sodium higher, than the DRI.

Most studies used different methodologies to determine adequate nutrient intake, therefore caution must be taken before making direct comparisons between studies. Kruzich and colleagues[42] also found suboptimal vitamin A and E intake among 13-38% of HIV-infected adolescents; however, the less stringent Estimated Average Requirement (EAR) was used to assess adequate nutrient intake. The EAR is the nutrient intake amount that is expected to meet the needs of only half of the healthy population.[28] The IOM[47] recommends comparing intake to the EAR for the general population. However, the World Health Organization recommends that children and adults with HIV meet at least the RDA;[16] therefore, our study compared mean intake of nutrients to the RDA. Zinc intake did not meet requirements in the Kruzich and colleagues' study,[42] but that was not the case in this study with mean zinc intake reaching 108% of the DRI for the

HIV+ group. Zuin et al.[41] only assessed intake of 4 nutrients using 3-day food diaries, but similarly found that calcium intake was well below the RDA in HIV-infected children. They also found poor dietary iron intake, which was not supported by our study.

Vitamin D, calcium, potassium, and vitamin E were the micronutrients consumed in the lowest amounts (HIV+: mean <60% of the DRI), and sodium intake was exceedingly excessive (HIV+=236% of AI). Proper intake of these micronutrients is vital for optimal health. Vitamin D and calcium are important for proper bone growth in our adolescent population,[49] and research suggests that low serum vitamin D is associated with CVD risk factors in US children and adolescents.[50] Due to the already increased risk factors for CVD in the HIV-infected population,[13,38,43,44] vitamin D intake is of even greater importance. In fact, studies on HIV-infected adults have shown associations between vitamin D status and markers for CVD, as well as immune function.[51,52] Consuming adequate potassium and staying within recommendations for sodium intake can help regulate blood pressure, an important factor in reducing CVD risk.[12] Furthermore 95% of our study population was African American, which is a race particularly sensitive to the effects of these key nutrients on blood pressure and cardiovascular problems.[12] The effects of these nutrients on the blood pressure of this study population should be explored in future studies. Vitamin E is important for immune function[42] and is an antioxidant that protects against oxidative damage, which is increased in HIV-infected individuals.[30] Stephensen et al.[30] concluded that HIV-infected youth have a greater need for vitamin E, as well as C, yet our HIV-study population is only consuming 54% of the vitamin E DRI for healthy individuals.

Macronutrients

The recommendation on the macronutrient breakdown of protein, carbohydrate and fat does not differ for the HIV-infected individual.[4,16,31,36] Protein and carbohydrate intake was sufficient and fell within the recommended AMDR for both groups. Past research shows consuming adequate protein is not a concern for HIV-infected youth. The dietary intake of all of the children studied by Zuin and associates[41] exceeded the RDA for protein. Henderson and colleagues[4] found the mean protein intake was 200% of the RDA among 38 HIV+ children, and Sharma et al.[32] found that mean protein intake ranged between 160-378% of the RDA in 126, HIV-infected 3-20 year olds.

The HIV-infected youth in this study had a mean percent fat intake from kilocalories that exceeded the recommendations, while the control group's intake remained within the AMDR. In Brazil, Tremeschin and colleagues[13] also found fat intake exceeded the AMDR (38.5% of kilocalories), but did not find any difference between the HIV-infected youth and the controls. Mean percent fat from kilocalories for the HIV-infected group in our study was significantly above the AMDR range maximum of 35%.

Intake Differences Between HIV-infected and Healthy Subjects

Analysis of the food recalls also shows HIV-infected youth present with poorer micro- and macronutrient intake compared to healthy controls despite similarities in caloric intake. The HIV+ group had significantly lower dietary folate, calcium, vitamin A, E, K, C, thiamin, riboflavin, pantothenic acid, copper, phosphorus, magnesium, manganese, and potassium intake. Some researchers[35] believe that adequate intake of these vitamins and minerals contribute to the slowing of HIV progression due to their

antioxidant effects and ability to reduce oxidative stress. Oxidative stress is considered as an important factor in the pathogenesis of the HIV disease.

Furthermore, the HIV+ group had significantly higher percent calories from fat and lower percent calories from carbohydrate compared to the control group. Alternatively, most studies did not find differences in nutrient intakes between the infected and the healthy children and adolescents.[4,13,32,41,42] The REACH study[7] did find that macronutrient intake was poorer in the HIV-positive group of adolescents due to higher intakes of fat, saturated fat and cholesterol compared to the non-infected controls.

Nutrient Intake Associations with HIV-Related Factors

Overall, research suggests that sufficient micronutrient status may contribute to improved immune status and survival in HIV-infected individuals. Baum and colleagues[24] found that as serum vitamin A, B-12, and zinc status improved, CD4+ cell counts increased in adult HIV-infected males. We found similar associations with the intake of these nutrients in our cohort of male and female youth. Percent DRI of vitamin A was positively correlated with nadir CD4+ count, and the percent DRI for zinc was positively associated with current CD4+ count, amongst all HIV-infected subjects. Dietary intake of riboflavin and magnesium was also positively associated with current CD4+ count, although similar correlations were not found in other studies. When we analyzed only subjects on ART medication, B-12 intake was also associated with CD4+ nadir, which supports the findings by Baum and colleagues.[24] Other studies also found similar associations between HIV progression biomarkers and serum B-12.[26] Furthermore in one of the few studies looking at children, Steenkamp and colleagues[19] found ART naïve children with abnormally low serum levels of zinc and vitamin A had

significantly lower CD4+ cell counts and higher viral loads. While analysis of our entire HIV cohort saw associations with zinc and vitamin A intake and CD4+ counts, in our subjects not on ART, viral load was only significantly negatively correlated with dietary protein intake. Therefore, we did not find evidence that adequate micronutrient intake was able to keep viral load down when ART medication was not being used. On the other hand, adequate protein intake in those HIV-infected youth not on ART may be important.

Unfortunately, all aforementioned studies assessed serum levels and not dietary intake, but it is worth noting similarities in correlations. Further investigation is warranted to determine whether nutrient intake data correlate with plasma nutrient concentrations in HIV+ youth and the potential impact of nutritional status on immune function and HIV progression. In studies of HIV-infected adults, correlations were found between serum concentrations and dietary intake of B-12,[26] vitamin A, and zinc,[24] which may be relevant for the associations found in our study.

Few studies have looked at correlations between dietary intake of nutrients and HIV-factors. In a study[27] of HIV-infected men that evaluated dietary intake, the researchers found that increased intake of zinc was associated with the progression of HIV and decreased CD4+ cell count, which we did not find. Kruzich and colleagues[42] found no associations between nutrient intakes and CD4+ cell counts.

In our study, kilocalories were negatively correlated with the current and nadir CD4+, suggesting that as our subjects increased their dietary caloric intake their immune status worsened. While it was a weak correlation, it was still significant. Previous studies looking at caloric intake associations found no significant associations with CD4 category, progression to AIDS,[27] or mortality.[21] However, these previous studies used

semi quantitative food frequency questionnaires and were done prior to the introduction of ART. The IOM recommends using at least two, 24-hour recalls on nonconsecutive days to assess usual intake,[47] as opposed to food frequency questionnaires, which is one of the strengths of our study. Likewise, we also saw a higher BMI was associated with poorer intake of most nutrients, which hint at poor diet choices among those with higher BMIs, since calorie intake showed no association with BMI. No additional regression analysis was performed due to the weak association, and to our knowledge this has not been assessed in prior studies. Additional studies should investigate this association.

When looking only at subjects on ART for greater than 6 months that have a viral load of less than 1000, there were no significant associations between nutrient intakes and CD4+ change. One might conclude that improved dietary intake did not contribute towards improvements in CD4+, or HIV-status; however, this information would be more useful if the study assessed nutrient intake and CD4+ count together at different points in time. This study only looked at average nutrient intake over the year and associations with CD4+ change that took place prior to the collection of food recalls.

CVD Risk Factors

Chronic infection and inflammation in HIV-infected individuals seems to increase atherosclerotic processes, including lipid abnormalities, lipodystrophy, and vascular structural changes in children infected with HIV, which are critical risk factors for CVD.[13,38,43,44] Our cohort of youth was less affected by lipodystrophy and dyslipidemia. Waist-to-hip ratios, one indicator of lipodystrophy, in our HIV-infected cohort were similar to healthy controls. However, lipodystrophy is better diagnosed by fat

redistribution, for instance visceral fat accumulation, and would be better assessed by looking at changes in waist-to-hip ratios over time.[13, 38] Furthermore, assessment of lipodystrophy is complicated due to growth;[38] therefore, any assessment done in a youth cohort would need to be treated with caution.

Mean lipid profiles were within healthy ranges for both groups, suggesting dyslipidemia is not a concern in this population. However, the HIV-infected group did have significantly higher mean triglycerides and significantly lower mean HDL-C. The prevalence of dyslipidemia among the HIV-infected youth was higher than healthy controls with 11.8% having high TC (controls=3%), 7.9% with high LDL-C (controls=3%), 9% with high TG (controls=0.8%), and 43.8% with low HDL-C (controls=5.3%). Other studies found similar results, including a study of a cohort of 94 children ages 1 through 18 that found 62% of the subjects on PI had dyslipidemia.[44] In a London study,[10] it was determined that 10% of children on ART required hyperlipidemia intervention. In contrast, Tremeschin and colleagues[13] found no statistical differences, among 4-17 year olds, in hyperlipidemia between the HIV-infected and control groups, aside from increased serum triglycerides in those subjects on PI. Our study did not assess differences in lipid values between those on PI versus other ART drugs, but did similarly find the HIV-infected group had higher triglyceride levels compared to the controls.

In the current study, TC and LDL-C was significantly higher in those HIV-infected youth on ART compared to those not currently on ART. Surprisingly, HDL-C was also significantly higher in those HIV-infected youth on ART, which suggests HDL-C may be offsetting some of the negatives associated with higher TC and LDL-C in this group.

