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The association between food insecurity and mortality among HIV-infected individuals on HAART

Sheri D. Weiser, MD, MPH^{1,2}, Kimberly A. Fernandes, MSC³, Eirikka K. Brandson, MPH³, Viviane D. Lima, PhD^{3,4}, Aranka Anema, MSc³, David R. Bangsberg, MD, MPH⁵, Julio S. Montaner, MD, FRCPC^{3,4}, and Robert S. Hogg, PhD^{3,6}

¹Positive Health Program, San Francisco General Hospital, UCSF

²Center for AIDS Prevention Studies, University of California, San Francisco (UCSF)

³BC Center for Excellence in HIV/AIDS, Vancouver, BC, Canada

⁴University of British Columbia, Department of Medicine

⁵Massachusetts General Hospital Center for Global Health, Harvard Medical School

⁶Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada

Abstract

Background—Food insecurity is increasingly recognized as a barrier to optimal treatment outcomes but there is little data on this issue. We assessed associations between food insecurity and mortality in HIV-infected antiretroviral therapy (ART)-treated individuals in Vancouver, British Columbia (BC), and whether body max index (BMI) modified associations.

Methods—Individuals were recruited from the BC HIV/AIDS drug treatment program in 1998 and 1999, and were followed until June 2007 for outcomes. Food insecurity was measured with the Radimer/Cornell questionnaire. Cox proportional hazard models were used to determine associations between food insecurity, BMI and non-accidental deaths when controlling for confounders.

Results—Among 1119 participants, 536 (48%) were categorized as food insecure and 160 (14%) were categorized as underweight (BMI <18.5). After a median follow-up time of 8.2 years, 153 individuals (14%) had died from non-accidental deaths. After controlling for adherence, CD4 counts, and socioeconomic variables, people who were food insecure and underweight were nearly two times more likely to die (Adjusted hazard ratio [AHR]=1.94, 95% Confidence interval [CI]=1.10-3.40) compared with people who were not food insecure or underweight. There was also a trend towards increased risk of mortality among people who were food insecure and not underweight (AHR= 1.40, 95% CI=0.91-2.05). In contrast, people who were underweight but food secure were not more likely to die.

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Corresponding Author: Sheri Weiser, MD, MPH, Positive Health Program, POB 0874 UCSF, San Francisco, CA 94143-1372, Sheri.Weiser@ucsf.edu, fax: 415-869-5395, Tel: 415-314-0665.

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Author contributions: RH and JM developed and maintained the regional population-based cohort within which this study took place. RH, EB, VL, and JM were responsible for design and implementation of the current study, and for acquisition of data. SW, RH, AA, KF and DB contributed substantially to conception of the idea for the manuscript, and to data analysis and interpretation. SW drafted the manuscript. SW, KF, EB, VL, AA, DB, JM, and RH contributed substantially to critical editing and revision of the manuscript. All authors approved the final version of the manuscript.

Conclusions—Food insecurity is a risk factor for mortality among ART-treated individuals in BC, particularly among individuals who are underweight. Innovative approaches to address food insecurity should be incorporated into HIV treatment programs.

Keywords

Food insecurity; HIV/AIDS; mortality; Vancouver

Introduction

The advent of highly active antiretroviral therapy (HAART) in 1996 has led to dramatic declines in HIV-related morbidity and mortality. ¹⁻³ Despite this success, significant disparities in HIV treatment outcomes remain, especially among the urban poor. Racial and ethnic minorities, homeless and marginally housed individuals, individuals with lower education and incomes, and people with a history of mental illness and substance abuse have been found to have lower rates of HAART utilization, initiation of HAART at later stages of disease, lower adherence to antiretroviral (ARV) therapy, and higher mortality rates. ⁴⁻¹⁵

