

Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Manka A. Banda

Date

Nutritional Indicators as Predictors of Opportunistic Infection among HIV-Positive Adults in
Kapiri, Zambia 2008-2009

By

Manka A. Banda
Master of Science in Public Health

Global Epidemiology

Kristin Wall, PhD
Committee Chair

Nutritional Indicators as Predictors of Opportunistic Infection among HIV-Positive Adults in
Kapiri, Zambia 2008-2009

By

Manka A. Banda

B.S. University of Maryland College Park, 2012
B.A., University of Maryland College Park, 2012

Thesis Committee Chair: Kristin Wall, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in Global Epidemiology
2016

Abstract

Nutritional Indicators as Predictors of Opportunistic Infection among HIV-Positive Adults in Kapiri, Zambia 2008-2009
By Manka Banda

Background: Body Mass Index (BMI) and Mid-Upper Arm Circumference (MUAC) are often used to assess malnutrition among people living with HIV (PLHIV) and predict HIV disease outcomes. These measures do not easily detect early changes in nutritional status, and impaired muscle strength, a condition occurring in disease-related malnutrition, may be a better measure of HIV-associated malnutrition and predictor of HIV disease progression. This study examined if, in addition to the typical anthropometric measures, measures of muscle strength and fatigue predict HIV disease progression.

Methods: From 2008-2009, HIV positive adult males and non-pregnant females were recruited and followed over a 9-month period at a Medecins Sans Frontiers (MSF) HIV clinic in Kapiri, Zambia. Diagnoses of any AIDS-Defining Opportunistic Infection (ADOI) were recorded and multivariate logistic regression models, stratified by sex and CD4 cell count, were assessed to determine the association between incident ADOI and baseline nutritional indicators.

Results: Twenty-eight male subjects (12%) and 47 female subjects (14%) were diagnosed with an ADOI. Seventeen (7.6%) PLHIV with high CD4 cell count (≥ 200 cells/mm³) and 37 (17.7%) with low CD4 cell count were diagnosed with an ADOI. Mean handgrip strength (OR=0.66, 95% CI: 0.55 – 0.78, $p < 0.0001$) and loss of appetite (OR=2.23, 95% CI: 1.01 – 4.93, $p = 0.0457$) were associated with incident ADOI among females. Mean handgrip strength was also found to be associated with ADOI among those with high CD4 cell count (OR=0.76, 95% CI: 0.62 – 0.93, $p = 0.0079$). Only MUAC was found to be significantly associated with incident ADOI in males and those low CD4 cell count.

Conclusions: As expected, lower MUAC was associated with incident ADOIs in this cohort of ART-naïve HIV-positive adults in Zambia, but surprisingly BMI was not. Two additional metrics of strength and fatigue may be clinically useful in predicting disease progression among women and people with higher initial CD4s. These findings warrant further study, and exploration of additional metrics of disease progression in men and sicker adults are needed.

Keywords: HIV disease outcomes, nutrition, opportunistic infections, Africa

Nutritional Indicators as Predictors of Opportunistic Infection among HIV-Positive Adults in
Kapiri, Zambia 2008-2009

By

Manka A. Banda

B.S. University of Maryland College Park, 2012
B.A., University of Maryland College Park, 2012

Thesis Committee Chair: Kristin Wall, PhD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Public Health
in Global Epidemiology
2016

BACKGROUND

Malnutrition, particularly wasting and micronutrient deficiencies which are common in people living with HIV (PLHIV) (1-4), is an important predictor of HIV disease outcomes and progression to AIDS (5-8). In clinical settings, Body Mass Index (BMI), Mid-Upper Arm Circumference (MUAC), and diet are often used to assess malnutrition among PLHIV to predict HIV disease outcomes (9,10). However, the sole use of these measures to identify HIV disease progression risks in PLHIV may be insufficient, as they do not easily detect early changes in nutritional status or distinguish between acute and chronic malnutrition (11). HIV-associated malnutrition - acute malnutrition caused by or exacerbated by HIV infection - may be a better predictor of HIV disease progression than chronic malnutrition (1).

Impaired muscle strength is a condition occurring in disease-related malnutrition, and various studies have shown a relationship between muscle strength and acute and chronic disease outcomes (11,12). This suggests that muscular strength and fatigue, when combined with other measures of malnutrition, may be a better measure of HIV-associated malnutrition and a better predictor of disease progression among PLHIV.

The purpose of this study was to determine if, in addition to the typical nutritional indicators used in clinical settings, measures of muscle strength and fatigue predict HIV disease progression. The study examines the association between a wide range of nutritional indicators, including muscle strength and fatigue, and incident AIDS-defining opportunistic infections (ADOIs) – a proxy measure of HIV disease progression. The occurrence of an incident opportunistic infection indicative of advanced HIV (stage 4), as described by the World Health Organization disease staging system for HIV infection and disease in adults and adolescents (13), was the outcome of interest in this study.

METHODS

Study Participants and Study Design

From 2008-2009, HIV-positive adults aged ≥ 18 years who attended HIV clinics sponsored by *Médecins Sans Frontières*'- Operational Centre Barcelona and Athens (MSF-OCBA) in Kapiri, Zambia, were enrolled in a 9-month prospective study. Enrolled patients were assessed at study admission and were followed during each of their regular visits (including hospitalizations and clinical consultations) and during quarterly nutritional follow-up visits (i.e., month 3 and month 6).

During each visit, MSF-OCBA HIV clinics used *Follow-Up of Clinical HIV Infection and AIDS* (FUCHIA v. 1.5.1) software to collect and store demographic, clinical, laboratory information. Nutritional information was collected separately using a survey administered at study admission and at the quarterly nutritional follow-up visits.

