Weight gain post-ART in HIV+ Latinos/as differs in the USA, Haiti, and Latin America

Lara E. Coelho[a,*], **Cathy A. Jenkins**[b], **Bryan E. Shepherd**[b], **Jean W. Pape**[c], **Fernando Mejia Cordero**[d], **Denis Padgett**[e], **Brenda Crabtree Ramirez**[f], **Beatriz Grinsztejn**[a], **Keri N. Althoff**[g], **John R. Koethe**[h], **Vincent C. Marconi**[i], **Phyllis C. Tien**[j], **Amanda L. Willig**[k], **Richard D. Moore**[g], **Jessica L. Castilho**[h], **Jonathan Colasanti**[i], **Heidi M. Crane**[l], **M. John Gill**[m], **Michael A. Horberg**[n], **Angel Mayor**[o], **Michael J. Silverberg**[p], **Catherine McGowan**[h], **Peter F. Rebeiro**[b,h] **on behalf of the North American AIDS Collaboration on Research and Design (NA-ACCORD) and the Caribbean, Central and South America network for HIV epidemiology (CCASAnet) of the International epidemiology Databases to Evaluate AIDS (IeDEA)**

[a]Instituto Nacional de Infectologia Evandro Chagas (INI), Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

[b]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA

[c]Groupe Haitien d'Etudes du Sarcome de Kaposi et des Infections Opportunistes, Port-au-Prince, Haiti

[d]Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru

[e]Instituto Hondureño de Seguridad Social & Hospital Escuela Universitario, Tegucigalpa, Honduras

[f]Deparatmento de Infectologia, Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán. Mexico City, Mexico

[g]Johns Hopkins University, Baltimore, MD, USA

[h]Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, TN, USA

[i]Emory University School of Medicine and Rollins School of Public Health, Atlanta, GA, USA

[j]Department of Medicine, University of California, San Francisco (UCSF), and the Department of Veterans Affairs Medical Center. San Francisco, CA, USA

*Corresponding author: Lara E. Coelho, Av. Brasil 4365, Manguinhos, Rio de Janeiro, RJ, Brazil, Zipcode: 21040-900, Phone: +55 21 38659121, lara.coelho@ini.fiocruz.br (L.E. Coelho).

[k]School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA

[l]University of Washington, Seattle, WA, US

[m]The University of Calgary, Calgary, AB, Canada

[n]Kaiser Permanente, Mid-Atlantic Permanente Research Institute, Rockville, MD, US

[o]Universidad Central del Caribe, Retrovirus Research Center, Bayamón, PR, US

[p]Kaiser Permanente Northern California, Oakland, CA, US

Summary

Background—An obesity epidemic has been documented among adult Latinos/as in Latin America and the United States (US); however, little is known about obesity among Latinos/as with HIV (PWH). Moreover, Latinos/as PWH in the US may have different weight trajectories than those in Latin America due to the cultural and environmental contexts. We assessed weight and body mass index (BMI) trajectories among PWH initiating antiretroviral therapy (ART) across 5 countries in Latin America and the Caribbean and the US.

Methods—ART-naÿve PWH 18 years old, enrolled in Brazil, Honduras, Mexico, Peru, and Haiti (sites within CCA-SAnet) and the US (NA-ACCORD) starting ART between 2000 and 2017, with at least one weight measured after ART initiation were included. Participants were classified according to site/ethnicity as: Latinos/as in US, non-Latinos/as in US, Haitians, and Latinos/as in Latin America. Generalized least squares models were used to assess trends in weight and BMI. Models estimating probabilities of becoming overweight/obese (BMI 25 kg/m^2) and of becoming obese (BMI 30 kg/m^2) post ART initiation for males and females were fit using generalized estimating equations with a logit link and an independence working correlation structure.

Findings—Among 59,207 PWH, 9% were Latinos/as from Latin America, 9% Latinos/as from the US, 68% non-Latinos/as from the US and 14% were Haitian. At ART initiation, 29% were overweight and 14% were obese. Post-ART weight and BMI increases were steeper for Latinos/as in Latin America compared with other sites/ethnicities; however, BMI at 3-years post ART remained lower compared to Latinos/as and non-Latinos/as in the US. Among females, at 3-years post ART initiation the greatest adjusted probability of obesity was found among non-Latinas in the US (15·2%) and lowest among Latinas in Latin America (8.6%). Among males, while starting with a lower BMI, Latinos in Latin America had the greatest adjusted probability of becoming overweight or obese 3-years post-ART initiation.

