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Research Article

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The Impact of Nutrition on CD4$^+$ Levels for HIV-positive Kenyan Adults

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Abstract

Background: HIV infection is highly prevalent in sub-Saharan Africa. Many people living with HIV infection in the region are malnourished or food insecure, which may affect HIV outcomes such as CD4$^+$ levels.

Study purpose and design: We conducted a cross-sectional study of ambulatory HIV-positive adult patients who lived in the vicinity of Kijabe, Kenya, a rural town served by the Kijabe Hospital outpatient clinic and 3 satellite clinics. All patients had received highly active antiretroviral therapy for at least 6 months. The purpose of the study was to determine the daily caloric and protein intake among these patients and their effects on CD4$^+$ levels.

Methods: All patients who consented to participate in the study completed dietary recall surveys to record their food and beverage intake for the previous 3 days. The medical records of the participants were reviewed to confirm that the respondents met the study inclusion criteria. Participant intake was compared to the recommended daily intake of calories and protein using predictive equations. Bivariate correlation was used to analyze the relationship between the CD4$^+$ level and meeting the recommended daily caloric and protein intake.

Results: Among the 122 participants who were eligible for the study, caloric and protein recommended intake, respectively, averaged 68.8% and 102.9% in males and 74.4% and 102.9% in females. There was a statistically significant positive correlation between protein consumption and CD4$^+$ levels for males but not for females.

Conclusion: The study results suggest that predictive equations currently in use underestimate protein recommendations for HIV-positive males. Further investigation is needed to re-evaluate current predictive equations and nutrient requirements in HIV-infected individuals. Research in these areas will likely benefit HIV outcomes as well as raise awareness of the importance to maximize local resources for food security.

Keywords: CD4$^+$ levels; Dietary recall; HIV; Kenya; Nutrition; Resource-poor

Abbreviations: AF: Activity Factor; BMR: Basic Metabolic Rate; BMI: Body Mass Index; HAART: Highly Active Antiretroviral Therapy; HB: Harris Benedict; HIV: Human Immunodeficiency Virus; IBW: Ideal Body Weight; SD: Standard Deviation; UNAIDS: Joint United Nations Programme on HIV/AIDS; WHO: World Health Organization

Introduction

Infection with the human immunodeficiency virus (HIV) affects public health worldwide. Of the 7 billion people in the world, an estimated 33.3 million are infected with HIV [1,2]. HIV infection is especially prevalent in sub-Saharan Africa; of the 883 million people in that part of the continent (13% of the world's population), 22.5 million are infected with HIV, representing 68% of all HIV cases worldwide [1-3]. Kenya is no exception; 6.7% of its adults are HIV positive [4].

People living with HIV are further burdened with another public health issue: malnutrition. Of the 842 million people estimated to be malnourished worldwide, 223 million (27%) live in sub-Saharan Africa. Of the 42 million people living in Kenya, 11 million (26%) are malnourished. Malnutrition and food insecurity are consequences of the economic status of a country [5]. Across Kenya, 45.9% of the population lives below the poverty line, most of who live in rural areas. This is understandable considering that the average gross national income per capita in Kenya is $840, compared to an average of over $50,000 in other industrialized nations [6].

Other investigators have demonstrated that malnutrition is associated with poor outcomes in HIV-infected individuals, including interruption of antiretroviral treatment, medication-associated complications, and decreased survival [7-10]. Given the effects of nutrition on the immune system this is not surprising. Schlesinger and Stekel describe caloric deficiencies associated with a blunted lymphocyte response while Li et al. note the adverse effects of protein malnutrition on amino acid metabolism [11,12]. In addition, nutritional supplementation has been shown to have a beneficial effect on HIV outcomes, such as decreased morbidity with vitamin A supplementation [13], delayed progression to World Health Organization (WHO) stage 4 with multivitamins in pregnant women [14], and improved immune cell number (CD4$^+$) with micronutrient supplementation [15].

Although the role of micronutrients is clearly defined in HIV infection, the effects of macronutrients, specifically protein, and caloric supplementation on HIV outcomes are not well established. Despite expansive literature emphasizing the benefits of increased caloric and protein intake in other catabolic states, such as burns and cancer [16-18], such benefits are not well defined for HIV infection. As a result, the likelihood of inappropriate supplementation and wasted resources increases among a population already succumbing to poverty-stricken living conditions.