Eligible patients were ART-naïve (a non-ART users prior to and upon admission into the study), strong enough to stand up and be measured anthropometrically, and not pregnant/lactating. Women who experienced pregnancy during the study were censored. This study was approved by the Office for Human Research Protections-registered Institutional Review Boards at Emory University and by the Research Ethic Committee at University of Zambia.

Outcome of Interest

The occurrence of an opportunistic infection (OI) indicative of advanced HIV was the outcome of interest in this study. According to the World Health Organization disease staging system for HIV infection and disease in adults and adolescents, certain HIV-related diseases are considered severe enough to require ART initiation regardless of the patient's clinical condition

or immune status and diagnosis the patient with stage 4 HIV. These conditions include: *HIV wasting syndrome, Pneumocystis pneumonia, Recurrent severe bacterial pneumonia, Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site), Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs), Extrapulmonary tuberculosis, Kaposi's sarcoma, Cytomegalovirus infection (retinitis or infection of other organs), Central nervous system toxoplasmosis, HIV encephalopathy, Extrapulmonary cryptococcosis including meningitis, Disseminated non-tuberculous mycobacterial infection, Progressive multifocal leukoencephalopathy, Chronic cryptosporidiosis (with diarrhoea), Chronic isosporiasis, Disseminated mycosis (coccidiomycosis or histoplasmosis), Recurrent non-typhoidal Salmonella bacteraemia, Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours, Invasive cervical carcinoma, Atypical disseminated leishmaniasis, Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy (13).* During each visit, participants were evaluated for these symptoms. Participants newly diagnosed with at least one of these conditions during the 9 month follow-up period were considered to have had the outcome event of interest.

Non-nutritional Covariates

Age, gender, CD4 cell count, diagnosis of a non-severe HIV-associated symptom and diagnosis of a severe opportunistic infection were recorded at the time of entry into the study. Based on the World Health Organization (WHO) disease staging system for HIV infection and disease in adults and adolescents,¹¹ non-severe HIV-associated symptom was coded as a binary variable describing a diagnosis of at least one of the following conditions: weight loss, minor mucocutaneous manifestations, herpes zoster, recurrent upper respiratory tract infections,

bedridden during the last month, oral hairy leukoplakia, unexplained chronic diarrhea > 1 month, unexplained prolonged fever > 1 month, oral candidiasis, vulvovaginal candidiasis > 1 month.

The occurrence of a severe opportunistic infection at baseline was also a binary variable created to describe the diagnosis of at least one of the stage 4 HIV-associated symptoms. CD4 cell count was not included in the analysis for the entire cohort or by gender due to high number of patients missing CD4 cell count measurements.

Nutritional Covariates

Loss of appetite and loss of weight were self-reported. BMI and MUAC were measured by staff, and for the purpose of the analysis, were considered in continuous and categorical forms. Height was measured to the closest millimeter using an estadiometer while weight was measured to the closest 100 grams using standing scales. MUAC was measured to the closest millimeter using non-stretchable measuring tape. BMI was categorized into normal ($BMI \geq 18.5$), mild thin ($18.5 > BMI \geq 17.0$), and moderate/severe thin ($BMI < 17.0$) using a derived grading system for adult chronic energy deficiency.¹² Similarly, MUAC was categorized into 3 sex-specific categories used in conditions of food scarcity¹³: severe/extreme wasting (Male: < 200 mm; Female: < 190 mm), undernourished (Male: 200-229 mm; Female: 190-219mm), normal (Male: ≥ 230 mm; Female: ≥ 220 mm).

Muscular strength and fatigue were measured using two separate tests – the handgrip strength test and the sphygmomanometer test. The handgrip strength test required participants to squeeze a hand dynamometer 10 times consecutively with maximum strength at 30-second intervals. Grip strength (psi) was recorded at each handgrip, and the following summary statistics were obtained from the ten handgrip readings: mean, media, slope, and percentage strength lost between the maximum reading and final reading.

$$\textit{Percent strength loss * (\%)} = \frac{(\textit{maximum reading} - \textit{final reading})}{\textit{maximum reading}} \times 100\%$$

$$\textit{Slope of measures} = \frac{(\textit{final reading} - \textit{maximum reading})}{\textit{\# trials between the maximum and final readings}}$$

The sphygmomanometer test required participants to repeatedly squeeze a rubber bulb connected to a sphygmomanometer for 60 seconds or until failure due to muscle fatigue. The “sphygmomanometer” device was designed such that the cumulative pressure readings (mmHg) resulting from repeated squeezing could be recorded.¹⁴ The length of the test, cumulative pressure reading at the end of the test and the total number of hand squeezes were recorded and used to compute the average squeeze strength (mmHg/squeeze).

Food security at household level was assessed by inquiring the occurrence of the four scenarios in the last four months prior to the visit: (1) unable to eat the preferred types of food due to lack of resources (mild insecurity), (2) having to eat a smaller or fewer meals than usual (moderate insecurity), (3) no food stored in the participant’s household (severe insecurity), and (4) sleeping with an empty stomach (extreme insecurity). All nutritional indicators except height are considered time-varying. For the purpose of the analysis, BMI and MUAC were considered in continuous and categorical forms.

Data Management and Statistical Analysis

Data cleaning and analyses were conducted using MS Excel, SAS v9.3 and SAS v9.4 (Cary, NC). All missing values for the covariates at baseline were imputed based on the next non-missing values in a subsequent visit. The distribution of non-nutritional and nutritional

covariates were described by sex and CD4 outcome using frequencies and percentages for categorical covariates or using means and standard deviations for continuous covariates. Fisher exact chi-square tests (for categorical variables) and two-sample equal variance t-tests for normally distributed data and Mann-Whitney U for non-parametric data (for continuous variables) were used to compare the distribution of covariates by gender, CD4 cell count and the occurrence of an opportunistic infection

Logistic regression models (SAS v9.3 GENMOD procedure) were used to assess univariate and multivariate associations between covariates and opportunistic infection outcome. Only the covariates that had a significant crude odds ratio ($p=0.05$) in the univariate analyses were included in the full multivariate logistic regression models by sex and CD4 count. Variables entered into the full multivariate logistic models were assessed for collinearity. When 2 or more covariates were associated with a Conditional Index greater than 30 and variance decomposition proportion greater than or equal to 0.5, one of the covariates was dropped. The decision about which covariate to drop was based on prior knowledge and the clinical meaningfulness of the variable. Once a variable was dropped, the reduced model was assessed for multicollinearity again, and when no other covariates were found to be problematic, backwards selection with a cut off of $p=0.05$ was used to derive the final model.