Interpretation—In the Americas, PWH gain substantial weight after ART initiation. Despite environmental and cultural differences, PWH in Latin America, Haiti and Latinos and non-Latinos in the US share similar BMI trajectories on ART and high probabilities of becoming overweight and obese over time. Multicohort studies are needed to better understand the burden of other metabolic syndrome components in PWH across different countries.

Keywords

Background

Obesity prevalence has risen steadily across the globe for the last 50 years. In 2016, 39% of adults worldwide were overweight and 13% were obese.[1] Although obesity prevalence increased in every country in the world, prevalence and trends vary between countries and can be associated with cultural and environmental contexts.[2] In the United States (US), in 2015–2016, 40% of adults were obese,[3] while in Latin America and the Caribbean (LAC), in 2016, 24% were obese.[4]

In parallel, studies of persons with HIV (PWH) have reported an increasing prevalence of obesity (as measured at antiretroviral therapy [ART] initiation).[5–8] In Canada and the US (The North American AIDS Cohort Collaboration on Research and Design [NA-ACCORD] cohort study) obesity prevalence among PWH starting ART increased from 11% in 1998–2000 to 17% in 2007–2010.[5] In a Swiss cohort of PWH, obesity prevalence was 4% in 2000 and 9% in 2012.[9] In a cohort of PWH from Rio de Janeiro, Brazil, obesity prevalence was 5% in 2000–2003 and 12% in 2012–2015.[6] In Lima-Callao, Peru, in 2016, among PWH initiating ART in 5 clinics, obesity prevalence was 11%[10] and in the Dominican Republic in 2012, obesity prevalence among PWH was 14%.[11]

Factors associated with weight gain and body mass index (BMI) increase are consistent across studies conducted in different regions of the globe (i.e., lower CD_4 cell counts, higher HIV viral load, female sex, Black race, and integrase strand transfer inhibitor (INSTI)-based ART regimens).[6,9,12,13] However, as in the general population, obesity prevalence in PWH varies across different countries and these differences may be driven by cultural and environmental factors.

In this study we aimed to evaluate weight and BMI trajectories over time, as well as probabilities of becoming overweight or obese, in PWH initiating ART across 5 countries in LAC and the US.

Methods

Study Population

The Caribbean, Central and South America network for HIV epidemiology (CCASAnet) and NA-ACCORD are multisite collaborations of cohort studies of PWH in LAC and in the US and Canada, respectively. Both cohort groups are members of the International epidemiology Databases to Evaluate AIDS (IeDEA) consortium of the US National Institutes of Health, and details of these collaborations have been published previously.[14,15] Briefly, both cohort groups collect standardized data on demographic variables, antiretroviral medication use, laboratory test results (including CD_4 count and HIV viral load), clinical diagnoses, weight and height measurements, and vital status. The activities of the NA-ACCORD and CCASAnet have been reviewed and approved by local institutional review boards for each site.

We present a longitudinal analysis of weight and BMI trajectories between 2000 and 2018 for PWH initiating ART in cohorts from Brazil, Honduras, Mexico, Peru, Haiti

(within CCASAnet), and the US (within NA-ACCORD). Adults aged 18 years, ART naÿve at cohort entry, with at least one weight measurement after ART initiation, and one height measurement on or after age 18 were included. ART regimens were classified as either non-nucleoside reverse transcriptase inhibitor (NNRTI)-based (reference for all analyses), protease inhibitor (PI)-based, or INSTI-based, according to the initial ART regimen prescribed. Participants initiating ART with triple nucleoside reverse transcriptase inhibitors or with a combination of core drugs classes (i.e. NNRTI plus PI or INSTI, PI plus INSTI) were excluded from the analyses; this was done because they represented a small sample of participants and to limit our study population to those initiating ART based on preferred first-line regimens.[16] Participants were classified according to their site and self-reported ethnicity as: Latinos/as in US,[17,18] non-Latinos/as in US, Haitians, and Latinos/as in Latin America (including PWH living in Brazil, Honduras, Mexico, and Peru).