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This cross-sectional study focuses on caloric and protein intake in ambulatory HIV-positive Kenyan adults receiving highly active antiretroviral therapy (HAART). We use predictive equations to determine the recommended daily caloric and protein intake for healthy adults and compare the actual caloric and protein intake of participants to an HIV outcome (CD4$^+$ level). We hypothesize that (1) on average, the recommended daily intake would not be met because of food insecurity, and (2) there will be a positive correlation between consuming the recommended daily intake and CD4$^+$ level.

Methods

Study participants

Participant demographic and clinical characteristics are described in Table 1. No socioeconomic data were available for our participants. However, our population consisted of rural agrarians who lived in the vicinity of Kijabe, Kenya, a town served by the Kijabe Hospital outpatient clinic and 3 satellite clinics.

Participants were enrolled in the study during monthly support group sessions held for HIV-positive patients. Adults who had WHO stage 3 or 4 HIV infection [19,20] and who had received HAART for at least 6 months were eligible for the study. Women who were pregnant and adults with incomplete medical records were excluded. For the purposes of the study, an adult was defined as ≥15 years of age for consistency with descriptions of the Joint United Nations Programme on HIV/AIDS (UNAIDS) [2].

Participant anthropometric data were gathered in the field and confirmed from the participants' medical records in the clinic. Data extracted from the medical records included age, sex, height, HIV diagnosis date, HAART initiation date, pregnancy history, WHO stage, current CD4$^+$ levels, and weight history.

The Institutional Review Board of the University of Texas Medical Branch in Galveston, Texas, USA approved the protocol before the start of the project. Signed consent was waived and replaced with verbal consent. Medical record numbers were used to maintain participant confidentiality.

Components of a typical Kenyan diet

Internet searches were performed to determine the ingredients that are typically used to prepare Kenyan foods and recipes. At the Kijabe Hospital cafeteria, study staff worked with the head cook during food preparation and recorded portion sizes, ingredients, food additives, and cooking methods. The foods served in the cafeteria are commonly consumed throughout Kenya. Study staff also worked with the registered dietitian at Kijabe Hospital to verify the recipes and ingredients. This information was supplemented by observation of common Kenyan foods prepared at various sites, including local restaurants, commercial and household kitchens, and town markets and grocery stores.

Tables 2 and 3 describe the 38 individual food items and 8 recipes we identified from the participant surveys. Commonly consumed foods include chapattis (unleavened flatbread), githeri (maize and kidney beans), sukuma wiki (kale stew), and ugali (cornmeal).

Travels to nearby regions to compare variations in foods revealed no major differences in diet. The regions we visited in Kenya and Tanzania were the Masai Mara National Reserve (African bush), Nairobi (urban), Kilimanjaro (rural), Lake Victoria (coastal), and Zanzibar (Muslim predominance). Dietary information was obtained through direct interviews with local people.

	Males (n=33)	Females (n=89)
Age, years [mean (range)]	42.4 (33.0-57.0)	39.4 (19.0-61.0)
BMI kg/m^2 [n (%)]		
<18.5	9 (27.3)	5 (5.6)
18.5–24.9	20 (60.6)	58 (65.2)
> 24.9	4 (12.1)	26 (29.2)
CD4+ level, cells/mm^3 [mean (range)]	297.6 (34.0–927.0)	351.1 (13.0-1010.0)
Time since diagnosis [months (range)]	29.0 (10.0–94.0)	33.0 (6.0-127.0)
Time since start of HAART [months (range)]	24.0 (7.0–80.0)	23.0 (6.0-97.0)
Average kilocalorie intake (kcal)	1712.0	1548.6
Average protein intake (g)	56.5	46.2

Abbreviations: BMI=body mass index; HAART=highly active antiretroviral treatment

Table 1: Demographics and clinical characteristics of HIV-infected people in Kijabe, Kenya.