RESULTS

Baseline non-nutritional and nutritional covariates

Descriptive statistics and the distribution of covariates for the total population and by gender are shown in Table 1.1. The cohort was comprised of 238 males (42%) and 334 females (58%). During the nine month follow up of the study, 28 male subjects (12%) and 47 female subjects (14%) were diagnosed with an ADOI.

Among the male subjects, those diagnosed with an ADOI were more likely to have a lower BMI (18.7 kg/m² vs 19.7 kg/m², $p=0.0077$), be classified as mildly thin (43% vs 18%, $p=0.0077$), have smaller MUAC (225.6 mm vs 239.5, $p=0.0105$) and be classified as undernourished (64% vs. 27%, $p= 0.003$) than those not diagnosed with an ADOI (Table 1.2). Additionally, they took longer to complete the sphygmomanometer test (51.7s vs 47s $p=0.0269$). They were less likely to be classified as having normal BMI (46% vs 70%, $p=0.0077$), or be classified as having normal MUAC (32% vs 67%, $p=0.0003$).

Among the female subjects, those diagnosed with an ADOI were more likely to have been diagnosed with a non-severe HIV-associated symptom (51% vs 33%, $p=0.049$), have lower BMI (18.8 kg/m² vs 21.0 kg/m², $p=0.0077$), be classified as moderately/severely thin (34% vs 10%, $p<0.0001$), have smaller MUAC (216.8 mm vs 246.9, $p<0.0001$) and be diagnosed with severe wasting (28% vs 4% $p= <0.0001$) than those not diagnosed with an ADOI (Table 1.3). Those diagnosed with ADOIs also performed worse on all measures of the sphygmomanometer test. They were less likely to be classified as having normal BMI (53% vs 76%, $p= <0.0001$), or be classified as having normal MUAC (53% vs 79%, $p= <0.0001$).

Among the those with high CD4 cell count, those diagnosed with an ADOI were more likely to have had a baseline opportunistic infection (12% vs 2%, $p=0.0332$), been diagnosed

with a non-severe HIV-associated symptom (59% vs 32%, $p=0.0273$), suffer from severe/extreme wasting (18% vs 2%, $p=0.0053$) and perform worse on all measures of handgrip strength test except the slope. In contrast, age, continuous MUAC, categorical MUAC, loss of appetite, mean and median handgrip strength, and percent of handgrip strength lost were significantly associated with incident OI among those with low CD4 cell count.

Univariate analysis (Table 2)

Among males, a significant association between ADOI and the following variables was found; continuous BMI, continuous MUAC, categorical MUAC and sphygmomanometer test length. Among women, categorical CD4 cell count, occurrence of non-severe HIV associated symptoms, continuous BMI, categorical BMI, continuous MUAC, categorical MUAC, loss of appetite, mean handgrip strength, median handgrip strength, percent handgrip strength lost and all measures of the sphygmomanometer test were significantly associated with incident ADOI. When continuous BMI and categorical BMI or continuous MUAC and categorical MUAC were both significantly associated with ADOI, only the categorical variable was entered into the full model because it was deemed more clinically meaningful. Though categorical CD4 count could have been entered into the full model for women, we decided to leave it out because including it would have reduced our sample size and event count considerably.

Among those with high CD4 count, continuous MUAC, categorical MUAC, mean handgrip strength, median handgrip strength, percent handgrip strength lost and total number of hand squeezes in the sphygmomanometer test were significantly associated with incident ADOI. As with male and female subject models, categorical MUAC, instead of continuous MUAC was entered into the full multivariate model. Among those with low CD4 count, occurrence of non-severe HIV associated symptoms, continuous BMI, categorical BMI, continuous MUAC,

categorical MUAC, loss of appetite, mean handgrip strength, median handgrip strength, percent handgrip strength lost, sphygmomanometer test length and cumulative hand squeeze strength were associated with incident ADOI. Categorical BMI and categorical MUAC were used in the full models.

Multivariate analysis (Table 3)

After backwards selection was performed, the only variable that remained in the final models for the male cohort and those with low CD4 cell count was categorical MUAC. The odds of incident ADOI among undernourished men was 2.19 times (95% CI: 1.18 – 4.06, $p=0.0125$) that among men with normal MUAC, and the odds of ADOI among men with severe wasting was 4.80 times (95% CI: 1.4 – 16.45, $p=0.0125$) that among men with normal MUAC. The same trend was seen among those with low CD4 cell count.

Mean handgrip strength ended up in the final models for both the female cohort and those with high CD4 cell count. Self-reported loss of appetite was also significantly associated with ADOI among females after adjusting for mean handgrip strength.

DISCUSSION

Among HIV positive, ART-naïve Zambians in this study, the association between nutrition indicators and incident opportunistic infection appeared to differ by sex and by CD4 cell count. It is important to explore such predictive metrics in ART-naïve persons since, even today, the majority of ART eligible HIV+ patients in sub-Saharan Africa are not able to access treatment (14).