PWH from Haiti were included in the analysis as a separate group from other countries in Latin America for several reasons including a generalized HIV epidemic (contrasting with concentrated epidemics in other Latin American countries);[19,20] greater representation of Haiti within CCASAnet relative to other sites (representing 60% of CCASAnet study population), particularly among females (77% of female population within CCASAnet); major socioeconomic differences between Haiti and other countries in Latin America;[21] as well as different background obesity estimates and trends in the general population relative to other countries in Latin America.

Outcomes of interest and covariates

Body weight and BMI measures were the outcomes of interest in the primary models; incidence of becoming overweight/obese and incidence of becoming obese were the outcomes of interest in the secondary models. Body weight and height were measured during routine follow-up at clinical sites and transmitted to NA-ACCORD and CCASAnet databases through standardized and audited electronic clinical research forms or directly from electronic health records. Regular validation of weights and heights were performed during regular site audits within CCASAnet; outliers were flagged by data coordinating centers and queries were sent to the sites. BMI was calculated as weight (kilograms) divided by height squared (meters [2]). Baseline measures were those closest to ART initiation within −180 to +30 days (for weights, heights, and CD_4 counts [cells/mm^3]) or within −180 days to +7 days (for HIV viral loads [copies/mL]). Missing baseline heights were imputed within a subject as the median of all available height measurements for an individual on or after 18 years of age. Body weights and BMI measures at 1 and 3 years post-ART were those closest to these time points (+/−180 days).

Statistical Analysis

Demographic and clinical characteristics were summarized as median and interquartile range (IQR) or as frequency (percent), when appropriate. Chi-square and Kruskal-Wallis tests were used for group and study period comparisons of categorical and continuous variables, respectively. To assess trends in body weight and BMI measure trajectories by site/ethnicity, generalized least squares models using a compound symmetric variance-covariance structure and multiply-imputed baseline measures were fit using separate models

for body weight and BMI. Covariates included in the model were time since ART initiation, the initial antiretroviral class regimen (NNRTI, PI, or INSTI), birth sex, year of ART initiation, and baseline weight (or BMI, depending on the outcome), age, CD_4 count (square-root transformed), and HIV viral load ($\log_{10}$ transformed). All continuous variables were fit with restricted cubic splines using 4 knots; two-way interactions between time and each of baseline body weight (or BMI), site/ethnicity, and birth sex were included in models along with an interaction between birth sex and site/ethnicity. Missing data (baseline weight, CD_4 count, and HIV viral load) were multiply imputed using predictive mean matching[22] and 10 imputation replications. Imputation models included all covariates in the main model as well as the outcome of interest.[23] Results from the models were summarized by birth sex and site/ethnicity.

Individuals were followed from ART initiation date until their last observed body body weight (BMI) measurement on or before December 31, 2018. Loss to follow-up (LTFU) was defined as no body weight measurement within 365 days of the cohort closing date or December 31, 2018, whichever came first. The cohort closing date was defined for each individual site as the 95th percentile of final body weight measurement dates within each site.

Secondary analyses estimated the probabilities of becoming overweight/obese (BMI 25 kg/m^2) and of becoming obese (BMI 30 kg/m^2) post ART initiation for males and females by site/ethnicity. These analyses included only the subset of PWH with no missing BMI information at baseline. In addition, overweight/obese PWH at baseline were excluded from the overweight/obesity probability models, while obese PWH at baseline were excluded from the obesity probability models. The association of site/ethnicity with the time-varying overweight/obese or obese incidence indicators were fit using separate generalized estimating equations with a logit link and an independence working correlation structure. The same covariates used in the body weight/BMI trend analyses were included in these models. As with the primary models, missing data were multiply imputed using 10 imputation replications with imputation models including all covariates in the main models along with the outcome of interest. All BMI measurements were used in these analyses (i.e., not just those at one and three years). Conditional probabilities were calculated from the models for men and women by site/ethnicity fixing all continuous covariates at their median values and ART class regimen as NNRTI-based.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation or writing of this report. All the authors had full access to the data in the study and had final responsibility for the decision to submit it for publication.