Food insecurity, defined as the "limited or uncertain availability of nutritionally adequate, safe foods or the inability to acquire personally acceptable foods in socially acceptable ways," ¹⁶ is also an important and under-recognized cause of disparities in health care access and health outcomes in marginalized populations. Food insecurity leads to worse health outcomes across a range of diseases and is associated with higher rates of heart disease, diabetes, obesity, and depression. ¹⁷⁻²² Food insecurity is also associated with increased hospitalizations and emergency department use, and postponing needed medical care and medications, even after controlling for other measures of socioeconomic status. ^{23, 24} Increasingly, food insecurity is becoming recognized as a key driver of the HIV epidemic internationally and as a potential cause of worse health outcomes among people living with HIV/AIDS. ^{25, 26} Studies from both San Francisco and Vancouver, BC, have found that nearly half of urban poor HIV-infected individuals in HAART treatment programs are food insecure. ^{16, 27} Food insecurity is independently associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco, an effect that appeared to be mediated through both behavioral and biologic pathways. ²⁷

No studies to date have specifically assessed the impact of food insecurity on mortality. In addition, no studies have looked at the extent to which possible negative HIV clinical outcomes associated with food insecurity are explained by poor nutritional status. We therefore set out to examine associations between food insecurity, body mass index, and non-accidental mortality among over 1100 ART-treated participants enrolled in BC's Province-wide Drug Treatment Program. We hypothesized that food insecurity would be independently associated with mortality and that body mass index would modify associations between food insecurity.

Methods

HIV/AIDS Drug Treatment Program

The BC Centre for Excellence in HIV/AIDS' Drug Treatment Program provides HAART free of charge to clinically eligible HIV-infected individuals throughout the province. All HAART patients are entered into an Oracle-based monitoring and evaluation reporting system that uses standardized indicators to prospectively track the antiretroviral use and clinical and laboratory status of HIV-1 infected individuals. Physicians enrolling an HIV-1 infected individual into the system must complete a drug request enrolment prescription

form, which compiles information on the applicant's age, ethnicity, address, past HIVspecific drug history, CD4 cell counts, plasma HIV-1 RNA, current drug requests, and enrolling physician data. The Providence Health Care Ethics Committee for Human Experimentation approved use of the Drug Treatment Program data for research purposes. In 1998-1999, a sample of participants from the BC drug treatment program participated in a self-administered survey as previously described. ¹⁶ Domains of inquiry for the survey included sociodemographic characteristics such as age, gender, ethnicity, housing status, income, employment and education; history of opportunistic infections and AIDS-defining illnesses; drug and alcohol use; incarceration, health and clinical status; and food insecurity.

Study Participants

Patients follow-up every one to three months to renew prescriptions and monitor HIV progression through laboratory tests. Participants were eligible if they were ARV naïve at the time they initiated HAART, and if they were >=18 years of age. All participants included in this study initiated HAART between 1992 and 1999. Eligible participants must have completed at least one questionnaire and undertaken at least two follow-up CD4 cell count and HIV plasma viral load tests. Participants were followed from admittance into the treatment until June 2007 for clinical outcomes. All study procedures were approved by the research ethics board of St. Paul's hospital and Providence Health Care.

Measures

The primary predictor was food insecurity, which was measured by a modified version of the Radimer/Cornell questionnaire. ^{28, 29} The Radimer/Cornell questionnaire covers a range of concepts such as insufficient food intake, the physical sensation of hunger, problems with household food supply, diet quality, anxiety related to food insecurity, and efforts made to maintain household food supplies.^{28, 29} We chose food insecurity at the individual level as our primary predictor (rather than at the household level) because we postulated that individual food insecurity would be most likely to impact upon malnutrition and mortality. As recommended by Kendall et al., individuals were categorized as food insecure at the individual level if they gave a minimum of 1 positive answer (often/sometimes) to any 1 out of the 8 items in the measure referring to individual food insecurity. If they answered one question in this manner they were deemed food insecure.

The primary outcome in the study was time to non-accidental mortality. This outcome was chosen to best approximate HIV-related mortality, as it excluded individuals who died from injuries, accidents, trauma, assaults, drug overdose, and suicide. Deaths were identified on a continuous basis through physician records and linkage with the BC Division of Vital Statistics. Event free subjects were censored in June of 2007.