As expected, lower MUAC indicating severe or extreme wasting was associated with incident ADOI among males (categorical MUAC) and females (continuous MUAC). Surprisingly, BMI was not associated with ADOI for either gender. Measures of muscular strength were considered in this study because BMI and MUAC alone may be insufficient to differentiate between chronic and HIV-disease specific under-nutrition. We did find that measures of muscular strength and fatigue were predictive of ADOI, but interestingly only for women and not men. Loss of appetite was also associated with opportunistic infection in adjusted models, but again only for women.

MUAC was also significantly associated with incident ADOI among patients with CD4 cell count less than 200 cell/mm³, but not for those with a CD4 count greater than or equal to 200 cell/mm³. The low number of incident ADOIs among those with high CD4 count in this study may explain why no association between MUAC and incident ADOI was noticed in this relatively healthy population (i.e., lack of power). However, it is possible that in HIV-infected individuals with high CD4 count, MUAC is truly not predictive of ADOI. In previous literature, increases in MUAC as a result of food supplementation have been associated with increases in CD4 count among HIV positive, ART naive persons in Sub-Saharan Africa (15). It is also well established that high CD4 cell count reduces the risk of opportunistic infection in HIV infected

persons, and a recent study of HIV infected persons followed in the Swiss HIV Cohort Study revealed that among patients with CD4 counts greater than 500/ μ L, chronic HIV infection was the cause of AIDS-defining opportunistic infections in a minority of cases; other immune-compromising conditions were more likely to explain opportunistic infections (16). If MUAC is predictive of high CD4 and among patients with high CD4 cell count, other immune-compromising infections unrelated to MUAC explain most OIs, then MUAC would likely not be associated with OI in this group of HIV patients.

Interestingly, measures of strength and fatigue did predict ADOI in those with higher CD4, but not lower CD4. Since our study population only dealt with ART-naïve patients, it could be that these differences arise from differences in the time between HIV infection and clinical assessment. If patients with lower CD4 were seen long after infection, and had become sicker, BMI and MUAC may have changed sufficiently to become more meaningful predictors than muscle strength. In later stages of malnutrition, muscle strength may be correlated with BMI and MUAC.

We examined measures of strength and fatigue because in clinical settings they allow us to diagnosis disease-associated malnutrition earlier than typical anthropometric measures. Our results indicate that, in clinical settings, these measures of strength and fatigue could be useful in predicting ADOIs for women and those with higher CD4 cell count, but not for men and those with lower CD4. Further studies looking at the different types of ADOIs these measures predict may be helpful in understanding the extent to which these predictors can be used in clinical settings. Additionally, when using these indicators in clinical settings it may be important to consider the time after HIV infection at which patients are assessed. There is also a need to look

at other measures of strength and fatigue in order to develop better predictors of HIV outcome among men and those who are sicker.

Strengths and Limitations

There are several limitations to this study that may have ultimately affected the results. Socioeconomic variables were not included in this analysis; therefore, the inability to control for such variables as potential confounders may have resulted in an inaccurate relationship between nutritional indicators and ADOI. This may have also impacted the overall response regarding food insecurity among the studied population. In addition, people who attend the clinic may share certain characteristics that are not necessarily representative of the general population, resulting in potential selection bias. Our follow-up was relatively short, and nutritional indicators of disease progression in longer-term cohorts are needed.

Conclusions

We found that, as expected, lower MUAC was associated with incident ADOIs in this cohort of ART-naïve HIV-positive adults in Zambia, but surprisingly that BMI was not. Interestingly, two additional metrics of strength and fatigue may be clinically useful in predicting disease progression among women and people with higher initial CD4s. These findings warrant further study, and exploration of additional metrics of disease progression in men and sicker adults are needed.

REFERENCES

1. Malvy D, Thiebaut R, Marimoutou C & Dabis F (2001) Weight loss and body mass index as predictors of disease progression to AIDS in adults. Aquitaine Cohort, France, 1985–1997. *J Am Coll Nutr* 20, 609–615.
2. J.H. Skurnick, J.D. Bogden,, H. Baker,, et al. Micronutrient profiles in HIV-1 infected heterosexual adults *J Acquir Immune Defic Syndr Hum Retrovirol*, 12 (1996), pp. 75–83
3. R. Ullrich, T. Schneider, W. Heise, et al. Serum carotene deficiency in HIV-infected patients: Berlin Diarrhoea/Wasting Syndrome Study Group *AIDS*, 8 (1994), pp. 661–665
4. G.C. John, R.W. Nduati, D. Mbori-Ngacha, et al. Genital shedding of human immunodeficiency virus type 1 DNA during pregnancy: association with immunosuppression, abnormal cervical or vaginal discharge, and severe vitamin A deficiency *J Infect Dis*, 175 (1997), pp. 57–62
5. R.D. Semba, A.M. Tang Micronutrients and the pathogenesis of human immunodeficiency virus infection *Br J Nutr*, 81 (1999), pp. 181–189
6. W.W. Fawzi, et al. A randomized trial of vitamin A supplements I relation to mortality among human immunodeficiency virus-infected and uninfected children in Tanzania *Pediatr Infect Dis J*, 18 (1999), pp. 127–133
7. R.D. Semba, et al. Vitamin A deficiency and wasting as predictors of mortality in human immunodeficiency virus-infected injection drug users *JIF*, 171 (1994), pp. 1196–1202
8. A.M. Tang, et al. Association between serum vitamin A and E levels and HIV-1 disease progression *AIDS*, 11 (1997), pp. 613–620
9. Wanke CA, Silva M, Knox TA, Forrester J, Speigelman D, Gorbach SL. Weight loss and wasting remain common complications in individuals infected with human