Results

Participants' characteristics

Among a total of 59,207 PWH included in the primary analysis, 9% were classified as Latinos/as from Latin America (3% from Peru, 3% from Brazil, 2% from Mexico and 1%

from Honduras), 9% as Latinos/as from the US, 68% as non-Latinos/as from the US, and 14% as Haitians (Table 1 and Suppl Table 1). Twenty percent of the study population were females and median age at ART initiation was 42 years (IQR 33,51). Females initiated ART at a younger age (median 38 years; IQR 30, 46) than males (median 44 years; IQR 34, 52).

At ART initiation, median CD_4 count was 287 cells/mm^3 (IQR 136, 459), with the lowest CD_4 counts observed among Latinos/as in Latin America, and the highest among non-Latinos/as in the US (Table 1). Baseline CD_4 counts increased from median 233 cells/mm^3(IQR 110, 369) in 2000–2009 to 357 cells/mm^3 (IQR 200, 549) in 2010–2017. The initial ART regimen was NNRTI-based among 59% of the study population, and this proportion varied widely across site/ethnicity categories, accounting for 83% of Latinos/as in Latin America, 48% of Latinos/as in the US, 51% of non-Latinos/as in US and 94% of Haitians. Over the study period (2000–2009 vs. 2010–2018), the proportion of PWH initiating ART with an NNRTI-based regimen remained relatively stable (61% and 57%, respectively). By contrast, the proportion of PWH initiating PI-based regimens decreased from 38% to 21% and the proportion of INSTI-based regimens increased from 1% to 22% (data not shown). Of note, 99% of INSTI users were from the US, with similar proportions observed among Latinos/as and non-Latinos/as: INSTIs accounted for the initial ART regimen among 16% of Latinos/as in the US (similar among females and males) and among 14% of non-Latinos/as in the US (females 17% and males 13%). Additional data on antiretrovirals in initial ART regimens in North and Latin America during the study period are provided in Suppl Table 2).

Median BMI at ART initiation was 24 kg/m^2 (IQR 21, 28) and remained stable throughout the study period (p-value 0·970, 2000–2009 vs. 2010–2018). The highest BMI at ART initiation was observed among Latinos/as and non-Latinos/as in the US and the lowest among Haitians. Twenty-nine percent of the study population were overweight, 14% had BMI ≥ 30kg/m^2. Moreover, 3% had BMI between 35–39·9kg/m^2 (obesity class 2) and 2% had BMI ≥ 40kg/m^2 (obesity class 3) at ART initiation. Highest prevalence of overweight and obesity were among Latinos/as and non-Latinos/as in the US (Table 1). Over the study period, the proportion of overweight or obese PWH at baseline remained relatively stable, at 29% and 13% in 2000–2009 and 27% and 16% in 2010–2018, respectively.

At 3 years post ART initiation, 34% of the participants were overweight, 18% were obese, and 2% had BMI ≥ 40kg/m^2 (obesity class 3), with the greatest proportions among Latinos/as and non-Latinos/as in the US. In addition, among participants with BMI between 30–34·9 kg/m^2 (obesity class 1) at baseline, 39% remained in the obesity class 1 category, 40% moved to obesity class 2 (BMI 35–39·9 kg/m^2), and 16% moved to obesity class 3 (BMI ≥ 40 kg/m^2) at 3 years post ART initiation. These percentages transitioning between obesity classes were similar though slightly higher among men (39%, 42%, and 18%, respectively) than women (37%, 35%, and 13%, respectively).

Factors associated with BMI changes after ART initiation

In our adjusted models, BMI gain was lower among PWH living in Latin America and Haiti relative to PWH from the US (Latinos and non-Latinos); BMI increase was greater among participants using INSTI-based regimens (adjusted estimated effect + 0.65 kg/m^2, 95%CI

0·51–0·80) and PI-based regimens (+0·15 kg/m^2, 95%CI 0·06, 0·23) compared to NNRTI users. BMI increase was also greater among women compared to men (+ 1·88 kg/m^2, 95%CI 1·74, 2·02) and among those with lower BMI at baseline. In addition, longer exposure to ART, lower baseline CD$_4$ count and higher baseline HIV viral load were associated with BMI increase over time.

Body weight and BMI trajectories among females

Among females, median BMI at ART initiation was 24 kg/m^2 (IQR 20, 28); 23 kg/m^2 (IQR 20, 26) among Latinas in Latin America, 26 kg/m^2 (IQR 23, 31) among Latinas in the US, 27 kg/m^2 (IQR 23, 33) among non-Latinas in the US and 22 kg/m^2 (IQR 19, 25) among Haitians.