Several risk factors for CVD were studied in 83 HIV-infected children in London.[43] Similar to our study, mean serum triglycerides were significantly higher and mean serum HDL-C was significantly lower in the HIV-infected children compared to the controls. This study also looked at vasculature in the groups and determined that the common carotid artery's IMT was significantly higher in the HIV infected children and FMD of the brachial artery was lower, showing this groups increased risk for atherosclerosis and CVD.

Considering the mean BMI, our HIV-positive group would not be categorized as overweight or obese, which is in contrast to findings of other studies in which the majority of the cohort was found to be overweight.[7] This suggests that our cohort may be in less danger of developing risk factors associated with CVD, and may also explain why mean lipid values fell within healthy standards.

Intake Compared to Recommendations for a Heart Healthy Diet

Given the research showing HIV-infected individual's increased risk factors for CVD, it is important to know whether HIV-infected youth follow a heart healthy diet, and if the intake of certain lipids and fiber influence nutritional markers of CVD. Research[38] suggests HIV-infected individuals with hyperlipidemia should limit fat intake to 30% of kilocalories, and the AND[36] suggests limiting trans fat, saturated fat and cholesterol intake to similar levels recommended by the AHA in these individuals. The AHA recommends total fat intake to be between 25 and 35% of total calories, saturated fat to be less than 7% of total calories, trans fats to be less than 1% of total calories, cholesterol to be less than 300mg per day, and to consume 14g of fiber per 1000 calories consumed per day, to reduce the risk of CVD.[19]

Our study revealed HIV-infected youth have poorer dietary intake compared to healthy youth due to greater intake of nutrients associated with increased risk of cardiovascular disease (i.e. fat and trans fat). The HIV-infected youth in this study had a mean percent fat intake from kilocalories that exceeded the AHA recommendation. In Brazil, Tremeschin and colleagues[13] also found fat intake exceeded the 35% recommendation. The same study found both HIV-infected and controls had excess intake of saturated fats, which is similar to what we found with both groups significantly exceeding the 7% recommendation and no significant difference between the groups (HIV+=11.55%; Controls=11.12%). Sharma et al.[32] also used 24-hour recalls to find their HIV-infected youth cohort had excess mean intake of saturated fat at greater than 12% of kilocalories.

Furthermore, our study revealed percent calories from trans fats significantly exceeded the 1% AHA recommendation in both HIV+ and controls, but the HIV+ group had significantly higher intake than the control group. Limiting saturated and trans fatty acids in the diet is associated with a lower risk of CVD, mostly due to its effects on LDL-C.[12]

Moreover, all but one subject between both groups did not meet fiber recommendations, and mean intake of fiber in both groups was significantly lower than the AHA's recommendation of 14g/1000kcal. The HIV+ group had significantly worse fiber intake than the control group. Increased dietary fiber, both insoluble and soluble, has been linked with lower CVD risk as well as decreased progression to CVD in high-risk individuals, such as the HIV-infected population.[12] In contrast to the REACH study,[7] dietary intake of cholesterol was within healthy recommendations for both groups.

Associations Between Diet and Lipid Profiles in HIV-infected Subjects

Pearson's correlation coefficients showed few weak associations between lipid profiles and intake of nutrients generally associated with altered serum lipids (fat, saturated fat, trans fat, cholesterol and fiber). It did show a positive correlation between fiber and serum triglycerides, which is unusual, but it was a very weak correlation and may be due to the majority of fiber intake being insoluble fiber; soluble fiber is generally associated with lower LDL-C. This study only looked a total fiber, and did not distinguish between soluble and insoluble.

In contrast to a study of adults with HIV by Barrios and colleagues,[11] we did not find a correlation between percent calories from fat and serum lipids in our cohort of HIV-infected youth, aside from a weak, positive relationship between trans fat intake and LDL-C. Surprisingly, as percent calories from fat increased, triglycerides decreased, but this was only a very weak association, and could not be explained. Shah et al.[40] also looked at correlations between lipid levels and specific nutrients and found trans fats were positively correlated with triglyceride levels. Moreover, soluble fiber intake was negatively correlated with total cholesterol, triglycerides, and non-HDL cholesterol. They did not find any associations between lipid levels and cholesterol and saturated fat intake. All previous studies assessing these correlations were in HIV-infected adults, and thus may not be applicable to our population. To our knowledge, these associations have not previously been explored in HIV-infected youths.

Study Limitations

While the relatively large sample size was a strength for this study, there were limitations. Often limitations arise when using 24-hour recalls, as they do with most methods used for assessing dietary intake. There was likely over- or under-reporting of food intake when collecting the 24-hour recalls from the youth or caregiver, and an evaluation of the over- or under-reporting would be valuable in determining the validity of the recalls. Also, some recalls were obtained by phone and may not have been as accurate as those obtained in the clinic. Additionally, the control group had fewer average recalls per subject, which could be a limitation since most of the controls only had 2 recalls while most of the HIV-infected youth had 4 recalls completed. This difference in recalls obtained from subjects was likely due to the ease of retrieving a 24-hour dietary recall from HIV-infected subjects since research investigators saw them in the clinic more for often for appointments.

The cross-sectional study design was also a limitation in that no cause and effect could be established from the associations found. Analysis of HIV-related factors and lipid levels with nutrient intakes in a sequential manner may have provided a causal link.

Furthermore, the BLOCK FFQ that was collected with the data was not used to validate the 24-hour recalls; however, FFQs have limitations as well in that it does not capture intake at different periods of time.

Moreover, the demographics of our study population may be a limitation. The results from the study may not be extrapolated to the entire pediatric population, as 95% of the subjects were African American. While most of the HIV diagnoses in the U.S. are African Americans, it is only 44%,[1] and as we saw there were differences in nutrient

intake between different races. Also, there was a wide age range among our subjects, which makes it more difficult to generalize results to a certain group. Analyzing the data among different age groups such as children, adolescents, and early adulthood, would be valuable.

Conclusion

While the HIV-infected youth in our study are consuming similar kilocalories to those without HIV, they are making poorer food choices, which may ultimately lead to poorer health outcomes. Unfortunately, HIV-infected youth have greater micronutrient needs in order to maintain immune status and are at greater risk for CVD. Despite these known issues associated with the disease, diet is a modifiable factor that these patients may be able to control to alter their health status in the long run. Currently nutritional needs are not being met and nutrition counseling is needed in this population to ensure nutrient dense foods are consumed. This study supports suggestions made by the AND as well as other studies that advise nutrition counseling is of utmost importance in HIV-infected youth. Providing nutrition counseling to youths, early on in the disease process, is likely to optimize health. While some may think supplements can support inadequacies in micronutrient intake, the World Health Organization[16] suggests that an adequate diet is the best method for meeting nutrient needs in HIV-infected individuals due to past research on supplementation. Medical nutrition therapy is known to improve immune status, progression of HIV, and risk of mortality.[35] Furthermore, nutrition education must be customized to the HIV-infected individual depending on age, race and sex, as differences between these groups were seen for suboptimal nutrient intakes. To our knowledge this was the first study to comprehensively study nutrient intake and

associations with lipid profiles as well as HIV-related factors in HIV-infected youth. I believe this study offers insight into the dietary intake of this population and possible associations with nutrients and immune status. And although poor diet was not reflected in serum lipid profiles, the increased dyslipidemia in the HIV-infected youth may, over time combined with poor diet, contribute towards CVD. Based on these results, longitudinal, randomized control trials should be performed to determine the impact of nutrition counseling and specialized diets on the health outcomes of youth with HIV.

REFERENCES

1. Centers for Disease Control and Prevention. HIV/AIDS Statistics and Surveillance page. Internet: http://www.cdc.gov/hiv/topics/surveillance/basic.htm (accessed on 16 October 2011).

2. State Health Facts. Estimated Numbers of Diagnoses of HIV Infection, All Ages, 2009**.** Available at: http://www.statehealthfacts.org/comparemaptable.jsp?ind=521&cat=11. Accessed on October 16, 2011.

3. Johann-Liang R, O'Neill L, Cervia J, Haller I, Giunta Y, Licholai T, and Noel G. Energy balance, viral burden, insulin-like growth factor-1, interleukin-6 and growth impairment in children infected with human immunodeficiency virus. *AIDS.* 2000; 14: 683-690.

4. Henderson R, Talusan K, Hutton N, Yolken R, Caballero B. Serum and plasma markers of nutritional status in children infected with the human immunodeficiency virus. *Journal of the American Dietetic Association.* 1997; 97(12): 1377-81.

5. Banerjee T, Pensi T, Banerjee D, and Grover G. Impact of HAART on survival, weight gain, and resting energy expenditure in HIV-1-infected children in India. *Annals of Tropical Paediatrics.* 2010; 30: 27-37.

6. Miller T. Nutrition in paediatric human immunodeficiency virus infection. *Proceedings of the Nutrition Society*. 2000; 59: 155-162.

7. Kruzich L, Marquis G, Wilson C, and Stephensen C. HIV-infected US youth are at high risk of obesity and poor diet quality: a challenge for improving short- and long-term health outcomes. *Journal of the American Dietetic Association.* 2004a; 104(10): 1554-1560.

8. Dube M, Stein J, Aberg J, Fichtenbaum C, Gerber J, Tashima K, Henry W, Currier J, Sprecher D, Glesby M. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV medicine association of the infectious disease society of America and the adult AIDS clinical trials group. *Clinical Infectious Diseases.* 2003; 37: 613-27.

9. Capili B and Anastasi J. HIV and hyperlipidemia: current recommendations and treatment. *Medsurg Nursing.* 2006; 15: 14-20

10. Rhoads M, Lanigan J, Smith C, Lyall E. Effect of specific ART drugs on lipid

changes and the need for lipid management in children with HIV. *J Acquir Immune Defic Syndr.* 2011; 57(5): 404-412.

11. Barrios A, Blanco F, Garcia-Benayas T, Gomez-Viera J, de la Cruz J, Soriano V, Gonzalez J. Effect of dietary intervention on highly active antiretroviral therapy-related dyslipidemia. *AIDS.* 2002; 16(15): 2079-2081.