- immunodeficiency virus in the era of highly active antiretroviral therapy. *Clin Infect Dis* (2000); 31: 803–805.
10. Tang AM, Forrester J, Spiegelman D, Knox TA, Tchetgen E, Gorbach SL. Weight loss and survival in HIV-positive patients in the era of highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* (2002); 31: 230–236.
 11. J. Humphreys, M.P. de la, S. Hirsch, G. Barrera, V. Gattas, D. Bunout Muscle strength as a predictor of loss of functional status in hospitalized patients *Nutrition*, 18 (2002), pp. 616–620
 12. D.R. Hunt, B.J. Rowlands, D. Johnston Hand grip strength—a simple prognostic indicator in surgical patients *JPEN J Parenter Enteral Nutr*, 9 (1985), pp. 701–704
 13. WHO Case Definition of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-related Disease in Adults and Children. France: World Health Organization; 2007.
 14. World Health Organisation (WHO), Joint United Nations Programme on HIV/AIDS (UNAIDS) and United Nations Children Fund (UNICEF), GLOBAL HIV/AIDS RESPONSE—Epidemic update and health sector progress towards Universal Access—Progress Report 2011. Geneva, WHO, UNAIDS, UNICEF. 2011.
 15. Maluccio, J.A., et al., Improving Health-Related Quality of Life among People Living with HIV: Results from an Impact Evaluation of a Food Assistance Program in Uganda. *PLoS One*, 2015. 10(8): p. e0135879.
 16. Gisler, Valentin, et al. "AIDS defining opportunistic infections in patients with high CD4 counts in the combination antiretroviral therapy (cART) era: things ain't what they used to be." *Journal of the International AIDS Society* 17.4 (2014).

Table 1.1: Nutritional assessment at baseline by gender among HIV + Adults in Kapiri, Zambia, 2008-2009

	Total (N = 572)		Men (N = 238)		Women (N = 334)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Non-nutritional covariates							
Age (years)	32.9	7.3	34.6	7.0	31.7	7.3	<.0001
Baseline CD4 (cell/mm ³)	252.5	202.2	234.6	173.0	265.2	219.8	0.562
Baseline Opportunistic infection	43	8%	21	9%	22	7%	0.3173
Occurrence of non-severe HIV-associated symptoms							0.0201
Yes	225	39%	107	45%	118	35%	
No	347	61%	131	55%	216	65%	
Anthropometry							
Continuous BMI (kg/m ²)	20.2	3.3	19.6	2.3	20.7	3.8	<.0001
Categorical BMI							0.0598
Normal	404	71%	160	67%	244	73%	
Mild Thin	93	16%	49	21%	44	13%	
Moderate/Severe Thin	75	13%	29	12%	46	14%	
Continuous MUAC (mm)	240.7	33.3	237.9	27.0	242.7	37.1	0.1163
Categorical MUAC							0.0004
Normal	398	70%	148	62%	248	75%	
Undernourished	131	23%	74	31%	56	17%	
Severe/Extreme Wasting	40	7%	15	6%	25	8%	
Appetite and Weight Loss							
Loss of Weight							0.004
Yes	455	80%	203	85%	252	75%	
No	117	20%	35	15%	82	25%	
Loss of Appetite							0.2083
Yes	299	52%	117	49%	182	54%	
No	273	48%	121	51%	152	46%	
Handgrip Strength/Fatigue Test							
Mean of measures (psi)	9.9	3.0	11.6	3.1	8.7	2.3	<.0001
Median of measures (psi)	9.9	3.1	11.6	3.1	8.6	2.4	<.0001
Slope of measures	-0.3	0.1	-0.3	0.1	-0.3	0.1	0.3364
Percent strength loss (%)	24.0	11.0	20.2	9.6	26.8	11.2	<.0001

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.1 Continued: Nutritional assessment at baseline by gender among HIV + Adults in Kapiri, Zambia, 2008-2009

	Total (N = 572)		Men (N = 238)		Women (N = 334)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Sphygmomanometer Test							
Test length (sec)	51.1	9.3	47.6	10.0	53.6	7.9	<.0001
Total number of grip	64.7	16.9	61.4	17.9	67.1	15.8	0.0001
Average grip strength (mmHg/grip)	2.2	0.9	2.4	0.9	2.0	0.8	<.0001
Cumulative handgrip strength (mmHg)	129.9	32.9	137.8	28.1	124.1	35.0	<.0001
Household Food Security							
Unable to eat preferred food							0.0807
Yes	238	42%	89	38%	149	45%	
No	331	58%	148	62%	183	55%	
Have smaller/fewer meals							0.0283
Yes	237	42%	86	36%	151	45%	
No	332	58%	151	64%	181	55%	
No food storage in household							0.0087
Yes	186	33%	63	27%	123	37%	
No	383	67%	174	73%	209	63%	
Sleeping empty stomach							0.0078
Yes	184	32%	62	26%	122	37%	
No	385	68%	175	74%	210	63%	

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.2: Nutritional assessment at baseline by new opportunistic infection among HIV + Adult Men in Kapiri, Zambia, 2008-2009

	Total (N =238)		Had New Infection (N=28)		No New Infection (N=210)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Non-nutritional covariates							
Age (years)	34.6	7.0	33.9	7.0	34.7	7.0	0.5835
Baseline CD4 (cell/mm ³)	234.6	173.0	185.0	126.5	241.2	177.6	0.1624
Baseline Opportunistic Infection	21	9%	3	11%	18	9%	0.7073
Occurrence of non-severe HIV-associated symptoms							0.8677
Yes	107	45%	13	46%	94	45%	
No	131	55%	15	54%	116	55%	
Anthropometry							
Continuous BMI (kg/m ²)	19.6	2.3	18.7	1.6	19.7	2.4	0.0375
Categorical BMI							0.0077
Normal	160	67%	13	46%	147	70%	
Mild Thin	49	21%	12	43%	37	18%	
Moderate/Severe Thin	29	12%	3	11%	26	12%	
Continuous MUAC (mm)	237.9	27.0	225.6	17.5	239.5	27.7	0.0105
Categorical MUAC							0.0003
Normal	148	62%	9	32%	139	67%	
Undernourished	74	31%	18	64%	56	27%	
Severe/Extreme Wasting	15	6%	1	4%	14	7%	
Appetite and Weight Loss							
Loss of Weight							0.229
Yes	203	85%	26	93%	177	84%	
No	35	15%	2	7%	33	16%	
Loss of Appetite							0.0883
Yes	117	49%	18	64%	99	47%	
No	121	51%	10	36%	111	53%	
Handgrip Strength/Fatigue Test							
Mean of measures (psi)	11.6	3.1	11.0	2.2	11.7	3.1	0.3105
Median of measures (psi)	11.6	3.1	11.0	2.3	11.7	3.2	0.2838
Slope of measures	-0.3	0.1	-0.3	0.1	-0.3	0.1	0.9813
Percent strength loss (%)	20.2	9.6	20.7	7.3	20.1	9.8	0.7664