At baseline, 1 year, and 3-years post-ART, the overall proportion of overweight females increased from 21% to 25% and 27%, respectively; and the proportion of obese females increased from 19% to 22% and 27%, respectively. Moreover, at 3-years post-ART the proportion of obese females increased from baseline in all site/ethnicity categories: from 9% to 16% among Latinas in Latin America, from 28% to 32% among Latinas in the US, from 35% to 42% among non-Latinas in the US and from 9 to 14% among Haitians.

Post-ART body weight and BMI adjusted trajectories were initially steeper for Latinas in Latin America compared to other sites/ethnicities, though BMI 3-years post ART remained lower among Latinas in Latin America compared to Latinas and non-Latinas in the US (Figure 1).

Body weight and BMI trajectories among males

Among males, median BMI at ART initiation was 24 kg/m^2 (IQR 22, 27); 22 kg/m^2 (IQR 20, 25) among Latinos in Latin America, 25 kg/m^2 (IQR 23, 28) among Latinos in the US, 25 kg/m^2 (IQR 22, 28) among non-Latinos in the US and 21 kg/m^2 (IQR 19, 23) among Haitians.

At baseline, 1 year, and 3 years post-ART, the overall proportion of overweight males increased from 31% to 36% and 36%, respectively; and the proportion of obese males increased from 13% to 17% and 19%, respectively. Moreover, at 3-years post-ART, relative to baseline, the proportion of obese males increased in all site/ethnicity categories: from 4% to 11% among Latinos in Latin America, from 13% to 20% among Latinos in the US, from 15% to 21% among non-Latinos in the US and from 2 to 3% among Haitians.

Similar to females, adjusted post-ART body weight and BMI trajectories were steeper for Latinos in Latin America, however, despite the sharp initial increase, BMI 3-years post ART remained lower compared to Latinos and non-Latinos in the US (Figure 1).

Supplementary Figure shows body weight and BMI trajectories when Haiti is included with the other CCASAnet sites (among females and males).

Probabilities of becoming overweight/obese and probabilities of becoming obese after ART initiation

Among 41,378 PWH with baseline BMI information, 23,594 PWH (22% females) who were non-overweight and non-obese at ART initiation (i.e., baseline BMI <25 kg/m^2) were included in the adjusted overweight/obesity probability models (Suppl Table 3) and 35,414 PWH (20% females) who were non-obese at ART-initiation (BMI <30 kg/m^2) were included in the adjusted obesity probability models (Suppl Table 4).

Among non-overweight/non-obese females, at 1-year post ART initiation, adjusted probabilities of becoming overweight/obese ranged from 28% in Latinas in the US to 33% in Latinas in Latin America. Over time, probabilities of becoming overweight/obese rose further, reaching 45% among Latinas in the US at 3-years post ART initiation (Figure 2). Among non-obese females, adjusted probability of becoming obese at 1-year post-ART initiation varied between 5% (Latinas in Latin America and Haitians) and 7·5% (Latinas and non-Latinas in the US). At 3-years post ART initiation, the greatest probabilities of obesity were found among non-Latinas in the US (15·2%) and lowest among Latinas in Latin America (8·6%).

Among non-overweight/non-obese males, the adjusted probability of becoming overweight/obese at 1-year post-ART initiation was greatest in Latinos in Latin America (32%), followed by Latinos in the US (24%), non-Latinos in the US (20%), and Haitians (18%). Over time, probabilities rose further for all site/ethnicities, with Latinos in Latin America also showing the greatest adjusted probability of becoming overweight/obese (39%) at 3-years post ART initiation (Figure 2). Among non-obese males, adjusted probabilities of becoming obese were somewhat similar at 1-year post ART initiation across all site/ ethnicities ranging from 2·9% for Haitians to 3·8% in Latinos in Latin America; these probabilities remained on rise over time, and at 3-years post ART-initiation they were almost twice compared to the 1st year post ART estimates, except for Haitians (which remained stable) (Figure 2).