12. Lichtenstein A, Appel L, Brands M, et al. Diet and lifestyle recommendations revision 2006: A scientific statement from the American Heart Association nutrition committee. *Journal of the American Heart Association.* 2006; 114:82-96.

13. Tremeschin M, Sartorelli D, Cervi M, Negrini B, Salomao R, and Monteiro J. Nutritional assessment and lipid profile in HIV-infected children and adolescents treated with highly active antiretroviral therapy. *Revista da Sociedad Brasileira de Medicina Tropical*. 2011; 44(3): 274-281.

14. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. October 14, 2011; 1–167.

15. Jahoor F, Abramson S, Heird W. The protein metabolic response to HIV infection in young children. *Am J Clin Nutr.* 2003; 78:182-9.

16. World Health Organization. Nutrient requirements for people living with HIV/AIDS. Geneva: World Health Organization; 2003.

17. Chao D, Rutstein R, Steenhoff A, Shanbhag M, Andolaro K, and Zaoutis T. Two cases of hypocalcemia secondary to vitamin D deficiency in an urban HIV-positive pediatric population. *AIDS.* 2003; 17(16): 2401-2403.

18. Fawzi W. Micronutrients and HIV type 1 disease progression among adults and children. *Clinical Infectious Diseases.* 2003; 37: 112-6.

19. Steenkamp L, Dannhauser A, Walsh D, Joubert G, Veldman FJ, Van der Walt E, Cox C, Hendricks MK, Dippenaar H. Nutritional, immune, micronutrient and health status of HIV-infected children in care centres in Mangaung. *S Afr J Clin Nutr* 2009;22(3):131-136

20. Pee S and Semba R. Role of nutrition in HIV infection: review of evidence for more effective programming in resource-limited settings. *Food and Nutrition Bulletin.* 2010;31(4): 313-344.

21. Tang A, Graham N, Saah A. Effects of micronutrient intake on survival in human immunodeficiency virus type 1 infection. *American Journal of Epidemiology.* 1996; 143(12): 1244-1256.

22. Baum MK Shor-Posner G, Lai S, Zhang G, Lai H, Sauberlich H, Page BJ. High

risk of HIV-related mortality is associated with selenium deficiency. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology.* 1997; 15 (5): 370-374.

23. Baeten JM, McClelland RS, Wener MH, Bankson DD, Lavreys L, Mandaliya K, Bwayo JJ, Kreiss JK. Relationship between markers of HIV-1 disease progression and serum beta-carotene concentrations in Kenyan women. *Int J STD AIDS.* 2007;18:202–6.

24. Baum MK, Shor-Posner G, Lu Y, Rosner B, Sauberlich HE, Fletcher MA, Szapocznik J, Eisdorfer C, Buring JE, Hennekens C. Micronutrients and HIV-1 disease progression. *AIDS*. 1995; 9: 1051-1056.

25. Tang AM, Graham N, Semba RD, Saah AJ. Association between serum vitamin A and E levels and HIV-1 disease progression. *AIDS*. 1997; 11: 613-620.

26. Tang AM, Graham N, Chandra RK, Saah AJ. Low serum vitamin B-12 concentrations are associated with faster human immunodeficiency virus type 1 (HIV-1) disease progression. *J. Nutr.* 1997; 127: 345-351.

27. Tang AM, Graham N, Kirby AJ, McCall DL, Willett W, Saah AJ. Dietary micronutrient intake and risk of progression to acquired immunodeficiency syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected homosexual men. *American Journal of Epidemiology.* 1993; 138(11): 937-951.

28. Otten JJ, Hellwig JP, Meyers LD. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements.* Washington, D.C.: The National Academies Press; 2006.

29. Food and Nutrition Board, Institute of Medicine. Dietary reference intakes. Applications in dietary assessment. Washington, DC: National Academy Press, 2010.

30. Stephensen C, Marquis G, Jacob R, Kruzich L, Douglas S, and Wilson C. Vitamin C and E in adolescents and young adults with HIV infection. *Am J Clin Nutr.* 2006;83: 870-9.

31. Tabi M and Vogel R. Nutritional counseling: an intervention for HIV-positive patients. *Issues and innovations in nursing practice.* 2006: 676-682.

32. Sharma T, Kinnamon D, Duggan C, Weinberg G, Furuta L, Bechard L, Nicchitta J, Gorbach S, and Miller T.. Changes in macronutrient intake among HIV-infected children between 1995 and 2004. *Am J Clin Nutr*. 2008; 88: 384-91.

33. Position of the American Dietetic Association: Nutrition Intervention and Human Immunodeficiency Virus Infection. *J Am Diet Assoc.* 2010; 110:1105-1119.

34. Baum MK, Shor-Posner G, Bonvehi P, Cassetti I, Lu Y, Mantero-Atienza E,

Beach RS, Sauberlich HE. Influence of HIV-infection on vitamin status and requirements. *Ann N Y Acad Sci* 1992;669:165–73.

35. Suttajit M. Advances in nutrition support for quality of life in HIV+/AIDS. *Asia Pac J Clin Nutr*. 2007; 16: 318-322.

36. American Dietetic Association. HIV/AIDS macronutrient composition. Available at http://www.adaevidencelibrary.com/template.cfm?template=guide_summary&key=2821

37. Institute of Medicine. *Dietary Reference Intakes: Recommended Intakes for Individuals*: 2010. Available at: http://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables Accessed on: October 24, 2011.

38. Miller T, Grant Y, Almeida D, Sharma T, Lipshultz S. Cardiometabolic disease in human immunodeficiency virus-infected children. *Journal of Cardiometabolic Syndrome*. 2008: 98-105.

39. Kim J, Spiegelman D, Rimm E, and Gorbach L. The correlates of dietary intake among HIV-positive adults. *Am J Clin Nutr*. 2001; 74: 852-61.

40. Shah M, Tierney K, Adams-Huet B, et al. The role of diet, exercise and smoking in dyslipidaemia in HIV-infected patients with lipodystrophy. *HIV Medicine.* 2005;6: 291-298.

41. Zuin G, Comi D, Fontana M, Tornaghi R, Brugnani M, Fadini S, and Principi N. Energy and nutrient intakes in HIV-infected children. *Pediatric AIDS and HIV Infection:Fetus to Adolescent.* 1994;5(3):159-161.

42. Kruzich L, Marquis G, Carriquiry A, Wilson C, Stephensen C. US youths in the early stages of HIV disease have low intakes of some micronutrients important for optimal immune function. *Journal of the American Dietetic Association.* 2004b; 104(7): 1095-1101.

43. Charakida M, Donald AE, Green H, Storry C, Clapson M, Caslake M, Dunn DT, Halcox JP, Gibb DM, Klein NJ, Deanfield JE. Early structural and functional changes of the vasculature in HIV-infected children: impact of disease and antiretroviral therapy. *Circulation*. 2005;112(1):103-9.

44. Taylor P, Worrell C, Steinberg S, et al. Natural history of lipid abnormalities and fat redistribution among human immunodeficiency virus-infected children receiving long-term, protease inhibitor-containing, highly active antiretroviral therapy regimens. *Pediatrics.* 2004; 114 (2): e235-42.

45. Vigano A, Bedogni G, Zuccotti G, et al. Both HIV-Infection and Long-Term Antiretroviral Therapy are Associated with Increased Common Carotid Intima-

Media Thickness in HIV-Infected Adolescents and Young Adults. *Current HIV Research*. 2010;8(5):411-417.

46. Triant VA, Lee H, Hadigan C, Grinspoon S. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab.* 2007;92(7): 2506-2512.

47. *Dietary Reference Intakes : Applications In Dietary Assessment / Subcommittee On Interpretation And Uses Of Dietary Reference Intakes And The Standing Committee On The Scientific Evaluation Of Dietary Reference Intakes* [e-book]. Washington, D.C.: National Academy Press, c2000.; 2000.

48. Portney L, Watkins P. *Foundations of Clinical Research: Applications to Practice*. 3rd ed. Upper Saddle River, New Jersey: Pearson/Prentice Hall; 2009.

49. Institute of Medicine. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, D.C.: National Academy of Sciences. 2011.

50. Ganji V, Zhang X, Shaikh N, and Tangpricha V. Serum 25-hydroxyvitamin D concentrations are associated with prevalence of metabolic syndrome and various cardiometabolic risk factors in US children and adolescents based on assay-adjusted serum 25-hydroxyvitamin D data from NHANES 2001-2006. *Am J Clin Nutr.* 2011; 94:225-33.

51. Ross AC, Judd S, Kumari M, Hileman C, Storer N, Labbato D*, et al.* Vitamin D is linked to carotid intima-media thickness and immune reconstitution in HIV-positive individuals. *Antivir Ther* 2011,16:555-563.

52. Choi AI, Lo JC, Mulligan K, Schnell A, Kalapus SC, Li Y*, et al.* Association of vitamin D insufficiency with carotid intima-media thickness in HIV-infected persons. *Clin Infect Dis* 2011,52:941-944.

CHAPTER IV

MANUSCRIPT IN STYLE OF JOURNAL

Habitual nutrient intake in HIV-infected youth and associations with HIV-related factors

Lindsey A Stricker[1], Murugi Ndirangu[1], Anita Nucci[1], Thomas R Ziegler[2], Vin Tangpricha[2], Grace A McComsey[3], Jennifer K Frediani[3], Erin C Millson[3], LaTeshia Seaton[4], Allison Ross Eckard[2,4]

[1]Georgia State University, Atlanta, Georgia, USA; [2]Emory University School of Medicine, Atlanta, Georgia, USA; [3]Case Western Reserve University, Cleveland, Ohio, USA; [4]Children's Healthcare of Atlanta, Atlanta, Georgia, USA

Correspondence and Reprints: Allison Ross Eckard, MD, Assistant Professor of Pediatrics, Pediatric Infectious Diseases, Emory University School of Medicine, 2015 Uppergate Dr., NE, Atlanta, GA 30322, Phone: 404-727-8224, Fax: 404-727-9223, E-mail: Allison.ross.eckard@emory.edu

Disclaimers: ACR has received research funding from Bristol-Myers Squibb, Cubist Pharmaceuticals, and GlaxoSmithKline. GAM serves as a consultant, speaker, and has received research funding from Bristol-Myers Squibb, GlaxoSmithKline, Gilead, and Tibotec. GAM currently chairs a DSMB for a Pfizer-funded study. ACG has received research funding from Bristol-Myers Squibb. All other authors declare no conflicts of interest.