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.2 Continued: Nutritional assessment at baseline by new opportunistic infection among HIV + Adult Men in Kapiri, Zambia, 2008-2009

	Total (N =238)		Had New Infection (N=28)		No New Infection (N=210)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Sphygmomanometer Test							
Test length (sec)	47.6	10.0	51.7	7.9	47.0	10.2	0.0269
Total number of grip	61.4	17.9	57.3	16.3	61.9	18.1	0.2189
Average grip strength (mmHg/grip)	2.4	0.9	2.8	1.5	2.4	0.8	0.055
Cumulative handgrip strength (mmHg)	137.8	28.1	140.8	25.7	137.4	28.4	0.5629
Household Food Security							
Unable to eat preferred food							0.529
Yes	89	38%	9	32%	80	38%	
No	148	62%	19	68%	129	62%	
Have smaller/fewer meals							0.6272
Yes	86	36%	9	32%	77	37%	
No	151	64%	19	68%	132	63%	
No food storage in household							0.5109
Yes	63	27%	6	21%	57	27%	
No	174	73%	22	79%	152	73%	
Sleeping empty stomach							0.5441
Yes	62	26%	6	21%	56	27%	
No	175	74%	22	79%	153	73%	

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.3: Nutritional assessment at baseline by new opportunistic infection among HIV + Adult Women in Kapiri, Zambia, 2008-2009

	Total (N =334)		Had New Infection (N=47)		No New Infection (N=287)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Non-nutritional covariates							
Age (years)	31.7	7.3	30.6	7.1	31.9	7.3	0.2851
Baseline CD4 (cell/mm ³)	265.2	219.8	196.5	239.2	275.4	215.5	0.0541
Baseline Opportunistic Infection	22	7%	3	6%	19	7%	0.9515
Occurrence of non-severe HIV-associated symptoms							0.0149
Yes	118	35%	24	51%	94	33%	
No	216	65%	23	49%	193	67%	
Anthropometry							
Continuous BMI (kg/m ²)	20.7	3.8	18.8	3.5	21.0	3.8	0.0001
Categorical BMI							<.0001
Normal	244	73%	25	53%	219	76%	
Mild Thin	44	13%	6	13%	38	13%	
Moderate/Severe Thin	46	14%	16	34%	30	10%	
Continuous MUAC (mm)	242.7	37.1	216.8	37.0	246.9	35.4	<.0001
Categorical MUAC							<.0001
Normal	248	75%	25	53%	225	79%	
Undernourished	56	17%	9	19%	48	17%	
Severe/Extreme Wasting	25	8%	13	28%	12	4%	
Appetite and Weight Loss							
Loss of Weight							0.097
Yes	252	75%	40	85%	212	74%	
No	82	25%	7	15%	75	26%	
Loss of Appetite							0.001
Yes	182	54%	36	77%	146	51%	
No	152	46%	11	23%	141	49%	
Handgrip Strength/Fatigue Test							
Mean of measures (psi)	8.7	2.3	6.8	2.0	8.9	2.3	<.0001
Median of measures (psi)	8.6	2.4	6.8	2.0	8.9	2.3	<.0001
Slope of measures	-0.3	0.1	-0.3	0.1	-0.3	0.1	0.4306
Percent strength loss (%)	26.8	11.2	34.3	13.7	25.6	10.3	<.0001

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests or Mann-Whitney U if non-parametric

Table 1.3 Continued: Nutritional assessment at baseline by new opportunistic infection among HIV + Adult Women in Kapiri, Zambia, 2008-2009

	Total (N =334)		Had New Infection (N=47)		No New Infection (N=287)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Sphygmomanometer Test							
Test length (sec)	53.6	7.9	56.3	6.6	53.3	8.0	0.0249
Total number of grip	67.1	15.8	61.8	16.2	67.9	15.6	0.0212
Average grip strength (mmHg/grip)	2.0	0.8	1.7	0.9	2.0	0.7	0.0059
Cumulative handgrip strength (mmHg)	124.1	35.0	99.2	48.7	127.7	31.0	<.0001
Household Food Security							
Unable to eat preferred food							0.3983
Yes	149	45%	18	39%	131	46%	
No	183	55%	28	61%	155	54%	
Have smaller/fewer meals							0.2109
Yes	151	45%	17	37%	134	47%	
No	181	55%	29	63%	152	53%	
No food storage in household							0.1836
Yes	123	37%	13	28%	110	38%	
No	209	63%	33	72%	176	62%	
Sleeping empty stomach							0.1984
Yes	122	37%	13	28%	109	38%	
No	210	63%	33	72%	177	62%	

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests or Mann-Whitney U if non-parametric

Table 1.4: Nutritional assessment at baseline by new opportunistic infection among those with high CD4 cell count in Kapiri, Zambia, 2008-2009