Food	Amount	Kilocalories (kcal)	Protein (g)
Avocado	½ medium	160	3
Banana	4 inches (″)	60	0
Beef (ground)	3 ounces (oz)	200	24
Beef stew	1 cup (c)	160	10
Biscuit (cookie)	1 piece	15	0
Butter	1 tablespoon (T)	100	0
Beans (kidney)	½ c	100	7
Bread/toast	1 piece	80	2
Carrots (raw)	1 medium	25	1
Chai tea	1 c (4:1 water:milk)	40	2
Chicken	3 oz	120	21
Chicken soup	1 c	170	12
Eggs	1 egg	70	7
Githeri (corn/beans)	1 c	170	8
Goat meat	3 oz	120	23
Green gram (mung)	½ c	105	7
Mandazi (fried bread)	1 large piece	400	12
Mandazi	1 small piece	130	2
Milk (whole)	1 c	150	8
Mukimo (potato vegetable mash)	1 c	220	10
Nuts (ground)	¼ c	200	5
Omena (fish)	½ c	35	9
Orange	1 medium	60	1
Orange juice	1 c	110	0
Pancake	1 piece	100	3
Pear	1 medium	100	1
Potato (boiled)	½ c	70	1
Queen cake (pound cake)	2 pieces (3″ × 2″)	250	4
Rice	1 c	240	4
Spinach (cooked)	½ c	40	2
Sugar	1 teaspoon (tsp)	15	0
Sukuma wiki (kale stew)	1 c	200	9
Tilapia	3 oz	70	16
Ugali (cornmeal)	1 c	180	3
Ugali	1 portion	270	5
Uji (porridge)	1 c	110	3
Yam/kunde	1 c	200	4
Yam	1 medium (5″ × 2″)	115	2

Table 2: Kilocalorie and protein content of common Kenyan foods.

Chapatti (1 medium piece), 180 kilocalories, 3 g of protein
1 cups white flour and 1 cup whole-wheat flour
1/2 tsp salt
1 T oil
2 T water to make dough
1 T soft butter
Pan fry oil
Chicken Soup (1 cup), 160 kilocalories, 6 g of protein
3 Cups water
2 Tomatoes
1 Onion
1 Small chicken
Githeri (1 cup), 170 kilocalories, 8 g of protein
2 Cups corn
2 Cups cooked beans
Water to cover
Salt and pepper to taste
Mandazi (1 medium piece), 400 kilocalories, 8 g of protein
3 tsp baking powder
1 tsp cream of tartar
2 cups flour
½ cup sugar
2 Eggs cracked
Mukimo (1 cup), 220 kilocalories, 12 g of protein
2 Cups corn
2 Cups beans
2 Cups potatoes
2 Cups kale/pumpkin leaves
Water, salt, pepper to taste
Sukuma wiki (1 cup), 200 kilocalories, 4 g of protein
Fat for frying
1 Onion
2 Tomatoes (medium)
2 T flour
2 Pounds of sukuma
Ugali (1 cup), 180 kilocalories, 3 g of protein
1 Cup water
1 Cup cornmeal
1 tsp salt
Ugi/Sorghum (thin) porridge (1 cup), 110 kilocalories, 3 g of protein
¼ Cup millet flour
½ Cup corn flour
¼ Cup sorghum flour
4 Cups water

Table 3: Kenyan recipes with kilocalorie and protein content.

Three-day recall surveys

Three-day dietary recall surveys were chosen based on previous validation and successful use in other studies in Kenya [21,22]. These surveys were a subjective record of all food and beverages consumed over the previous 3 days.

After giving their consent, participants were given the survey to record their food and beverage intake. To help participants determine portion sizes, measuring cups were displayed and food samples were brought to each study site. To assist with data collection, native Kenyan volunteers were taught interview skills and were trained by the principle investigator to take dietary histories. Medical records were used to determine which respondents met the study inclusion criteria.

Predictive equations

Several steps were required to compare actual dietary intake to that recommended for the participants. First, to acquire the actual dietary intake, study staff used each participant's dietary recall survey to calculate the individual caloric (kilocalorie) and protein (gram) averages for the 3-days recorded [23]. Next, daily caloric recommendations were obtained by three steps: (1) the Harris-Benedict (HB) formula was used to calculate the basal metabolic rate (BMR) of each participant, (2) the BMR was multiplied by an activity factor of 1.3 to calculate recommended caloric intake, and (3) the recommended intake was multiplied by a factor of 25% according to WHO recommendations for people with stage 3 or 4 HIV infection [24]. We elected to use the HB equation because of its usefulness for group assessments in ambulatory populations [25,26]. We chose an activity factor of 1.3 (moderate) after direct observation of males and females at work in our study areas [27]. Because WHO does not recommend that HIV-positive adults increase their protein intake [24], we used the WHO recommendation of 0.83 g/kg for daily protein intake (equivalent to that of an otherwise healthy adult) for both male and female participants [18]. Finally, we used the Robinson formula [28] to calculate ideal body weight (IBW), which we used in all our equations. Table 4 provides a summary of each equation.