Sources of Support: The study was supported by research grants to Dr. Ross from GlaxoSmithKline, Emory-Egleston Children's Research Center, Emory's Center for AIDS Research (P30 AI050409), and NICHD (R01 HD070490). The funding agencies have no access to the raw data and no role in the analysis or writing of this manuscript.

Short title: Nutrient intake of HIV youth

List of abbreviations:

AHA	American Heart Association
AI	Adequate Intake
AIDS	Acquired Immunodeficiency Syndrome
AMDR	Acceptable Macronutrient Distribution Range
ART	Antiretroviral Therapy/Treatment
BMI	Body Mass Index
CD4	Cells that are targeted by the HIV virus
CDC	Centers for Disease Control and Prevention
CVD	Cardiovascular Disease
DRI	Dietary Reference Intake
EAR	Estimated Average Requirements
FFQ	Food Frequency Questionnaire
HAART	Highly Active Antiretroviral Therapy
HDL-C	Serum High-Density Lipoprotein Cholesterol
HIV	Human Immunodeficiency Virus

HIV+	HIV-infected subjects
HIV-	HIV-negative controls
IOM	Institute of Medicine
LDL-C	Serum Low-Density Lipoprotein Cholesterol
NDS-R	Nutrition Data System for Research Software
RDA	Recommended Dietary Allowance
TC	Total Serum Cholesterol
TG	Serum Triglycerides
UL	Tolerable Upper Intake Level
WHO	The World Health Organization

ABSTRACT

Background: Few studies have evaluated habitual nutrient intake among HIV-infected youth in the United States, even though diet may influence disease progression and chronic complication risk.

Objective: This study determined micro- and macronutrient intake in HIV-infected youth, and investigated relationships among nutrient intake, demographics, lipid profiles, and HIV-related factors.

Design: HIV-infected subjects and healthy controls 1-25 years old were prospectively enrolled. Concomitant demographic, clinical and laboratory data were collected. Nutrient intake was assessed via 24-hr dietary recalls performed every 3 months for one year, analyzed with NDS-R software, and compared to Dietary Reference Intakes (DRIs) and Acceptable Macronutrient Distribution Ranges (AMDRs).

Results*:* Subjects with ≥2 food recalls were analyzed (175 HIV+; 43 controls). Groups were similar in age, race, sex, body mass index, and kilocalorie intake. Both groups did not meet DRI for several micronutrients. HIV+ subjects had lower %DRI than controls for vitamins A, E, pantothenic acid, magnesium, calcium, folate and potassium. Percent kilocalories from fat was above normal and higher in HIV+ patients. Caloric intake was negatively correlated with current and nadir CD4 counts. Zinc, riboflavin, and magnesium %DRI were positively associated with current CD4+ count. In HIV+ subjects not on antiretroviral therapy, HIV-1 RNA levels were negatively correlated with protein intake.

Conclusions: HIV+ youth have inadequate intake of several essential nutrients and poorer dietary intake compared to controls. Intake of some nutrients was associated with HIV-related factors. Further investigation is warranted to determine the impact of nutrition on HIV progression and chronic complication risk in this population.

INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC), there were almost 43,000 new diagnoses of HIV infection in the United States in 2009, with 20% between the ages of 0 and 24 years (1). Nutritional deficiencies are common among people with HIV, including HIV-infected youth (2-8). In HIV-infected adults, nutritional deficiencies have been shown to affect immune status, disease progression and mortality (7-15).

With the advent of highly-active antiretroviral therapy (HAART), concerns over nutritional deficiencies in the HIV-infected population have shifted from AIDS wasting syndrome, growth stunting, and chronic diarrhea to newly-described long-term complications associated with chronic HIV infection secondary to increased inflammation, oxidative stress, and immune activation (6-7, 16-23). For example, HIV-infected individuals have an increased risk of cardiovascular disease (CVD) that have been shown to be associated with nutritional deficiencies in other populations, as well as within the HIV population (24-26). In addition, HIV-infected individuals are at an increased risk of lipid abnormalities and metabolic syndrome, which have been shown to improve with dietary intervention in the general population (18,22-22,24, 26-28).

Like HIV-infected adults, increased risk for CVD, and metabolic abnormalities occurs among HIV-infected youth (18,22,29-32). Combined with a rising prevalence of obesity in this population and higher nutritional risk due to growth and development demands, nutritional deficiencies in this population are particularly alarming (29,33). Moreover, chronic immune activation and increased oxidative stress in HIV-infected youth may result in increased nutrient needs beyond the recommended intakes (6,20,34),

while those individuals with hyperlipidemia or metabolic dysfunction may need to decrease their fat, trans fat, saturated fat, and cholesterol intake (30,36). To date, however, few studies have investigated nutritional intake among HIV-infected youth, despite the serious implications for HIV disease progression and complication development in this population (2,6,17,29, 36-38). And, notably, the few studies that have investigated this important topic used less stringent methods than what is recommended for nutrient intake assessment and/or only explored a few micronutrients.

Thus, the primary objective of this study was to comprehensively evaluate the micro- and macronutrient intake in HIV-infected youth. Secondary objectives included (1) to compare the nutrient intake in HIV-infected youth to that of current intake recommendations, (2) to compare the nutrient intake in HIV-infected youth to that of healthy controls, (3) to assess the associations between dietary intake and serum lipid levels, and (4)to determine if nutrient intake is associated with HIV-related variables.

METHODS

Study Population

All patients between the ages of 1-25 years old with documented HIV-1 infection enrolled at the Ponce Youth HIV Clinic of the Grady Health System in Atlanta, GA, USA were eligible for this study. Participants were recruited over a 10-month period of time while they were at the clinic for their regular HIV monitoring visits. Over 95% of approached patients consented to study participation.

Controls were recruited with advertisement flyers hung in the HIV clinic and by word of mouth, and selected so that the overall group matched the HIV-infected subjects

in age, sex, and race. Healthy controls included relatives of the hospital staff, relatives of HIV-infected patients, and HIV-negative patients seen at the clinic. Controls were eligible if they self-reported to be free of chronic disease and had no recent or current infection. Potential subjects ≥13 years of age were screened for HIV infection before enrollment with OraQuick Advance Rapid HIV Test (OraSure Technologies, Inc, Bethlehem, PA, USA). Controls <13 years of age were assumed HIV-uninfected unless they were considered at high-risk for having or contracting HIV. Exclusion criteria for controls were the same as for the infected group.

All parents or legal guardians and subjects ≥18 years of age provided written informed consent to participate in the study, and those subjects 17 years of age signed the written consent along with their parent or legal guardian. Subjects 6-10 years old gave verbal assent and those 11-16 years gave written assent. The Institutional Review Boards of Emory University and Grady Health Systems approved the study, and all ethical principles of the institutions were followed throughout the study.

Study Design

Each subject underwent anthropometric, clinical, laboratory, and nutritional intake assessments at enrollment. Subjects were then followed prospectively and one additional nutritional intake assessment was obtained per subject for each season of the year during routine clinic visits or by telephone interview. Only subjects with ≥2 nutritional assessments obtained during different seasons were included in the study. All nutritional intake assessments and data entry were performed by registered dietitian-

trained investigators and were overseen by registered dietitians.

Nutritional Assessments

Nutritional assessments were obtained for each season of the year by means of a 24-hour diet recall in order to capture seasonal changes in dietary intake as well as day-to-day variation in diet. Each subject reported food intake over the last 24 hours. The amounts were entered into Nutrition Data System for Research (NDS-R). NDS-R is a dietary analysis program designed for the collection and analysis of 24-hour dietary recalls and provides a detailed analysis of macro- and micro-nutrient intake in units per day. Subjects had to have ≥2 nonconsecutive, 24-hour food recalls to be included in the analysis, as per the Institute of Medicine (IOM) recommendations for dietary intake analysis (39).

Nutritional status was assessed using Dietary Reference Intakes (DRIs), which are the nutrient reference values derived from years of scientific research (40-41). Micronutrient intake was compared to the Recommended Dietary Allowance (RDA) or the Adequate Intake (AI), if no RDA existed for the nutrient. Individual recalls were assigned to an IOM life stage group, based on the subject's gender and age on the day of the assessment. Due to collection of recalls taking place over time, subjects could have multiple life stage groups and multiple DRIs for one micronutrient; therefore, percent DRIs were calculated for each recall for each nutrient and subsequently averaged for each subject. Thus, percent DRI was used for all micronutrient analysis. A total of 22 micronutrients were analyzed.

Mean macronutrient intake was compared to the Acceptable Macronutrient Distribution Ranges (AMDR). Fat, saturated fat, trans fat, cholesterol and fiber intake were compared to the recommendations of the American Heart Association (AHA) for the general population (total fat intake:25-35% of total calories; saturated fat: <7% of total calories; trans fats: <1% of total calories; cholesterol: < 300 mg per day; fiber: 14g per 1000 calories consumed per day)(26). Normal lipoprotein profile levels were considered 200 mg/dL, 130 mg/dL, 40 mg/dL, and 140 mg/dL for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG), respectively (2,28).

Clinical Assessments

Clinical measurements included weight, height, and waist and hip measurements (with standardized measurements based on procedure recommendations from the Metabolic Study Group of the AIDS Clinical Trials Group). All HIV-infected subjects and controls (or guardians) completed questionnaires in order to obtain relevant demographic and medical information (including vitamins and supplements). An extensive chart review was conducted for the HIV+ subjects, including detailed information on time of HIV diagnosis, past and current medical diagnoses, antiretroviral therapy (ART) use, and CD4 cell count nadir.