	Total (N = 224)		Had New Infection (N=17)		No New Infection (N=207)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Non-nutritional covariates							
Age (years)	33.1	6.9	33.2	6.7	33.1	7.0	0.9197
Baseline Opportunistic Infection	7	3%	2	12%	5	2%	0.0332
Occurrence of non-severe HIV-associated symptoms							0.0273
Yes	77	34%	10	59%	67	32%	
No	147	66%	7	41%	140	68%	
Anthropometry							
Continuous BMI (kg/m ²)	20.8	3.3	19.4	2.9	20.9	3.3	0.0854
Categorical BMI							0.4823
Normal	171	76%	11	65%	160	77%	
Mild Thin	33	15%	4	24%	29	14%	
Moderate/Severe Thin	20	9%	2	12%	18	9%	
Continuous MUAC (mm)	248.1	31.5	230.8	35.3	249.5	30.8	0.0186
Categorical MUAC							0.0053
Normal	179	81%	12	71%	167	81%	
Undernourished	35	16%	2	12%	33	16%	
Severe/Extreme Wasting	8	4%	3	18%	5	2%	
Appetite and Weight Loss							
Loss of Weight							0.3517
Yes	178.0	79%	15.0	88%	163.0	79%	
No	46	21%	2	12%	44	21%	
Loss of Appetite							0.0987
Yes	102	46%	11	65%	91	44%	
No	122	54%	6	35%	116	56%	
Handgrip Strength/Fatigue Test							
Mean of measures (psi)	10.3	2.9	8.4	3.3	10.5	2.8	0.0056
Median of measures (psi)	10.3	2.9	8.5	3.2	10.4	2.8	0.0089
Slope of measures	-0.3	0.1	-0.3	0.1	-0.3	0.1	0.5919
Percent strength loss (%)	22.9	9.8	28.6	15.6	22.5	9.1	0.0149

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.4 Continued: Nutritional assessment at baseline by new opportunistic infection among those with high CD4 cell count in Kapiri, Zambia, 2008-2009

	Total (N = 224)		Had New Infection (N=17)		No New Infection (N=207)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Sphygmomanometer Test							
Test length (sec)	50.2	9.5	52.2	9.0	50.0	9.5	0.3758
Total number of grip	66.2	17.1	57.8	18.4	66.9	16.9	0.0415
Average grip strength (mmHg/grip)	2.2	0.8	2.1	0.9	2.2	0.8	0.8751
Cumulative handgrip strength (mmHg)	134.2	29.3	124.0	44.8	134.9	27.8	0.1641
Household Food Security							
Unable to eat preferred food							0.5158
Yes	101	45%	6	38%	116	56%	
No	122	55%	10	63%	112	54%	
Have smaller/fewer meals							0.4923
Yes	102	46%	6	38%	96	46%	
No	121	54%	6	38%	111	54%	
No food storage in household							0.8571
Yes	79	35%	6	38%	73	35%	
No	144	65%	10	63%	73	35%	
Sleeping empty stomach							0.8262
Yes	78	35%	6	38%	72	35%	
No	145	65%	10	63%	135	65%	

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.5: Nutritional assessment at baseline by new opportunistic infection among those with low CD4 cell count in Kapiri, Zambia, 2008-2009

	Total (N = 209)		Had New Infection (N=37)		No New Infection (N=172)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Non-nutritional covariates							
Age (years)	33.9	7.3	31.2	7.0	34.4	7.2	0.0141
Baseline Opportunistic Infection	25	12%	3	8%	22	13%	0.4259
Occurrence of non-severe HIV-associated symptoms							0.1248
Yes	103	49%	14	38%	89	52%	
No	106	51%	23	62%	83	48%	
Anthropometry							
Continuous BMI (kg/m ²)	19.6	3.0	18.9	3.2	19.8	2.9	0.0830
Categorical BMI							0.1345
Normal	139	67%	20	54%	119	69%	
Mild Thin	35	17%	7	19%	28	16%	
Moderate/Severe Thin	35	17%	10	27%	25	15%	
Continuous MUAC (mm)	233.6	32.0	219.2	31.9	236.8	31.2	0.0022
Categorical MUAC							0.0084
Normal	125	60%	14	38%	111	65%	
Undernourished	64	31%	17	46%	47	27%	
Severe/Extreme Wasting	19	9%	6	16%	13	8%	
Appetite and Weight Loss							
Loss of Weight							0.3599
Yes	176.0	84%	33	89%	143	83%	
No	33	16%	4	11%	29	17%	
Loss of Appetite							0.0257
Yes	124	59%	28	76%	96	56%	
No	85	41%	9	24%	76	44%	
Handgrip Strength/Fatigue Test							
Mean of measures (psi)	9.4	3.0	8.4	2.6	9.6	3.1	0.0414
Median of measures (psi)	9.4	3.1	8.3	2.6	9.6	3.1	0.0313
Slope of measures	-0.3	0.1	-0.3	0.1	-0.3	0.1	0.2831
Percent strength loss (%)	24.8	12.3	29.0	13.4	24.0	11.9	0.0325

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 1.5 Continued: Nutritional assessment at baseline by new opportunistic infection among those with low CD4 cell count in Kapiri, Zambia, 2008-2009

	Total (N = 209)		Had New Infection (N=37)		No New Infection (N=172)		p-value (2-tailed)*
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	
Sphygmomanometer Test							
Test length (sec)	51.4	9.1	54.2	7.6	50.8	9.3	0.0597
Total number of grip	61.4	16.4	59.1	17.5	61.9	16.2	0.3941
Average grip strength (mmHg/grip)	2.2	1.0	2.3	1.6	2.2	0.8	0.5319
Cumulative handgrip strength (mmHg)	127.1	34.6	120.7	40.2	128.4	33.4	0.2539
Household Food Security							
Unable to eat preferred food							0.2541
Yes	79	38%	11	30%	68	40%	
No	129	62%	26	70%	103	60%	
Have smaller/fewer meals							0.2541
Yes	79	38%	11	30%	68	40%	
No	129	62%	26	70%	103	60%	
No food storage in household							0.1598
Yes	59	28%	7	19%	52	30%	
No	149	72%	30	81%	119	70%	
Sleeping empty stomach							0.1798
Yes	58	28%	7	19%	51	30%	
No	150	72%	30	81%	120	70%	