Discussion

In this study among almost 60,000 PWH initiating ART in six countries in the Americas over the past 15 years, we found that PWH substantially gained body weight after ART initiation. This large and diverse study population allowed us to demonstrate that body weight and BMI trajectories after ART initiation differed among Haitians, Latinos/as in Latin America and in Latinos/as and non-Latinos/as in the US. Latinos/as in Latin America and Haitians initiated ART with lower median BMI, and Latinos/as in Latin America had steeper body weight gain and BMI increase following ART initiation relative to PWH in the US. However, despite the sharp upward trajectories, 3-years post ART BMI estimates remained lower among Latinos/as in Latin America and Haitians compared to Latinos/as and non-Latinos/as in the US. Moreover, among males, Latinos in Latin America had the greatest adjusted probability of becoming overweight/obese and of becoming obese post ART initiation. Among females, Latinas in the US had the greatest probability of becoming overweight/obese while non-Latinas in the US had the greatest probability of becoming obese at 3-years post ART initiation.

In the early 90s, a study found that Nigerian men and women living in the US had a BMI 20–25% greater than their counterparts living in Nigeria, demonstrating that environmental factors are related to obesity burden.[24] Similarly, a large (N=16,415) study of Latinos living at 4 sites in the US (Chicago, Miami, Bronx - New York; San Diego) recruited in 2008–2011 found overall high age-standardized prevalence of obesity among Latin women (42·4%) and men (36·5%) from all backgrounds (countries of birth). They also found that the prevalence of obesity varied by country of birth (higher among Puerto Ricans and lowest among migrants from South America) and according to the site of residency (highest among residents of Bronx and lowest among residents in Miami). Most notable was that the strongest predictor of moderate and severe obesity was prolonged length of residency in the US. Moreover, the effect of duration of residency in the US was consistent across all origins, reinforcing the deleterious effect of exposure to an obesogenic environment as a risk factor for obesity.[25] In our analysis of the past 20 years, we also show among PWH that, Latinos/as living the in the US have greater BMI than Latinos/as PWH living in Latin America and Haitians (both at ART- and post ART-initiation). Among females, prevalence of obesity at ART initiation was at least 3-times higher in the Latinas living in the US compared to Haitians and Latinas in Latin America. Among males, prevalence of obesity was 6-times higher in the Latinos living in the US than in Haitians, and 3-times higher than in Latinos in Latin America, reinforcing the hypothesis of environmental drivers of obesity acting on PWH living in the US. In the general adult population, significant differences in the prevalence of obesity exist across countries included in these analyses. In 2016, the prevalence of obesity in Haiti was 20·5% (men: 16·4%, women: 24·3%); in Honduras, 19·1% (men: 14·1%, women: 24·5%); in Peru, 19·1% (men: 14·7%, women: 23·5%); in Brazil, 22·3% (men: 18·5%, women: 25·9%); in Mexico, 28·4% (men: 28·4%, women: 32·6%) and in the US, 37·3% (men: 36·5%, women: 38·2%).[26] Notably, in the US in 2017–2019, the prevalence of obesity among Latinos/as adults was 33·8% (versus 39·8% among non-Latinos Black and 29·9 among non-Latinos White adults).[27] In all six countries included in the present study, prevalence estimates of obesity among PWH at ART- and post-ART initiation were lower than the estimates for their respective general adult population. Low CD_4 counts and high viral loads at ART initiation, as well as enrollment in earlier years than the obesity data presented here could explain the gap between PWH included in the study and the general population observations. Low baseline CD_4 count and high viral load have been associated with lower body weight and BMI measures at ART initiation[5,6] as observed in our study. Conversely, low baseline CD_4 count and high viral load have been associated with BMI increase and obesity incidence after ART initiation,[5,6,12] highlighting the risk of overweight and obesity development among late ART initiators. In addition, we found that the use of INSTI-based regimens was associated with BMI increase after ART initiation. The risk effect of INSTI drugs on body weight gain and obesity has been described in different populations,[6,12,13] with differential effects observed for individual drugs (dolutegravir and bictegravir were associated with greater body weight gain than elvitegravir).[12,13] In our study, we were not able to fully study the effect of individual INSTI drugs on body weight and BMI trajectories over time due to small numbers of participants initiating INSTI-based regimens in Latin America and Haiti (< 1%) during the study period. Use of INSTIs in countries of Latin America has recently increased but was very limited in the study period included in our analyses. For instance, in a cohort study from Brazil,

with participants initiating ART between 2000–2015 (n=1567), only 0·9% used INSTI-based regimens, and raltegravir represented 93% of the INSTI-based regimens.[6] Future studies are needed to understand the differential effects of INSTIs (and modern INSTI drugs) in PWH living in LAC.