Laboratory Assessments

Lipoprotein profiles were obtained after at least an 8-hour fast. CD4 cell counts and HIV-1 RNA were obtained from the HIV-infected subjects.

Statistical Analysis

Demographics, clinical characteristics, and laboratory parameters are described by HIV status. Continuous measures are described by means/standard deviations, and nominal variables are described with frequencies/percentages. Variables that were not normally distributed were log transformed and parametric tests were performed. If the variables were not normally distributed after log transformations, non-parametric tests were used for analysis.

Statistical tests used to make group comparisons and to compare variables to standards included: Chi-squared for categorical variables, one-sample and independent t-tests for normally distributed means, and Mann-Whitney U test for non-normally distributed means.

One-way analysis of variance (ANOVA) and Bonferroni post-hoc comparisons were used to determine differences in nutrient intakes between races. Pearson's correlation coefficient or Kendall's Tau were used to investigate associations between nutrient intake and variables of interest. A P-value <0.05 was considered significant. All analyses were carried out using SPSS 18.0.

RESULTS

Study Population

175 HIV-infected subjects and 43 healthy controls were included in the analysis. Subject characteristics are summarized in Table 1. Groups were matched for age, race, sex, body mass index (BMI), and waist-to-hip ratio. The prevalence of dyslipidemia was higher in the HIV+ group compared to controls (TC=11.8% vs. 3%; LDL-C=7.9% vs. 3%; HDL-C=43.8% vs. 5.3%; and TG=9% vs. 0.8%). Mean HDL-C was significantly

lower in the HIV-infected group and mean triglycerides were significantly higher in the HIV-infected group. No significant differences existed between groups for TC and LDL-C.

Dietary Intake, Comparison to Standards, and Between-Group Differences

Recalls that were obvious outliers (<500 kilocalories or >5000 kilocalories in one 24-hour period) were excluded from the analysis. A total of 674 24-hour recalls were analyzed. 558 recalls were analyzed for the HIV+ group (mean = 3.2 recalls per subject): 75 subjects with four recalls (43%), 58 subjects with three recalls (33%), and 42 subjects with two recalls (24%). The control group had 113 recalls analyzed (mean = 2.6 recalls per subject): 7 subjects had four recalls (16%), 13 subjects had three recalls (30%), and 23 subjects had two recalls (53%).

Mean (standard deviation (SD)) intake for the HIV+ group was 1953.9 ± 610.87 kilocalories, and 1990 ± 540.8 kilocalories for the control group (P = 0.723).

Mean percentage of DRI intake of all micro- and macronutrients analyzed for the HIV+ and control groups are presented in Table 2 and **Figure 1**. For the HIV-infected group, mean micronutrient intake was less than 100% of the DRI for vitamin A, vitamin D, vitamin E, pantothenic acid, folate, calcium, magnesium, and potassium (all P < 0.001), with a prevalence of suboptimal intake at 82%, 99%, 93%, 73%, 61%, 93%, 87%, and 100% of subjects, respectively. Ninety-nine percent of HIV-infected subjects consumed greater than the recommended DRI for sodium with the mean intake significantly greater than the DRI (P < 0.001). For the controls, micronutrient intake was less than 100% of the DRI for vitamin A**,** vitamin D, vitamin E, calcium, magnesium, and potassium, and greater than the recommended DRI for sodium (all P < 0.001) with a

prevalence of suboptimal intake at 67%, 95%, 93%, 86%, 74%, 100%, and 100% of subjects, respectively.

Among nutrients that were consumed in sufficient amounts within the HIV+ group, the HIV+ group nonetheless had a significantly lower percent DRI compared to controls for vitamin K (-37.6%, P = 0.038), vitamin C (-42.6%, P = 0.003), thiamin (-25.45%, P = 0.029), riboflavin (-42%, P = 0.002), copper (-18.2%, P = 0.048), phosphorus (-20%, P = 0.033), manganese (-18.1%, P = 0.044).

Mean percentage of calories from carbohydrate and protein fell within the AMDR for both groups. Fat intake significantly exceeded the AMDR only for HIV-infected subjects (P = 0.018) (**Figure 2**). Compared to AHA recommendations, both groups had significantly less fiber intake and greater percentage of calories from saturated fat and trans fat, but normal cholesterol intake. The HIV+ group had significantly higher % kilocalories from fat and trans fat, and significantly lower % kilocalories from carbohydrate (-2.9%, P = 0.014) compared to the control group, but no difference in protein intake (P = 0.177).

Within the HIV-infected group, females had significantly lower calorie intake (-387 kcal, P < 0.001) and mean percent DRI for folate (-0.184%, P = 0.004), pantothenic acid (-0.182%, P = 0.000), vitamin D (-0.09%, P = 0.002), calcium (-0.17%, P < 0.001), and potassium (-0.085%, P < 0.001). African Americans had a lower percent DRI of vitamin D (-26.2%, P = 0.027) and calcium intake (-31.2%, P = 0.017) than Caucasians. Latinos had significantly lower percent fat intake from calories compared to African Americans (-10.8%, P = 0.003) and Caucasians (-10.1%, P = 0.031).

Associations Between Nutrient Intake and Serum Lipid Levels

Within the HIV-infected group, there was a positive correlation between trans fat intake and serum LDL-C ($r = 0.158$, $P = 0.040$), as well as between fiber intake and serum triglycerides ($r = 0.157$, $P = 0.041$). There was a negative correlation between total fat intake and serum triglycerides ($r = -0.170$, $P = 0.027$). In the control group there was a positive correlation between cholesterol intake and serum triglyceride levels ($r = 0.315$, $P = 0.040$).

Associations Between Nutrient Intake and HIV-Related Factors

Age was positively associated with intake of calories, phosphorus, sodium, and fat (Table 3). Body mass index was negatively correlated with percent DRI of vitamin A, vitamin D, vitamin E, riboflavin, thiamin, niacin, pantothenic acid, vitamin B6, folate, vitamin B12, magnesium, iron, zinc, copper, potassium, and selenium.

Within the HIV-infected group, calorie intake was negatively correlated with current CD4+ cell count and nadir CD4+ cell count. The percent of DRI for vitamin A was positively associated with nadir CD4+ cell count count. The percent of DRI for zinc, magnesium, and riboflavin was positively associated with current CD4+ cell count.

Among HIV-infected subjects currently on ART, riboflavin and B12 intake was positively associated with CD4+ cell count nadir. Current CD4+ cell count was positively associated with magnesium and zinc intake. For subjects on ART for >6 months with an HIV-1 RNA <1000 copies/mL, there were no significant associations between nutrient intake and change in CD4+ cell count after starting ART (current-nadir CD4).

There were no significant correlations with CD4+ cell counts among those subjects currently not on ART. However, HIV-1 RNA was negatively correlated with protein intake ($r = -0.296$, $P = 0.046$).

DISCUSSION

This study showed that the nutrient intake in HIV-infected youth did not meet dietary guidelines for a number of critical micronutrients, including vitamins A, D, E, pantothenic acid, folate, calcium, magnesium, potassium, and sodium. Vitamin D, calcium, potassium, and vitamin E were consumed in the lowest amounts, while sodium intake was exceedingly excessive.

HIV-infected youth also had poorer micro- and macronutrient intake compared to healthy controls despite similarities in caloric intake. Proper nutrient intake is vital for optimal health in the HIV-infected population, as many micronutrients have been associated with diseases known to be increased in this population. For example, HIV-infected individuals are at an increased risk of CVD (2, 22, 30-31, 42-43). Low serum vitamin D concentrations are associated with CVD risk factors in children and adults, in both the HIV-infected and HIV-uninfected populations (42-45). Furthermore, consuming recommended amounts of potassium and sodium can help regulate blood pressure, another important factor in reducing CVD risk (26).

Importantly, in our cohort of HIV-infected youth, we did observe a greater prevalence of dyslipidemia and significantly higher mean TG and significantly lower HDL-C than healthy controls. Moreover, the HIV-infected youth in this study had a percent total fat, trans fat, and saturated fat intake from kilocalories that exceeded

recommendations, and fiber intake was less than recommendations in all but one subject. Fat and fiber intake aberrations have been associated with CVD risk in the general adult population. For example, limiting dietary intake of saturated and trans fat is associated with a lower risk of CVD, mostly due to its positive effects on LDL-C (26). Increased dietary fiber, both insoluble and soluble, has been linked with lower CVD risk and decreased progression to CVD in high-risk adults (26).

Adult HIV studies have also shown associations between trans fat intake and serum TG levels (24), as well as between percent calories from fat and serum TC and TG (46). Despite these findings previously found in adults, there were few meaningful associations between nutrient intake and lipid profiles in our cohort of HIV-infected youth. These associations have not been previously studied in HIV-infected youth, and thus, nutrient intake may not have the same relationship to serum lipid levels as found in adults. Alternatively, inadequate power and/or confounding factors may have played a role. These relationships should be analyzed more systematically in future studies, given the high prevalence of dyslipidemia and high fat intake within this population.

Importantly, appropriate micronutrient levels may contribute to improved immune status and survival in HIV-infected individuals (7, 8, 10-15, 47-49). For instance, Baum and colleagues found that as serum vitamin A, B12, and zinc status improved, CD4+ cell counts increased in HIV-infected adult males (12). This association between micronutrient sufficiency and HIV disease status has been repeated in other studies (5, 12, 14-15), despite some conflicting data which investigated micronutrient intake (38). Notably, Steenkamp, *et al* showed that in ART-naïve children with abnormally low serum levels of zinc and vitamin A had significantly lower CD4+ cell counts and higher

366 HIV-1 RNA levels (5). Decreased vitamin D concentrations have also been associated
367 with increased mortality and HIV disease progression among several HIV-infected
368 populations, including in children born to HIV-infected woman with vitamin D
369 deficiency (48-49). Similarly, vitamin E is important for immune function and is a
370 potent antioxidant, which may be particularly important in HIV-infected individuals who
371 have increased oxidative stress (6, 38).