Statistical analysis

All data obtained from the 3-day dietary recall surveys, the medical chart review, and our predictive equations (HB and WHO) were entered into an Excel spreadsheet and analyzed using MedCalc version 11.3.1.0 (MedCalc Software, Ostend, Belgium). Subjects where separated into groups by sex for analysis. Age in years was treated as a continuous variable. Student's t-test and one-way analysis of variance were used for between group and within group comparisons. Associations were estimated with Pearson's product-moment correlation coefficient. Distribution assumptions were met with Student's t-test and Pearson's correlation coefficient. Bivariate correlation was used to analyze the relationship between $CD4^+$ level and consumption of the recommended daily caloric and protein intake. Statistical significance was set at $p \leq 0.05$.

Results

Participant data

As depicted in Table 1, the average $CD4^+$ levels for male participants (297.6 cells/mm^3) were less than those for female participants (351.1 cells/mm^3). For both sexes, most participants were diagnosed with HIV within 3 years prior to the study. The median time since initiation of HAART to the time of the survey was 24.0 months for males (range 7.0-80.0 months) and 23.0 months for females (range 6.0-97.0 months).

Three-day dietary recall survey data

Three-day dietary recall surveys were collected during meetings of the HIV support groups that were held outside the clinics in churches, outdoor areas, and other places. A total of 201 surveys were completed. Of these, 79 did not meet the study inclusion criteria because the respondents had incomplete medical records (n=29), had received HAART for <6 months (n=30), or were pregnant (n=20). For the final analysis, 122 (60.7%) surveys were used.

Predictive equation data

Caloric intake: Over 3 days, males averaged 1712.0 (standard deviation [SD] ± 577.8) calories and females averaged 1548.6 (SD ±

Harris-Benedict (HB) equation for kilocalories
Males: ((66+(13.7 × weight (kg))+(5 × height (cm)) – (6.8 × age))*AF)*WHO)
Females: ((655+(9.6 × weight (kg))+(1.8 × height (cm)) – (4.7 × age)*AF)*WHO)
World Health Organization equation for protein
Males and females: 0.83 g protein/kg IBW
Robinson formula for IBW
Males: IBW (kg)=52 kg+1.9 kg for each inch over 5 feet
Females: IBW (kg)=49 kg+1.7 kg for each inch over 5 feet

Abbreviations: AF=activity factor; Harris-Benedict (HB); IBW=ideal body weight; WHO=World Health Organization

Table 4: Predictive equations for kilocalories, protein, and ideal body weight (IBW).

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483.9) calories per day (*p*=0.20; Table 1). Using the HB equation, caloric intake averaged 68.8% (SD ± 23.3) among males and averaged 74.4% (SD ± 24.4) in females. There was no statistically significant difference between sexes (*p*=0.25).

Protein intake: Over 3 days, males averaged 56.5 (SD ± 25.6) grams and females averaged 46.2 (SD ± 18.2) grams of protein per day (Table 1). The WHO predictive equation was used to compare the recommended daily protein intake of 0.83 g/kg with the means of the actual daily protein intake of the participants. On average, males consumed 102.9% (SD ± 46.4) and females consumed 102.9% (SD ± 43.6) of daily recommended protein. There was no statistically significant difference between the sexes (*p*=0.94).

CD4$^+$ levels and nutrient intake: There was no correlation between CD4$^+$ levels and consuming the recommended daily caloric intake in either male or female participants (males: r=0.104, *p*=0.654; females: r=0.042, *p*=0.765; Figures 1 and 2). However, there was a statistically significant correlation between CD4$^+$ levels and consuming the recommended daily protein intake for males (r=0.706, *p*=0.000351; Figure 3); for females, there was no statistically significant correlation (r=-0.174, *p*=0.177; Figure 4).