Of importance, despite initiating ART with lower median BMI (10% were underweight and 65% were normal weight), Latinos (males) in Latin America had the greatest adjusted probability of becoming overweight/obese or obese 3-years post-ART initiation. High probabilities were also found for female Haitians, who had the lowest BMI at ART initiation (17% were underweight and 58% normal weight) and the second greatest adjusted probability of being overweight/obese (40%) and obese post-ART initiation (12%). Heterogeneity in the dynamic of obesity burden (i.e., steepness of the trends, acceleration periods) across countries have been described for the general population,[28] but is not yet well documented among PWH. Data from the NCD Risk Factor Collaboration shows trends of BMI and obesity across countries over the past 40 years. After the year 2000, BMI increase slowed for both sexes in most of the high-income countries, including the US. In Latin America, among women the BMI increase also slowed after 2000, while among men BMI increase accelerated.[29] Dynamics in secular trends of obesity across the countries can also be explained by the obesity transition framework, which postulates predictable and sequential 4-stage transition in which a country may fall. The proposed stages use obesity prevalence estimates by gender, age (adults versus children) and socioeconomic status (low *versus* high) to classify a country. This framework provides useful insights to understand the findings in our study. According to it, in 2016, Brazil and Mexico were at stage 2 of obesity transition, which is characterized by a large increase in the prevalence among adults, a smaller increase among children, and a narrowing of the gender gap and socioeconomic differences among women, while the US was already at stage 3, when the prevalence of obesity among those with lower socioeconomic status surpasses that among those with higher socioeconomic status and plateaus in obesity may be observed among women with high socioeconomic status and children.[30]

Altogether, our findings help understand how the obesity transition has affected PWH living in different countries in the Americas. A dramatic demographic and nutrition transition was observed in LAC driven by rapid urbanization processes, income increases, dietary changes (expanded access to ultra-processed food and fast food), as well as decrease in physical activity.[31] Currently, over 60% of the general adult population in Latin America and the Caribbean are overweight, and 24% are obese. The most striking rise in obesity prevalence was recorded for the Caribbean region: in 1975, 6% of adults were obese contrasting with 25% in 2016[31]. Moreover, despite the region's economic growth, income and wealth concentration prevail, and Latin America remains the most inequitable region in the globe, with the top 10% of individuals in the income distribution capturing 54% of the national income.[32,33] Most disadvantaged populations are exposed to worse environmental conditions, have less access to healthy food and places to exercise, are more exposed to violence and chronic stress, increasing their risk of obesity and obesity-related health issues.[34,35] A large study evaluating obesity prevalence by socioeconomic status among 479,809 adults living in 13 countries in Latin America found that obesity prevalence increased in the region over the past 20 years, with larger increases among rural residents

and the most disadvantaged groups.[36] Finally, the obesity and HIV epidemics overlap, with both of them disproportionately affecting the most vulnerable populations,[30,37,38] resulting in a synergistic deleterious combination of chronic diseases which poses a large public health challenge among populations least-served by health strategies, thus reinforcing the need to understand biological and structural mechanisms driving obesity in PWH.

Obesity increases the risk of metabolic and cardiovascular diseases, osteoarthritis, Alzheimer's Disease and depression, and some cancers, leading to reduced quality of life and disability; it is also associated with decreased life expectancy.[39,40] Nonetheless, health care providers often fail to recognize obesity as a progressive and chronic disease, therefore diagnosis and treatment is delayed to a point that surgical treatment is warranted.[2] Also, stigma associated with being HIV-positive or having AIDS has been associated with overweight and obesity in PWH.[41,42] Moreover, HIV infection and obesity may interact synergistically, increasing the burden of non-communicable diseases in PWH. Obesity prevention and treatment needs to be reinforced among HIV care providers. Medical and family history of obesity and metabolic diseases should be assessed, protocols for BMI and waist circumference monitoring should be implemented in HIV routine care,[43] as well as screening for obesity-related comorbidities. Currently, obesity treatment mostly relies on physical activity and dietary interventions, however, unfortunately, these interventions are usually poorly successful in the long term. Pharmacological and surgical treatments exist but remain rarely available and unaffordable for most patients.[2]