372 In our current study, we found some notable correlations between nutrient intake
373 and variables used to assess HIV disease status. Vitamin A intake was positively
374 correlated with nadir CD4+ cell count, and zinc, riboflavin, and magnesium intake were
375 positively associated with current CD4+ cell count. In subjects not on ART and with
376 uncontrolled viremia, CD4+ cell count was not significantly correlated with zinc, niacin
377 or vitamin A intake, as was shown in a previous studies (10, 15), but HIV-1 RNA was
378 negatively correlated with dietary protein intake. This may suggest that HIV-infected
379 individuals, especially when their viremia is not suppressed with ART, may be in an
380 increased metabolic state, requiring additional protein. Studies showing a higher rate of
381 protein oxidation in HIV-infected children corroborate this finding (34).

382 Total intake of kilocalories was negatively correlated with current and nadir
383 CD4+ cell counts, which may suggest that individuals with more advanced HIV disease
384 (i.e. with a lower CD4 count and lower CD4 nadir) require a higher amount of calories
385 compared to individuals with higher CD4 counts. This is consistent with the
386 aforementioned findings suggesting that individuals not on ART with uncontrolled
387 viremia may have not only greater protein needs, but increased kilocalorie intake overall.
388 When an individual's immune system is highly immunocompromised and overwhelmed

with viremia, this may help to preserve immune function and/or allow a faster immune reconstitution once ART is initiated. Previous studies evaluating caloric intake did not find any associations between CD4 category and progression to AIDS (15), or mortality (10). However, these previous adult studies used semi-quantitative food frequency questionnaires, instead of the IOM's recommendation to use at least two, 24-hour recalls on nonconsecutive days to assess usual intake (39), and were also done in the pre-ART era. Thus, further investigation is warranted to determine total kilocalorie and protein needs at various clinical and virological stages of disease in HIV-infected youth. In HIV-infected adults, medical nutrition therapy has been shown to improve immune status, progression of HIV, and risk of mortality (21).

Despite the important findings in our study, there were several limitations, including a cross-sectional design which cannot prove causality, a relatively small control group, and a wide-age range among our subject population. In addition, while the IOM recommends using 24-hour recalls to determine nutrient intake (39), they do have drawbacks. Due to their recall nature, there was likely over- or under-reporting of food intake. We tried to account for this by omitting recalls that were clear outliers. Regardless, 24-hour dietary recalls still remain the best method for adequately assessing diet and making comparisons to DRIs (39). Similarly, we are assuming that dietary intake is correlated with serum levels, and this may not be the case. However, in studies investigating HIV-infected adults, correlations were found between serum concentrations and dietary intake of B12 (14), vitamin A, and zinc (12). Additional studies are needed to determine whether nutrient intake data correlate with serum nutrient concentrations in

411 our current study population, and whether the serum nutrient status has an impact on
412 immune status and HIV progression in HIV-infected youth.

413 Our study was comprised of 95% African Americans, which limits our ability to
414 generalize the results. However, this race is particularly sensitive to the effects of these
415 key nutrients on blood pressure and cardiovascular problems and may benefit the most
416 from improving their nutrient intake based on these results (26). Finally, due to the large
417 number of variables that were tested in univariate fashion, there was a risk of Type I
418 errors. However, these exploratory data provide a substrate from which to design future
419 longitudinal, randomized-controlled trials.

420 Nevertheless, this study offers insight into the diet of this vulnerable population
421 and possible associations with HIV-related variables and chronic complication risk. The
422 important point is the high prevalence of suboptimal nutrient intake among HIV-infected
423 children and young adults, which could have a serious impact on their long-term
424 morbidity and mortality.

425 These results are novel as few studies have evaluated nutrient intake in HIV-infected
426 youth, and none has used 24-hour food intake recall data compared to the current micro-
427 and macronutrient RDAs, which are the gold standards according to WHO and IOM (9,
428 39). Diet is a modifiable factor, and providing nutrition counseling early on in the
429 disease process is likely to optimize health and improve long-term outcomes.
430 Longitudinal, randomized-controlled trials are also needed not only to determine the
431 impact of nutrition counseling on the nutrient status of HIV-infected youth, but to better
432 define their actual intake requirements necessary to attenuate risk of chronic
433 complications, such as CVD, and minimize disease progression.

ACKNOWLEDGEMENTS

Lindsey Stricker was involved in research design, data analysis, data interpretation, and manuscript writing. Thomas Ziegler, Vin Tangpricha and Grace McComsey were involved in study design, data interpretation, and manuscript writing; LaTeshia Seaton enrolled subjects and collected data. Murugi Ndirangu and Anita Nucci were involved in research design and data interpretation. Jennifer Frediani and Erin Millson were involved in data analysis and data interpretation. Allison Eckard was involved in study design, data collection, data analysis, data interpretation, and manuscript writing.

REFERENCES

1. Centers for Disease Control and Prevention. HIV/AIDS Statistics and Surveillance page. Internet: http://www.cdc.gov/hiv/topics/surveillance/basic.htm (accessed on 16 October 2011).
2. Tremeschin M, Sartorelli D, Cervi M, Negrini B, Salomao R, and Monteiro J. Nutritional assessment and lipid profile in HIV-infected children and adolescents treated with highly active antiretroviral therapy. Revista da Sociedad Brasileira de Medicina Tropical 2011; 44(3): 274-281.
3. Chao D, Rutstein R, Steenhoff A, Shanbhag M, Andolaro K, and Zaoutis T. Two cases of hypocalcemia secondary to vitamin D deficiency in an urban HIV-positive pediatric population. AIDS 2003; 17(16): 2401-2403.
4. Fawzi W. Micronutrients and HIV type 1 disease progression among adults and children. Clin Infect Dis 2003; 37: 112-6.

5. Steenkamp L, Dannhauser A, Walsh D, Joubert G, Veldman FJ, Van der Walt E, Cox C, Hendricks MK, Dippenaar H. Nutritional, immune, micronutrient and health status of HIV-infected children in care centres in Mangaung. S Afr J Clin Nutr 2009;22(3):131-136
6. Stephensen C, Marquis G, Jacob R, Kruzich L, Douglas S, and Wilson C. Vitamin C and E in adolescents and young adults with HIV infection. Am J Clin Nutr 2006;83: 870-9.
7. Pee S and Semba R. Role of nutrition in HIV infection: review of evidence for more effective programming in resource-limited settings. Food and Nutrition Bulletin 2010;31(4): 313-344.
8. Baum MK Shor-Posner G, Lai S, Zhang G, Lai H, Sauberlich H, Page BJ. High risk of HIV-related mortality is associated with selenium deficiency. JAIDS AND HR 1997; 15 (5): 370-374.
9. World Health Organization. Nutrient requirements for people living with HIV/AIDS. Geneva: World Health Organization; 2003.
10. Tang A, Graham N, Saah A. Effects of micronutrient intake on survival in human immunodeficiency virus type 1 infection. Am J Epidemiol 1996; 143(12): 1244-1256.
11. Baeten JM, McClelland RS, Wener MH, Bankson DD, Lavreys L, Mandaliya K, Bwayo JJ, Kreiss JK. Relationship between markers of HIV-1 disease progression and serum beta-carotene concentrations in Kenyan women. Int J STD AIDS 2007;18:202–6.
12. Baum MK, Shor-Posner G, Lu Y, Rosner B, Sauberlich HE, Fletcher MA,

480 Szapocznik J, Eisdorfer C, Buring JE, Hennekens C. Micronutrients and HIV-1
481 disease progression. AIDS 1995; 9: 1051-1056.
482 13. Tang AM, Graham N, Semba RD, Saah AJ. Association between serum vitamin
483 A and E levels and HIV-1 disease progression. AIDS 1997; 11: 613-620.
484 14. Tang AM, Graham N, Chandra RK, Saah AJ. Low serum vitamin B-12
485 concentrations are associated with faster human immunodeficiency virus type 1
486 (HIV-1) disease progression. J. Nutr 1997; 127: 345-351.
487 15. Tang AM, Graham N, Kirby AJ, McCall DL, Willett W, Saah AJ. Dietary
488 micronutrient intake and risk of progression to acquired immunodeficiency
489 syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected
490 homosexual men. Am J Epidemiol 1993; 138(11): 937-951.
491 16. Johann-Liang R, O'Neill L, Cervia J, Haller I, Giunta Y, Licholai T, and Noel G.
492 Energy balance, viral burden, insulin-like growth factor-1, interleukin-6 and
493 growth impairment in children infected with human immunodeficiency virus.
494 AIDS 2000; 14: 683-690.
495 17. Henderson R, Talusan K, Hutton N, Yolken R, Caballero B. Serum and plasma
496 markers of nutritional status in children infected with the human
497 immunodeficiency virus. J Am Diet Assoc 1997; 97(12): 1377-81.
498 18. Dube M, Stein J, Aberg J, Fichtenbaum C, Gerber J, Tashima K, Henry W,
499 Currier J, Sprecher D, Glesby M. Guidelines for the evaluation and management
500 of dyslipidemia in human immunodeficiency virus (HlV)-infected adults
501 receiving antiretroviral therapy: recommendations of the HIV medicine
502 association of the infectious disease society of America and the adult AIDS

clinical trials group. Clin Infect Dis 2003; 37: 613-27.