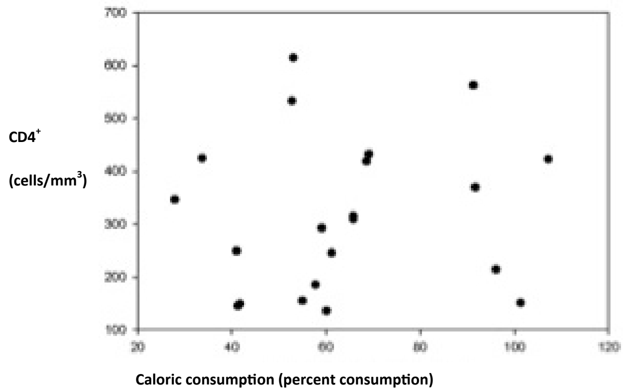

Figure 1: Scatter plot showing the percentages of recommended calories consumed versus CD4$^+$ levels among male participants. Pearson correlation coefficient r=0.104, p=0.654.

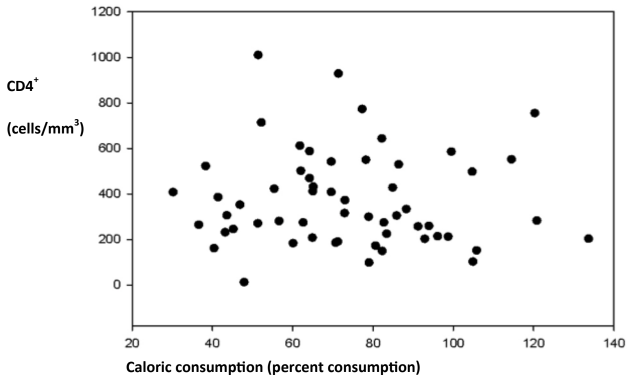

Figure 2: Scatter plot showing the percentages of recommended calories consumed versus CD4$^+$ levels among female participants. Pearson correlation coefficient r=0.042, *p*=0.765.

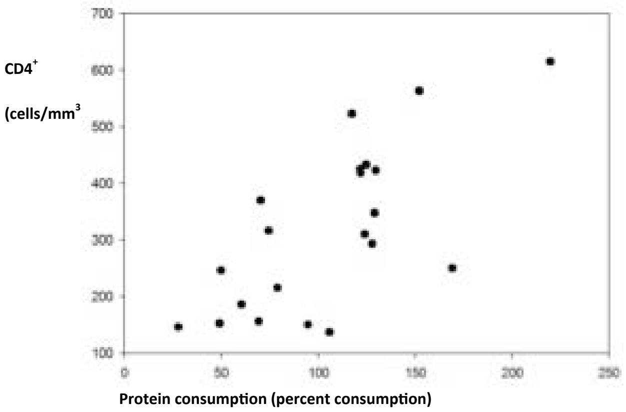

Figure 3: Scatter plot showing the percentages of recommended protein consumed versus CD4$^+$ levels among male participants. Pearson correlation coefficient r=0.706, *p*=0.000351.

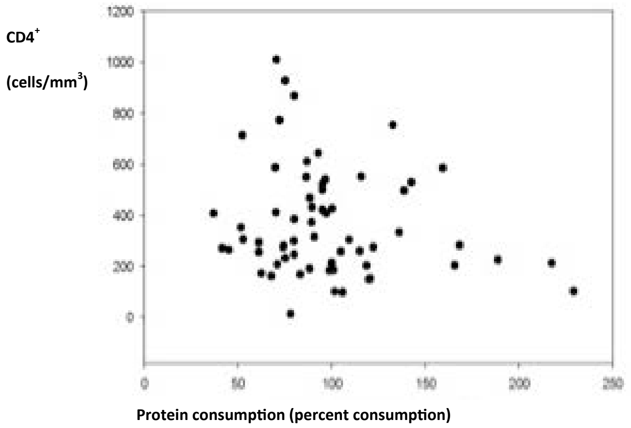

Figure 4: Scatter plot showing the percentages of recommended protein consumed versus CD4$^+$ levels and female participants. Pearson correlation coefficient r=-0.174, *p*=0.177.

Discussion

Though we hypothesized that caloric and protein recommendations would not be met in the HIV-infected Kenyan adults that we surveyed, we found that the average participant met the majority of recommendations. Both sexes met more than 65% of the recommended daily caloric intake and more than 100% of the recommended daily protein intake. Given the amount of added fat and oils in Kenyan foods (Tables 2 and 3), it is not surprising that many of the participants met the majority of recommended daily caloric intake. Although fat is not nutrient-dense, it is kilocalorie-dense and has a low cost/kilocalorie value. In contrast, it was surprising that many of the participants met the recommended daily intake of protein, because animal products are too expensive for most Kenyans. However, Kenyans eat several protein-rich non-animal foods (e.g., legumes, sukuma wiki). Unfortunately, non-animal proteins do not mimic the amino acid content of animal proteins [27].