Low body mass index (BMI) was evaluated as a possible effect modifier in the relationship between food insecurity and non-accidental mortality, and was defined as a BMI <18.5. ³⁰ The BMI, which was obtained at the time of the survey in 1998/1999, is calculated from weight and height measurements, using the formula weight in kg divided by height in m^{-2} . The BMI reflects protein and fat reserves, and a person with a low BMI is underweight for their height.³¹

Covariates for the study included age (continuous), sex (male versus female), ethnicity (aboriginal or non-aboriginal), annual income (>=\$10,000/year versus < \$10,000/year which approximates the low income cut off for Canada), education (>=high school graduation versus < high school graduation), history of treatment in a drug or alcohol program (yes versus no), CD4 cell count (continuous +100 cells), number of years on HAART (continuous), season of the interview (Winter, Spring, Summer, Fall), and log viral load

(continuous). CD4 cell counts and viral loads were the most recent values obtained within 6 months prior to the survey date. Unstable housing was defined as living in a hotel, boarding house, group home, jail, in the street, or having no fixed address at the time of the survey. History of injection drug use was defined as having ever injected illicit drugs (by physician or self-report). Adherence was estimated using pharmacy refill data during the year preceding the survey, and was estimated by dividing the number of months of medication dispensed by the number of months of follow-up. Individuals were defined as non-adherent if they received ARVs for less than 95% of the follow-up period as previously described. ^{32, 33} This measure of adherence has been found to be independently associated with mortality in previous studies. ^{33, 34} All covariates were obtained at the time of the baseline survey in 1998/1999, except where indicated above.

Statistical Analysis

Cox proportional hazard confounder models were used to determine the association between food insecurity, BMI and non-accidental deaths when controlling for other confounders. Data were analyzed using SAS software version 9.1.3. (SAS Institute, Cary, North Carolina, Version 9) Data are presented within categories as frequencies [n (%)] or as median and interquartile range (IQR). We compared categorical variables between groups using Pearson's χ^2 test, and comparisons of continuous variables were carried out using Wilcoxon's rank-sum test. We first assessed the association between food insecurity and non-accidental deaths when controlling for several baseline confounders using Cox proportional hazards. Variable selection was conducted using a backward-selection method suggested by Maldonado and Greenland, by first including all variables in the model and then dropping one variable at each step using the relative change in the coefficient for the variable related to food security as a criterion until the maximum change from the model exceeded 10%. ³⁵ This method has been used in several previous papers, both from our Centre ^{36, 37} and elsewhere, ³⁸ and has been found to perform well with regard to minimizing bias. ³⁵ Next, in testing BMI for effect modification, we tried to determine whether the relationship between food insecurity and mortality was equally strong in each strata defined by BMI. If the association between food insecurity and mortality differed significantly across the different levels of body mass index, then there would be statistical interaction between food security and BMI, indicating that the effect of food insecurity on survival varies depending on the BMI level. For this analysis, we created a 4-level categorical variable combining food insecurity (present or absent) and BMI (>=18.5 or <18.5). Diagnostic procedures yielded no evidence of multi-collinearity or overly influential outliers in any of the models.

Results

In total, 1214 individuals were recruited into the drug treatment cohort. Of these, 1119 individuals (92%) had consistent follow-up during all years of the study and were included in the analysis. At the time of the interview, 536 participants (48%) were food insecure. The median age of all participants was 41 years, 91% of participants were male, 42% had completed high school, and 21% had a history of IDU (Table 1). The median CD4 cell count was 380 (IQR 220-540), the median viral load was 2.6 (log 10 copies/ml)² (IQR 2.6-3.3), 4.6% had an AIDS diagnosis, and 22% were less than 95% adherent during the first year of follow-up. The overall all cause mortality was 16.4% and 13.7% died by non-accidental deaths during the study period.

Examining participant characteristics according to food security status, a significantly higher proportion of women and individuals of aboriginal descent were food insecure. Food insecurity was also significantly associated with lower median ages, lower median CD4 cell counts and higher viral loads, fewer years on HAART, history of injection drug use, history

of enrollment in an alcohol or drug treatment program, lower education, and unstable housing (Table 1). In addition, 62% of individuals who were food insecure were non-adherent with their HAART regimens compared to 38% of individuals who were food secure (p<0.001). Twenty-two percent of individuals who were food insecure died by non-accidental deaths, compared to 11% of individuals who were food secure.