19. Rhoads M, Lanigan J, Smith C, Lyall E. Effect of specific ART drugs on lipid changes and the need for lipid management in children with HIV. J Acquir Immune Defic Syndr 2011; 57(5): 404-412.
20. Baum MK, Shor-Posner G, Bonvehi P, Cassetti I, Lu Y, Mantero-Atienza E, Beach RS, Sauberlich HE. Influence of HIV-infection on vitamin status and requirements. Ann N Y Acad Sci 1992;669:165–73.
21. Suttajit M. Advances in nutrition support for quality of life in HIV+/AIDS. Asia Pac J Clin Nutr 2007; 16: 318-322.
22. Charakida M, Donald AE, Green H, Storry C, Clapson M, Caslake M, Dunn DT, Halcox JP, Gibb DM, Klein NJ, Deanfield JE. Early structural and functional changes of the vasculature in HIV-infected children: impact of disease and antiretroviral therapy. Circulation 2005;112(1):103-9.
23. Banerjee T, Pensi T, Banerjee D, and Grover G. Impact of HAART on survival, weight gain, and resting energy expenditure in HIV-1-infected children in India. Ann Trop Paediatr 2010; 30: 27-37.
24. Shah M, Tierney K, Adams-Huet B, et al. The role of diet, exercise and smoking in dyslipidaemia in HIV-infected patients with lipodystrophy. HIV Medicine 2005;6: 291-298.
25. Triant VA, Lee H, Hadigan C, Grinspoon S. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab 2007;92(7): 2506-2512.

526 26. Lichtenstein A, Appel L, Brands M, et al. Diet and lifestyle recommendations
527 revision 2006: A scientific statement from the American Heart Association
528 nutrition committee. Journal of the American Heart Association 2006; 114:82-96.
529 27. Capili B and Anastasi J. HIV and hyperlipidemia: current recommendations and
530 treatment. Medsurg Nursing 2006; 15: 14-20
531 28. National Institute of Health. National Cholesterol Education Program. ATP III
532 Guidelines At-A-Glance Quick Desk Reference. Bethesda, MD: National Heart,
533 Lung, and Blood Institute; 2001.
534 29. Kruzich L, Marquis G, Wilson C, and Stephensen C. HIV-infected US youth are
535 at high risk of obesity and poor diet quality: a challenge for improving short- and
536 long-term health outcomes. J Am Diet Assoc 2004; 104(10): 1554-1560.
537 30. Miller T, Grant Y, Almeida D, Sharma T, Lipshultz S. Cardiometabolic disease
538 in human immunodeficiency virus-infected children. Journal of Cardiometabolic
539 Syndrome 2008: 98-105.
540 31. Taylor P, Worrell C, Steinberg S, et al. Natural history of lipid abnormalities and
541 fat redistribution among human immunodeficiency virus-infected children
542 receiving long-term, protease inhibitor-containing, highly active antiretroviral
543 therapy regimens. Pediatrics 2004; 114 (2): e235-42.
544 32. Vigano A, Bedogni G, Zuccotti G, et al. Both HIV-Infection and Long-Term
545 Antiretroviral Therapy are Associated with Increased Common Carotid Intima-
546 Media Thickness in HIV-Infected Adolescents and Young Adults. Current HIV
547 Research 2010;8(5):411-417.
548 33. Position of the American Dietetic Association: Nutrition Intervention and Human

549 Immunodeficiency Virus Infection. J Am Diet Assoc 2010; 110:1105-1119.
550 34. Jahoor F, Abramson S, Heird W. The protein metabolic response to HIV
551 infection in young children. Am J Clin Nutr 2003; 78:182-9.
552 35. American Dietetic Association. HIV/AIDS macronutrient composition. Internet:
553 http://www.adaevidencelibrary.com/template.cfm?template=guide_summary&ke
554 y=2821
555 36. Sharma T, Kinnamon D, Duggan C, Weinberg G, Furuta L, Bechard L, Nicchitta
556 J, Gorbach S, and Miller T.. Changes in macronutrient intake among HIV-
557 infected children between 1995 and 2004. Am J Clin Nutr 2008; 88: 384-91.
558 37. Zuin G, Comi D, Fontana M, Tornaghi R, Brugnani M, Fadini S, and Principi N.
559 Energy and nutrient intakes in HIV-infected children. Pediatric AIDS and HIV
560 Infection:Fetus to Adolescent 1994;5(3):159-161.
561 38. Kruzich L, Marquis G, Carriquiry A, Wilson C, Stephensen C. US youths in the
562 early stages of HIV disease have low intakes of some micronutrients important for
563 optimal immune function. J Am Diet Assoc 2004; 104(7): 1095-1101.
564 39. Institute of Medicine. Dietary Reference Intakes : Applications In Dietary
565 Assessment / Subcommittee On Interpretation And Uses Of Dietary Reference
566 Intakes And The Standing Committee On The Scientific Evaluation Of Dietary
567 Reference Intakes [e-book]. Washington, D.C.: National Academy Press, 2000.
568 40. Otten JJ, Hellwig JP, Meyers LD. Dietary Reference Intakes: The Essential
569 Guide to Nutrient Requirements. Washington, D.C.: The National Academies
570 Press, 2006.
571 41. Institute of Medicine. Dietary Reference Intakes: Recommended Intakes for

572 Individuals: 2010. Internet: http://fnic.nal.usda.gov/dietary-guidance/dietary-
573 reference-intakes/dri-tables (accessed 24 October 2011).
574 42. Ross AC, Judd S, Kumari M, Hileman C, Storer N, Labbato D*, et al.* Vitamin D is
575 linked to carotid intima-media thickness and immune reconstitution in HIV-
576 positive individuals. Antivir Ther 2011,16:555-563.
577 43. Choi AI, Lo JC, Mulligan K, Schnell A, Kalapus SC, Li Y*, et al.* Association of
578 vitamin D insufficiency with carotid intima-media thickness in HIV-infected
579 persons. Clin Infect Dis 2011,52:941-944.
580 44. Ganji V, Zhang X, Shaikh N, and Tangpricha V. Serum 25-hydroxyvitamin D
581 concentrations are associated with prevalence of metabolic syndrome and various
582 cardiometabolic risk factors in US children and adolescents based on assay-
583 adjusted serum 25-hydroxyvitamin D data from NHANES 2001-2006. Am J Clin
584 Nutr 2011; 94:225-33.
585 45. Ross AC, Judd S, Ziegler TR, Camacho-Gonzalez AF, Fitzpatrick AM, Hadley
586 GR, Grossmann RF, Seydafkan S, Seaton L, Mulligan MJ, Rimann N, Tangpricha
587 V, McComsey GA. Risk factors for vitamin D deficiency and relationship with
588 cardiac biomarkers, inflammation, and immune restoration in HIV-infected youth.
589 Antiviral Therapy, in press.
590 46. Barrios A, Blanco F, Garcia-Benayas T, Gomez-Viera J, de la Cruz J, Soriano V,
591 Gonzalez J. Effect of dietary intervention on highly active antiretroviral therapy-
592 related dyslipidemia. AIDS 2002; 16(15): 2079-2081.
593 47. Ross AC, McComsey GA. The role of vitamin D deficiency in the pathogenesis
594 of osteoporosis and in the modulation of the immune system in HIV-infected

patients. Clinic Rev Bone Miner Metab 2012. DOI 10.1007/s12018-012-9131-0.

48. Mehta S, Giovannucci E, Mugusi FM, Spiegelman D, Aboud S, Hertzmark E, Msamanga GI, Hunter D, Fawzi WW. Vitamin D status of HIV-infected women and its association with HIV disease progression, anemia, and mortality. PLoS ONE 2010; 5(1): e8770. doi:10.1371/journal.pone.0008770

49. Viard JP, Souberbielle JC, Kirk O, Reekie J, Knysz B, Losso M, Gatell J, Pedersen C, Bogner JR, Lundgren JD, *et al.* Vitamin D and clinical disease progression in HIV infection: results from the EuroSIDA study. AIDS 2011 June 19; 25(10): 1305–1315. doi: 10.1097/QAD.0b013e328347f6f7.

Table 1. Subject Characteristics

Mean ± SD or no. (%)		**HIV+ (n=175)**	**Controls (n=43)**	**P-value**
Age (Years)		17.44 ± 4.79	17.26 ± 6.14	0.688
Race	Black	166 (94.9%)	39 (90.7%)	0.183
	White	6 (3.4%)	4 (9.3%)	
	Latino	3 (1.7%)	0 (0%)	
Gender	Male	94 (53.7%)	24 (55.8%)	0.804
	Female	81 (46.3%)	19 (44.2%)	
Body Mass Index (kg/m^2)		22.53 ± 5.72	22.16 ±5.17	0.813
Waist-to-Hip Ratio		0.85 ± 0.08	0.83 ±0.07	0.124

Total Cholesterol (mg/dL)	155.29 ±38.929	150.67 ± 31.471	0.473
LDL-Cholesterol (mg/dL)	94.66 ± 26.217	87.86 ± 28.779	0.138
HDL-Cholesterol (mg/dL)	44.1 ± 15.923	51.16 ± 13.009	0.001
Triglycerides (mg/dL)	84.35 ± 53.8	58.56 ± 23.757	0.001
Currently on ART	119 (68%)		
ART-naïve	25 (14%)		
Perinatally-infected	113 (64%)		
Time from HIV diagnosis (years)	10.9 ± 10.4		
CD4+ cell count (cells/mm^3)	499 ± 361		
CD4+ cell count %	26.3 ± 12.1		
CD4+ cell count nadir (cells/mm^3)	291 ± 267		
ΔCD4 (nadir-current) cell count (N=156)	208 ± 255		
HIV-1 RNA <1000 copies/mL	101 (58%)		
Cumulative NRTI use (months)	74.3 ± 65.2		
Cumulative PI use (months)	53.3 ± 54.5		

ART, antiretroviral therapy; NRTI, nucleoside/nucleotide analogue reverse transcriptase inhibitor; PI, protease inhibitor