For categorical variables, p-values from Chi-square tests (or Fisher's Exact)

For continuous variables, p-values from t-tests (if normally distributed) or Mann-Whitney U (if non-parametric)

Table 2: Unadjusted logistic model of new opportunistic infection over time among HIV + Adults in Kapiri, Zambia,

	Male			Female			CD4 >= 200 at baseline			CD4 < 200 at baseline						
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value				
Non-nutritional covariates																
Age (years)	0.98	0.93	1.04	0.582	0.98	0.94	1.02	0.2849	1.00	0.94	1.08	0.9193	0.97	0.94	1.01	0.1395
Baseline Opportunistic Infection	1.28	0.35	4.66	0.7077	0.96	0.27	3.39	0.9521	5.39	0.96	30.14	0.0551	0.60	0.20	1.76	0.5147
Continuous CD4	1.00	1.00	1.00	0.1619	1.00	1.00	1.00	0.0581	1.00	1.00	1.00	0.8641	1.00	0.99	1.00	0.5147
Categorical CD4	0.44	0.17	1.15	0.094	0.35	0.16	0.76	0.0084								
Occurrence of non-severe HIV-associated syrr	1.07	0.49	2.36	0.8678	2.14	1.15	3.99	0.0165	2.99	1.09	8.19	0.0336	1.22	0.69	2.14	0.4976
Yes																
No																
Anthropometry																
Continuous BMI (kg/m ²)	0.82	0.68	0.99	0.0381	0.82	0.73	0.91	0.0002	0.85	0.70	1.02	0.0834	0.83	0.74	0.92	0.0006
Categorical BMI																
Normal																
Mild Thin	1.49	0.90	2.48	0.1249	2.10	1.45	3.04	<.0001	1.40	0.71	2.78	0.3305	1.54	1.00	2.36	0.0494
Moderate/Severe Thin	2.22	0.80	6.13	0.1249	4.42	2.11	9.24	<.0001	1.97	0.50	7.73	0.3305	2.36	1.00	5.58	0.0494
Continuous MUAC (mm)	0.98	0.96	1.00	0.0116	0.98	0.97	0.99	<.0001	0.98	0.96	1.00	0.0189	0.98	0.97	0.99	<.0001
Categorical MUAC																
Normal																
Undernourished	2.08	1.16	3.71	0.0135	2.81	1.84	4.30	<.0001	2.16	1.01	4.63	0.0471	2.11	1.27	3.49	0.0037
Severe/Extreme Wasting	4.32	1.35	13.76	0.0135	7.89	3.37	18.46	<.0001	4.68	1.02	21.46	0.0471	4.44	1.62	12.16	0.0037
Appetite and Weight Loss																
Loss of Weight	2.42	0.55	10.70	0.2428	2.02	0.87	4.71	0.1026	2.02	0.45	9.19	0.3607	2.06	0.89	4.77	0.09
Yes																
No																
Loss of Appetite	2.02	0.89	4.58	0.0929	3.16	1.55	6.45	0.0016	2.34	0.83	6.56	0.1069	2.53	1.35	4.76	0.0039
Yes																
No																
Handgrip Strength/Fatigue Test																
Mean of measures (psi)	0.93	0.82	1.07	0.3097	0.65	0.55	0.77	<.0001	0.75	0.61	0.92	0.0068	0.86	0.77	0.95	0.0037
Median of measures (psi)	0.93	0.82	1.06	0.2832	0.65	0.55	0.77	<.0001	0.76	0.62	0.94	0.0104	0.85	0.77	0.94	0.0023
Slope of measures	1.04	0.04	28.35	0.9812	0.31	0.02	5.68	0.4296	3.76	0.03	466.37	0.5904	0.33	0.03	3.59	0.3655
Percent strength loss (%)	1.01	0.97	1.05	0.7653	1.07	1.04	1.10	<.0001	1.06	1.01	1.11	0.0188	1.04	1.01	1.06	0.0039

Table 3. Multivariable logistic model of new opportunistic infection among HIV + Adults in Kapiri, Zambia, 2008-2009

	OR	95% CI		p-value
Male (N=226, events = 26)				
Categorical MUAC				
Normal	ref			
Undernourished	2.19	1.18	4.06	0.0125
Severe/Extreme Wasting	4.80	1.40	16.45	0.0125
Female (N=308, events=39)¹				
Loss of Appetite				
No	ref			
Yes	2.23	1.01	4.93	0.0475
Handgrip Strength/Fatigue Test				
Mean of measures (psi)	0.66	0.55	0.78	<.0001
Female (N=308, events=39)²				
Continuous MUAC	0.98	0.97	0.99	0.0024
Handgrip Strength/Fatigue Test				
Percent strength loss (%)	1.04	1.01	1.08	0.0189
Sphygmomanometer Test				
Cumulative handgrip strength (mmHg)	0.99	0.98	1.00	0.0229
High CD4 (CD4 ≥200 cells/μL) (N=214, events=16)				
Handgrip Strength/Fatigue Test				
Mean of measures (psi)	0.76	0.62	0.93	0.0079
Low CD4 (CD4 <200 cells/μL) (N=192, events=31)				
Categorical MUAC				
Normal	ref			
Undernourished	2.13	1.18	3.83	0.0118
Severe/Extreme Wasting	4.53	1.40	14.67	0.0118

¹MUAC was treated as categorical variable in full model²MUAC was treated as continuous variable in full model