Factors associated with non-accidental mortality

In unadjusted analyses (see Table 2, first column), individuals who were food insecure were more than two times more likely to die compared to individuals who were not food insecure (Hazard Ratio [HR]=2.15, 95% CI=1.55-3.00). Higher age, female gender, lower CD4 cell counts, higher viral loads, lower HAART adherence, lower income, history of injection drug use and drug or alcohol treatment, history of unstable housing, and aboriginal ethnicity were all significantly associated with morality.

The second column of Table 2 shows factors associated with non-accidental mortality when adjusting for all possible confounders excluding BMI. In adjusted analyses, individuals who were food insecure were 50% more likely to die compared with individuals who were not food insecure (AHR=1.51, 95% CI=1.03-2.23). Individuals with higher CD4 counts were less likely to die, and individuals who were older and had a history of injection drug use were significantly more likely to die in adjusted analyses. In our analyses, we created a 4level categorical variable combining levels of food insecurity (food insecure and food secure) and BMI (Underweight: BMI<18.5 verus normal weight: BMI>=18.5) and found that BMI was an effect modifier in the relationship between food insecurity and mortality. The third column of Table 2 presents models showing the interaction between food insecurity, body mass index and mortality. After controlling for all confounders, individuals who were both food insecure and underweight were nearly two times more likely to die compared to individuals who were neither food insecure nor underweight (AHR=1.94, 95% CI=1.10-3.40). There was also a trend towards increased risk of mortality among individuals who were food insecure but had normal weights (AHR=1.40, 95% CI=0.91-2.05). In contrast, individuals who were underweight but food secure were not more likely to die.

Figure 1 shows the crude Kaplan Meier of survival stratified by food security status and body mass index. The mortality rate was quite distinct among the different food security status and body mass index groups, with food insecure and underweight individuals having the highest mortality rates (log-rank test P-value: <0.0001). When only food secure patients were considered, the mortality rate was similar for those who were underweight and at normal weights (log-rank test P-value, 0.71). When only food insecure patients were considered, the mortality rate was similar for those who were underweight and at normal weights (log-rank test P-value 0.43). When only underweight patients were considered, the mortality rate was elevated for those who were food insecure (log-rank test P-value 0.008). When only normal weight patients were considered, the mortality rate was elevated for those who were food insecure (log-rank test P-value 0.008). When only normal weight patients were considered, the mortality rate was elevated for those who were food insecure (log-rank test P-value 0.008). When only normal weight patients were considered, the mortality rate was elevated for those who were food insecure (log-rank test P-value 0.008). When only normal weight patients were considered, the mortality rate was elevated for those who were food insecure (log-rank test P-value 0.008).

Discussion

While malnutrition has been found to be associated with mortality for individuals both on and off HAART in both developed and developing countries, ³⁹⁻⁴⁷no previous studies to our knowledge have examined the association between food insecurity and mortality. We found that HAART-treated individuals who were food insecure were significantly more likely to die of non-accidental deaths compared to individuals who were not food insecure. The very high prevalence of food insecurity in our study sample (48%) has been previously reported in this population, ¹⁶ and suggests that the negative impacts of food insecurity on health outcomes may be experienced by a large proportion of urban poor HIV-infected individuals.

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These results are also consistent with our previous work in San Francisco, where we found that 49% of HIV-infected individuals on HAART were food insecure and that food insecurity was significantly associated with incomplete viral load suppression among homeless and marginally housed individuals. ²⁷ Taken together, these results argue that food insecurity should be an important target for intervention for HIV-infected individuals on HAART to improve clinical outcomes and decrease mortality. Our findings support recommendations by the World Health Organization, the Joint United Nations Programme on HIV/AIDS, and the World Food Program that food assistance should be integrated into HIV AIDS programming where possible. ⁴⁸⁻⁵⁰While these recommendations are typically aimed at under-resourced settings, our findings suggest that targeted food supplementation coupled with other measures to alleviate poverty should also be a priority among urban poor HIV-infected individuals in well-resourced settings.