608

Table 2. Mean % Dietary Reference Intakes

	HIV-Infected (N=175)		Controls (N=43)	
	Mean (± SD) Intake that Met DRI	Mean (± SD) Intake That Did Not Meet DRI[2]	Mean (± SD) Intake That Met DRI	Mean (± SD) Intake That Did Not Meet DRI[2]
		MICRONUTRIENTS		
Vitamin A	--	77.6% ± 120	--	96.8% ± 75.0
Vitamin D	--	27.0% ± 21.3	--	36.0% ± 31.8
Vitamin E	--	54.1% ± 33.7	--	64.6% ± 27.9
Vitamin K[1]	115.0% ± 120.9	--	152.7% ± 146.0	--
Vitamin C	127.8% ± 109.4	--	170.4% ± 110.8	--
Thiamin	145.3% ± 53.6	--	170.8% ± 79.8	--
Riboflavin	154.5% ± 69.3	--	196.4% ± 101.4	--
Niacin	259.7% ± 84.2	--	285.4% ± 90.3	--
Pantothenic Acid [1]	--	87.5% ± 38.2	106.1% ± 54.8	--
B-6	143.0% ± 58.8	--	162.2% ± 64.8	--
Folate	--	96.8% ± 48.3	114.1% ± 54.4	--
B-12	208.4% ± 327.8	--	225.3% ± 178.0	--
Calcium	--	57.6% ± 27.2	--	69.5% ± 30.7
Phosphorus	117.1% ± 53.5	--	137.1% ± 58.6	--
Magnesium	--	63.7% ± 30.4	--	80.2% ± 40.4

Manganese [1]	114.8% ± 53.6	--	133.0% ± 48.9	--
Iron	126.6% ± 69.7	--	131.2% ± 66.8	--
Zinc	108.3% ± 46.9	--	111.7% ± 41.6	--
Copper	133.7% ± 174.0	--	151.9% ± 95.6	--
Selenium	206.6% ± 77.5	--	228.4% ± 85.8	--
Sodium [1]	--	236.3% ± 83.1	--	247.2% ± 74.3
Potassium [1]	--	39.5% ± 14.1	--	45.0% ± 12.7

MACRONUTRIENTS (% of total kilocalories)

	Mean (± SD) Intake Within AMDR	**Mean (± SD) Intake Exceeds AMDR**	**Mean (± SD) Intake Within AMDR**	**Mean (± SD) Intake Exceeds AMDR**
Fat	--	36.0% ± 5.7[3]	33.8% ± 5.1	--
CHO	48.2% ± 7.0	--	51.0% ± 5.6	--
Protein	15.7% ± 3.6	--	14.9% ± 2.6	--

AHA RECOMMENDATIONS[4]

Mean % (± SD) of AHA recommended intake

	Met	**Did not meet [2]**	**Met**	**Did not meet [2]**
Saturated fat	--	165.0% ± 32.8	--	158.8% ± 31.1
Trans- fat	--	145.1% ± 55.3	--	115.0% ± 57.1

Cholesterol	85.0% ± 45.0	--	87.7% ± 43.6	--
Fiber	--	43.3% ± 13.7	--	48.8% ± 15.7

[1] Micronutrient with adequate intake (AI); micronutrients without superscript have recommended dietary allowance (RDA)

[2]Significantly suboptimal intake with P <0.001

[3]Significantly suboptimal intake with P <0.05

[4]AHA recommendations: Saturated fat = 7% of kcals; trans-fat = 1% of kcals; cholesterol = 300mg/day; fiber = 14g/1000kcal

AHA, American Heart Association; AMDR, acceptable macronutrient distribution range; CHO, carbohydrate; DRI, dietary reference intake

609
610
611
612
613
614
615
616
617
618
619
620
621

Table 3. Associations between nutrient intake and HIV-related factors

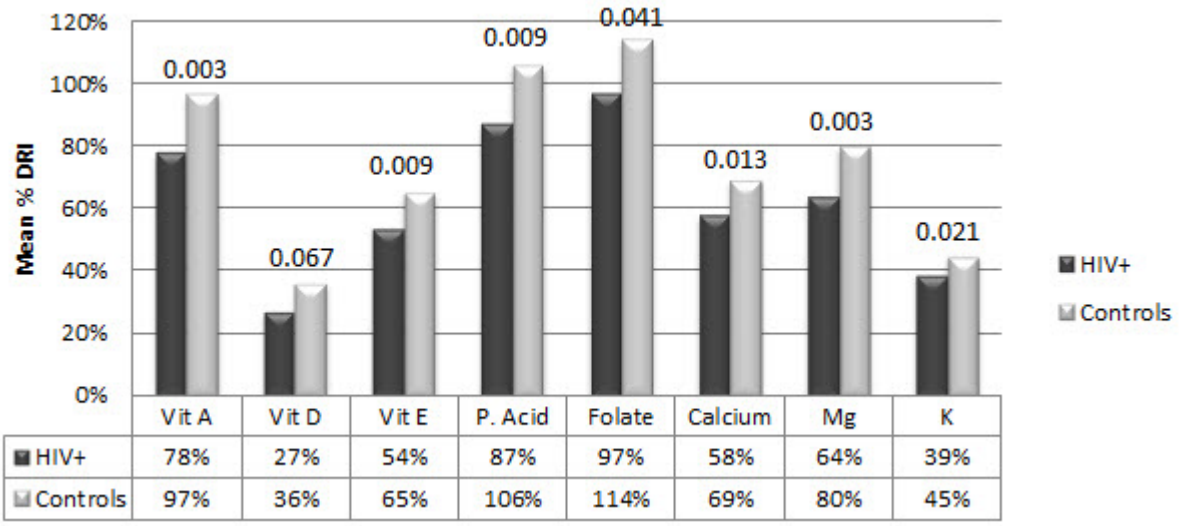
	Age		BMI		Current CD4+		Nadir CD4+	
	r	*P*	r	*P*	r	*P*	r	*P*
Calories	0.152	0.003	--	--	-0.116	0.024	-0.105	0.041
Phosphorus	0.253	<0.001	--	--	--	--	--	--
Sodium	0.133	0.027	--	--	--	--	--	--
Fat	0.122	0.017	--	--	--	--	--	--
Vitamin A	--	--	-0.135	0.008	--	--	0.102	0.047
Vitamin D	--	--	-0.108	0.034	--	--	--	--
Vitamin E	--	--	-0.179	<0.001	--	--	--	--
Riboflavin	--	--	-0.201	<0.001	0.120	0.019	0.129[1]	0.033[1]
Thiamin	--	--	-0.184	<0.001	--	--	--	--
Niacin	--	--	-0.162	0.002	--	--	--	--
Pantothenic Acid	--	--	-0.146	0.004	--	--	--	--
Vitamin B6	--	--	-0.173	0.001	--	--	--	--
Folate	--	--	-0.190	<0.001	--	--	--	--
Vitamin B12	--	--	-0.129	0.012	--	--	0.122[1]	0.044[1]
Magnesium	--	--	-0.229	<0.001	0.141 0.140[1]	0.006 0.020[1]	--	--
Iron	--	--	-0.122	0.017	--	--	--	--

Zinc	--	--	-0.179	<0.001	0.128 0.188[1]	0.013 0.050[1]	--	--
Copper	--	--	-0.210	<0.001	--	--	--	--
Potassium	--	--	-0.110	0.032	--	--	--	--
Selenium	--	--	-0.163	0.001	--	--	--	--

r=Pearson's correlation coefficient

[1] Includes only HIV+ subjects currently on antiretroviral medication (N=119)

No significant correlations were found between nutrients and those variables without numbers reported in the table, or for those nutrients not listed in the table.



	Vit A	Vit D	Vit E	P. Acid	Folate	Calcium	Mg	K
HIV+	78%	27%	54%	87%	97%	58%	64%	39%
Controls	97%	36%	65%	106%	114%	69%	80%	45%

Figure 1.

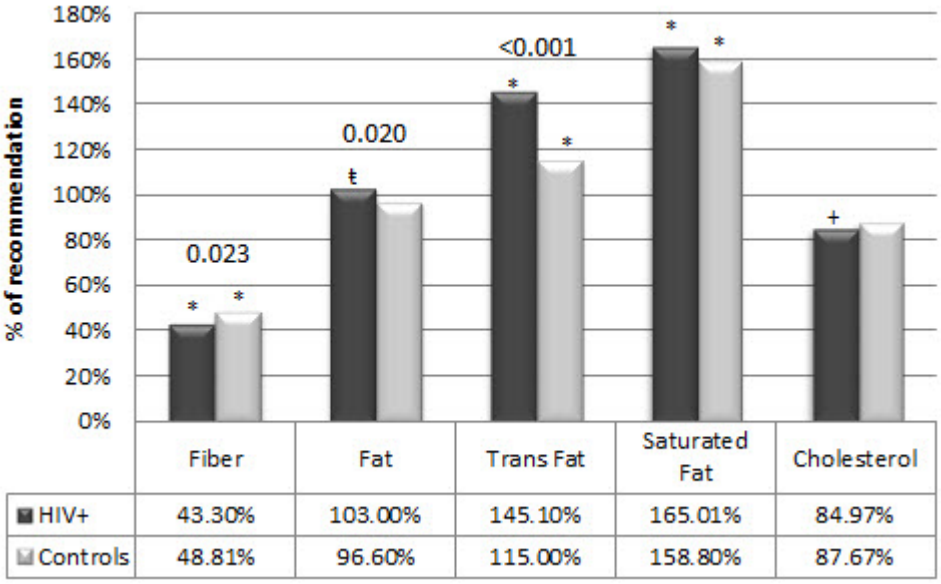

180%
160%
140%
120%
100%
80%
60%
40%
20%
0%
% of recommendation
0.023
0.020
<0.001
*
†
+
Fiber
Fat
Trans Fat
Saturated Fat
Cholesterol
HIV+
43.30%
103.00%
145.10%
165.01%
84.97%
Controls
48.81%
96.60%
115.00%
158.80%
87.67%

Figure 2.

668 FIGURE LEGEND

669

670 Figure 1. HIV+ Micronutrient Intake Deficiencies: Differences Between Groups in Mean

671 % DRI intake.

672

673 Figure 2. Differences Between Mean % Intake of AHA recommendation.

674 * denotes a significant difference from AHA recommendations with a P-value < 0.001

675 + denotes significantly within AHA recommendations with P-value <0.001

676 ŧ denotes significant difference from AHA recommendations with a P-value < 0.05

677 P-values above the bars show significant differences between HIV+ and Controls

678

679