Though we hypothesized that there would be a positive correlation between CD4$^+$ levels and meeting the recommended daily intake of calories and protein, we only found a positive correlation between CD4$^+$ levels and daily protein intake in males. We found it interesting that this occurred only with protein and only in males.

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There are several reasons why this finding might have occurred. First, unlike caloric predictive equations, the WHO protein predictive equation does not account for sex. Females typically have less muscle mass than males [29] and therefore, their protein needs are less [30]. Woods and Connors accounted for sex, recommending 100-150 g/day in HIV-positive males and 80-100 g/day in HIV-positive females [31]. Next, unlike caloric predictive equations, neither HIV diagnosis nor disease severity is accounted for in the protein predictive equation. Coyne-Meyers and Trombley noted in their review that some investigators recommend 1.0 to 1.4 g/kg for maintenance and 1.5 to 2.0 g/kg to promote anabolism for individuals infected with HIV [32]. Further, in our study, we observed that males had lower average CD4$^+$ levels than females. These absences of adjustments for sex, HIV-positive diagnosis, and severity of disease lead us to conclude that the WHO protein predictive equation may underestimate protein recommendations in males.

In the absence of a definitive standard for predicted protein recommendations, we elected to use the WHO predictive equation to allow comparison with other international studies. However, our findings infer that establishment of an international standard for a predictive protein recommendation equation in HIV-positive adults is incomplete and needs to be further investigated.

Protein quality versus quantity

Another explanation for why we found a positive correlation between CD4$^+$ levels and protein intake only in males could be the quality of protein consumed. Since non-animal proteins do not mimic the amino acid content of animal proteins, solely meeting a numerical value of recommended protein intake may not fully describe one's nutritional state. Failure to consume complete proteins (found in animal proteins or complementary non-animal proteins) could impair protein metabolism, especially in HIV-infected individuals. This impaired metabolism then leads to reduced humoral and cellular immunity and altered barrier function in highly metabolically active mucosal surfaces, resulting in increased infections and susceptibility to viral replication, which ultimately lowers CD4$^+$ levels [27]. Therefore, if females in our study had consumed higher quality protein sources, this could also explain their higher CD4$^+$ levels. Nevertheless, we did not observe significant differences in protein source consumption between males and females. However, a complete amino acid profile would be needed for a definitive answer.

Study limitations

There were several limitations in the design of our study. First, it is cross-sectional which did not permit longitudinal data. Because the dietary information was collected on a one-time basis, we could not recontact the participants to gather missing information. Additionally, the use of a recall survey may potentially have introduced bias and caused the observed differences between males and females. Although such bias was overcome to some extent by displaying measuring utensils and food samples at the study sites, it was still necessary for the subjects to remember what and how much they had eaten.

The need to obtain primary data in the field led to other limitations. The medical records we reviewed were paper charts that were located in four clinics separated by considerable distance. If more information was needed from a medical record, transit time and poor retrieval systems often resulted in the exclusion of a survey.

Furthermore, the association we observed between CD4$^+$ levels and protein intake could also be explained by reverse causality. Finally, because we did not analyze the amino acid content of the proteins or other nutrients the participants consumed, we were unable to analyze potential correlations between protein quality or other nutrients and CD4$^+$ levels.

Conclusion

We found that the typical HIV-positive participant in our study met his or her recommended daily caloric and protein intake. Further investigation is needed to determine the importance of nutrient quality versus quantity and HIV outcomes. We also found a positive correlation between meeting the recommended daily protein intake and CD4$^+$ levels in HIV-positive Kenyan males. We concluded that the WHO protein predictive equation for HIV-positive males might underestimate their dietary needs. Further study is warranted to obtain a protein predictive equation for HIV-infected adults that accounts for sex, HIV diagnosis, and HIV disease severity.

These findings and observations raise new questions that, if answered, could greatly improve the healthcare of HIV-infected people. The findings of additional investigations may result in higher efficiency of nutrition interventions, reduced food waste, and decreased cost. Specifically, these subtle, small changes may lead to advances that could benefit millions in resource-poor areas.

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