Another key finding was that body mass index (BMI) modified associations between food insecurity and mortality in that the effects of food insecurity on mortality were most pronounced among individuals who were also underweight. There is a rich body of literature examining the impacts of malnutrition on HIV clinical, immunologic and virologic outcomes. Studies from both Westernized and developing settings have shown that malnutrition, measured by low body mass index (BMI) and low albumin, hastens progression to immunologic decline, opportunistic infections, AIDS and death in untreated individuals.^{39-43, 51-56} In terms of the impact of malnutrition on HIV outcomes for patients on HAART, Tang et al. has shown that loss of weight and of lean body mass remain independent predictors of mortality in the HAART era among patients in Massachussets.⁴⁴ Similarly, studies from Westernized settings have found associations between weight loss or low BMI and higher HIV RNA levels. 57, 58 Negative impacts of poor nutritional status have also been shown in sub-Saharan Africa where several studies reported that low BMI and low hemoglobin were predictive of mortality, especially in the early phases of HAART initiation. ⁴⁵⁻⁴⁷ Our findings, coupled with those of others, suggests that interventions using targeted food supplementation may have the most benefit among individuals who are both food insecure and underweight.

It is interesting that associations between low body mass index and mortality in this study were not seen among individuals who were food secure, and that there was a trend towards increased risk of mortality among individuals who were food insecure but not underweight. This suggests that associations seen between nutritional status and mortality among HAART-treated individuals in other studies may be mediated to some extent by food insecurity. It also suggests that the adverse impact of food insecurity on mortality may be explained in part by mechanisms other than poor nutritional status. In terms of possible additional biologic mechanisms to explain associations between food insecurity and mortality, food insecurity may also impede optimal absorption of certain antiretroviral drugs, which may contribute to treatment failure, progression to AIDS and death. For instance, several protease inhibitors such as nelfinavir and ritonavir require food for maximal absorption, and the absence of food may negatively affect the pharmikokinetics of these drugs. ⁵⁹⁻⁶¹

As for behavioral mechanisms, we found that food insecurity was significantly associated with antiretroviral adherence at baseline, so it is likely that lower adherence to HAART may have contributed to negative clinical impacts of food insecurity. Since we did not collect longitudinal data on food insecurity, we were unable to better explore interactions between food insecurity and adherence over time and how they may have affected mortality. Other studies have also found associations between food insecurity and HAART non-adherence. A number of qualitative and small quantitative studies have reported that food insecurity is an important barrier to HAART adherence in under-resourced settings. ⁶²⁻⁶⁴ Similarly, in a

study among nearly 5000 HIV-infected individuals in France, food privation was associated with increased odds of HAART non-adherence among heterosexual men and a trend towards increased odds of non-adherence among heterosexual women. ⁶⁵ Associations between food insecurity and non-adherence have also been reported for other diseases such as tuberculosis. ^{66, 67} More studies are needed to better understand the role of HAART non-adherence and treatment interruptions in mediating the negative clinical impacts of food insecurity.

Food insecurity was strongly associated with both baseline drug and alcohol use, as well as with markers of socioeconomic status such as low income, lower education and unstable housing. While these factors were controlled for in our confounder models, socioeconomic status is a complex concept that may not be adequately captured by income, education and housing status, and we did not evaluate all drugs of abuse. Consequently, it is possible that low socioeconomic status and drug abuse may in part account for associations seen between food insecurity and mortality. In addition, other studies have found associations between food insecurity and depression^{17, 18, 20}, and depression is well known to be associated with worse clinical outcomes and mortality among individuals on HAART. ⁶⁸ Consequently, it is possible that depression and other mental illnesses may also be on the causal pathway between food insecurity and poor health outcomes.

There were a number of other important limitations that may affect interpretation of our results. As previously mentioned, we did not gather longitudinal data on food insecurity so were unable to better assess interactions between food insecurity, body mass index, adherence and viral load suppression over time to better understand mechanisms for how food insecurity may impact upon mortality. In addition, we did not use more comprehensive measures of nutritional status such as anthropometry, lab markers of overall nutrition, nutrient assays and body composition measures. Future studies should use more rigorous measures of nutritional status in further exploring interactions between food insecurity, nutritional status and clinical outcomes. Few patients were HAART naïve at the time of the food security interview and it is likely that the impacts of food insecurity on clinical outcomes and mortality may be different among people first initiating HAART. Finally, as with all observational studies, bias is inherent due to uncontrolled confounders.

In conclusion, we found that nearly half of HAART-treated patients from the BC HIV Drug Treatment Program were food insecure and that food insecurity strongly and significantly increased the likelihood of mortality. The effect of food insecurity on mortality was most pronounced in individuals who were also underweight. Addressing food insecurity and relieving hunger among the urban poor is an important goal by itself to improve quality of life and overall health. The potential impact of food support on mortality for HIV-infected individuals on HAART provides additional rationale for meeting broad needs, including food provisions, for urban poor individuals living with HIV/AIDS. Novel interventions to alleviate food insecurity and poverty among urban poor individuals in resource-rich settings are needed to avoid clinical deterioration and excess mortality. Towards this goal, clinicians caring for HIV-infected individuals may consider working in multi-disciplinary teams that include both case managers and nutritionists. These teams can screen individuals for food insecurity and poor nutritional status, inquire about barriers to food access, and help individuals who are food insecure identify reliable sources of good quality food in their communities.

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Figure 1.

Crude Kaplan-Meier Survival Probabilities for the 1119 Patients Stratified by Food Security and BMI Levels.

People remaining in the study	0 months	20 months	40 months	60 months	80 months	100 months
Food Insecure/Underweight	87 (7.8%)	75 (6.7%)	73 (6.5%)	68 (6.1%)	62 (5.5%)	40 (3.6%)
Food Insecure/Not Underweight	449 (40.1%)	418 (37.4%)	394 (35.2%)	362 (32.4%)	331 (29.6%)	156 (13.9%)
Food Secure/Underweight	73 (6.5%)	70 (6.3%)	68 (6.1%)	65 (5.8%)	60 (5.4%)	38 (3.4%)
Food Secure/Not Underweight	510 (45.6%)	485 (43.3%)	464 (41.5%)	442 (39.5%)	428 (38.2%)	232 (20.7%)

Table 1

A Comparison of Baseline Socioeconomic and Clinical Characteristic by Food Security Status

Variable	Food Secure N=583 N (column %)	Food Insecure (N=536) N (column %)	Totals (column %)	P-value
Gender,				
Female	36 (6.2)	57 (10.6)	93 (8.3)	0.01
Male	547 (93.8)	479 (89.4)	1026 (91.7)	
Age				
Median	42.0	39.0	1119	< 0.001
Interquartile range	36.0-48.0	35.0-45.0		
AIDS diagnosis				
Yes	31 (5.3)	21 (3.9)	52 (4.6)	0.27
No	552 (94.7)	515 (96.1)	1067(95.4)	
Aboriginal status				
Yes	35 (6.0)	89 (16.6)	124 (11.1)	< 0.001
No	548 (94.0)	447 (83.4)	995 (88.9)	
CD4 Cell Count (per 100 cells) ¹				
Median	4.0	3.6	3.8	< 0.001
Interquartile range	2.4-5.6	2.0-5.33	2.2 - 5.4	
Plasma HIV viral load (log 10 copies/ml) 2				
Median	2.6	2.6	2.6	0.01
Interquartile range	2.6-3.0	2.6-3.5	2.6 - 3.3	
Adherence (>=95%) 3				
Yes	489 (83.9)	381 (71.2)	870 (77.8)	< 0.001
No	94 (16.1)	154 (28.8)	248 (22.2)	
History of injection drug use ⁴				
No	514 (90.2)	330 (64.2)	844 (77.9)	< 0.001
Yes	56 (9.8)	184 (35.8)	240 (22.1)	
Ever enrolled in an alcohol or drug treatment program? 5				
No	500 (90.1)	383 (74.8)	883 (82.8)	< 0.001
Yes	55 (9.9)	129 (25.2)	184(17.2)	
High School Education or greater				
No	202 (34.6)	272 (50.7)	474 (42.4)	< 0.001
Yes	381 (65.4)	264 (49.3)	645 (57.6)	
Income (<= Canadian \$10000)				
No	493 (89.0)	244 (49.5)	717 (69.8)	< 0.001

Variable	Food Secure N=583 (column %)	N Food Insecure (N=536) N (column %)	Totals (column %)	P-value
Yes	61 (11.0)	249 (50.5)	310 (30.2)	
Stable Housing? 6				
No	13 (2.3)	51 (9.8)	64 (5.9)	< 0.001
Yes	553(97.7)	469 (90.2)	1022 (94.1)	
Body Mass Index (BMI)				
Underweight (BMI < 18.5)	73 (12.5)	87 (16.2)	160 (14.3)	0.09
Not Underweight (BMI >=18.5)	510 (87.5)	449 (83.8)	959 (85.7)	
Number of years on ART				
Median	2.75	2.25	2.50	<.0001
Interquartile range	1.42 - 4.83	1.08 - 3.33	1.25 - 4.00	
Non-accidental deaths				
No	529 (90.7)	437 (81.5)	966 (86.3)	<.0001
Yes	54 (9.3)	99 (18.5)	153 (13.7)	
All-cause mortality				
No	520 (89.2)	416 (77.6)	936 (83.7)	< 0.0001
Yes	63 (10.8)	120 (22.4))	183 (16.4)	
Season survey completed				
Winter	304 (52.1)	264 (49.2)	568 (50.7)	0.309
Spring	123 (21.1)	138 (25.8)	261 (23.3)	
Summer	61 (10.5)	56 (10.5)	117 (10.5)	
Fall	95 (16.3)	78 (14.5)	173 (15.5)	

¹Data missing for 86 patients.

 2 Data missing for 20 patients.

 $^{\mathcal{S}}$ Data missing for 1 patient.

⁴Data missing for 35 patients.

⁵Data missing for 52 patients.

⁶Data missing for 33 patients.

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Table	2
Probability of Non-Accidental Deaths	

Variable	Unadjusted Model HR, 95% CI	Adjusted Model HR, 95% CI	Adjusted Model with BMI as Possible Effect Modifier HR, 95% CI
Male vs. Female	0.59 (0.37,0.95)	-	-
Age (+ x/years)	1.04 (1.02,1.06)	1.05 (1.03,1.07)	1.05 (1.03,1.07)
CD4 Cell Count (per 100 cells)	0.79 (0.72 0.86)	0.80 (0.74,0.87)	0.80 (0.74, 0.88)
Log10 Viral Load	1.63 (1.40,1.90)	-	-
< high school vs. >= high school	1.68 (1.22,2.30)	-	-
Income <10000 vs >=10000	1.92 (1.37,2.70)	-	-
History of injection drug use (Yes vs. No)	3.44 (2.49,4.76)	3.46 (2.40,4.99)	3.43 (2.38, 4.94)
Ethnicity (Native vs. Non-Native)	1.90 (1.25,2.88)	-	-
Ever been in an Alcohol or Drug program (Yes vs. No)	2.33 (1.63,3.32)	-	-
Number of years on ART (for every year increase)	0.97 (0.89 - 1.06)	-	-
Adherence >=95% vs. <95%	0.44 (0.32 – 0.62)	-	-
Stable housing (Yes vs No)	0.55 (0.32,0.95)	-	-
Food Insecure? (Yes vs. No)	2.15 (1.55,3.00)	1.51 (1.03,2.23)	NA
Food Secure and not underweight	1.00 (-)		1.00 (-)
Food Secure and underweight	0.70 (0.28,1.76)		0.70 (0.28,1.78)
Food insecure and not underweight	1.93 (1.35,2.77)		1.40 (0.91,2.05)
Food Insecure and underweight	2.81 (1.69,4.69)		1.94 (1.10,3.40)
Season survey completed			
Winter	1.00 (-)		
Spring	0.87 (0.58,1.31)		
Summer	0.88 (0.50, 1.54)		
Fall	1.06 (0.67,1.65)		