Our study has several limitations. First, there could be possible residual confounding from unmeasured or mismeasured covariates among the study population, particularly related to environmental context, socio-economic status (e.g., individual income, employment, education, etc.), dietary composition, and treatments/interventions for obesity, which were unmeasured; on the other hand, in CCASAnet and NA-ACCORD cohorts, data collection is standardized and audited, allowing for robust measures of individual-level health status while in clinical care. Second, most of the study population included in the studies are from urban sites, limiting the generalizability to more rural populations; however, this representation is in accordance with the burden of HIV in the Americas. Third, we have limited our study population to ART initiators, possibly imposing a selection bias in the earlier years of the study period; moreover, participants were categorized according to their first ART regimen core class (NNRTI, PI or INSTI), and ART switch, modifications, or virologic failure were not taken into account. Further, we could not quantitatively assess how trends in weight and BMI among PWH differed from the HIV-negative general population nor the role of HIV or ART themselves in observed weight gain, as we did not have HIV-negative or ART non-user comparator populations, nonetheless trends in weight and obesity available for the general population from the countries included in the study were presented qualitative comparisons above. Also, models were not adjusted by the particular nucleoside reverse transcriptase inhibitors included in the regimens. It is worth mentioning that tenofovir alafenamide, found to be associated with body weight gain in randomized clinical trials,[13,44] was used by a negligible proportion of US and non-US participants during the study period. Finally, small numbers of non-US PWH used INSTI-based regimens during the study period (over 99% of INSTI users were from the US), which constrains our ability to study body weight gain and BMI trajectories among INSTI users in Latin America and

Haiti., Differential effects of INSTI drugs (i.e., dolutegravir, bictegravir, elvitegravir) on body weight gain have been demonstrated;[12,13] although important to consider, these effects were not analyzed in the present study due to limited use of INSTI regimens in Latin America and Haiti.

Conclusion

The burden of overweight and obesity is high among PWH initiating ART across six countries in the Americas. Further, PWH substantially gained body weight after ART initiation in both North and Latin America. Despite environmental and cultural differences, PWH in Latin America, Haiti and the US share concerning BMI trajectories and high probabilities of becoming overweight and obese over time. Further multicohort studies are needed to better understand the burden of other metabolic syndrome components in PWH across different countries, as well as the effect of individual drugs in PWH living in Latin America and the Caribbean.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

Data sharing

Data are made available to all authors and external collaborators upon reasonable request, in accordance with internal scientific review guidelines (https://www.ccasanet.org/collaborate/). External requests should be directed to CCASAnet Program Coordinator, Ms. Hilary Vansell (hilary.vansell@vumc.org).

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Research in context

Evidence before this study

Obesity prevalence has steadily increased in the world for the past half century; however, prevalence and trends vary between countries and can be associated with cultural and environmental contexts. In persons with HIV (PWH), obesity prevalence is also on the rise; furthermore, factors associated with HIV infection progression and antiretroviral therapy have been implicated in weight gain and obesity incidence.

Added value of this study

In this study, a diverse population of almost 60,000 PWH initiating ART in six countries in the Americas over the past 20 years were included. PWH substantially gained weight after ART initiation in both North and Latin America. Weight and BMI trajectories after ART initiation differed in Haitians, Latinos/as in Latin America and in Latinos/as and non-Latinos/as in the US. Latinos (males) in Latin America had the greatest probability of becoming overweight/obese and of becoming obese post ART initiation. Among females, Latinas in the US had the greatest probability of becoming overweight/obese while non-Latinas in the US had the greatest probability of becoming obese.

Implications of all the available evidence

The burden of obesity and overweight in PWH is increasing worldwide. Despite environmental and cultural differences, PWH in Latin America, Haiti and the US share concerning BMI trajectories and high probabilities of becoming overweight and obese over time. Obesity is a major risk factor for cardiovascular diseases, diabetes and other non-communicable diseases. Among PWH, metabolic and inflammatory consequences of obesity are likely amplified. Further research is needed to understand the burden of other metabolic syndrome components and their consequences in PWH.
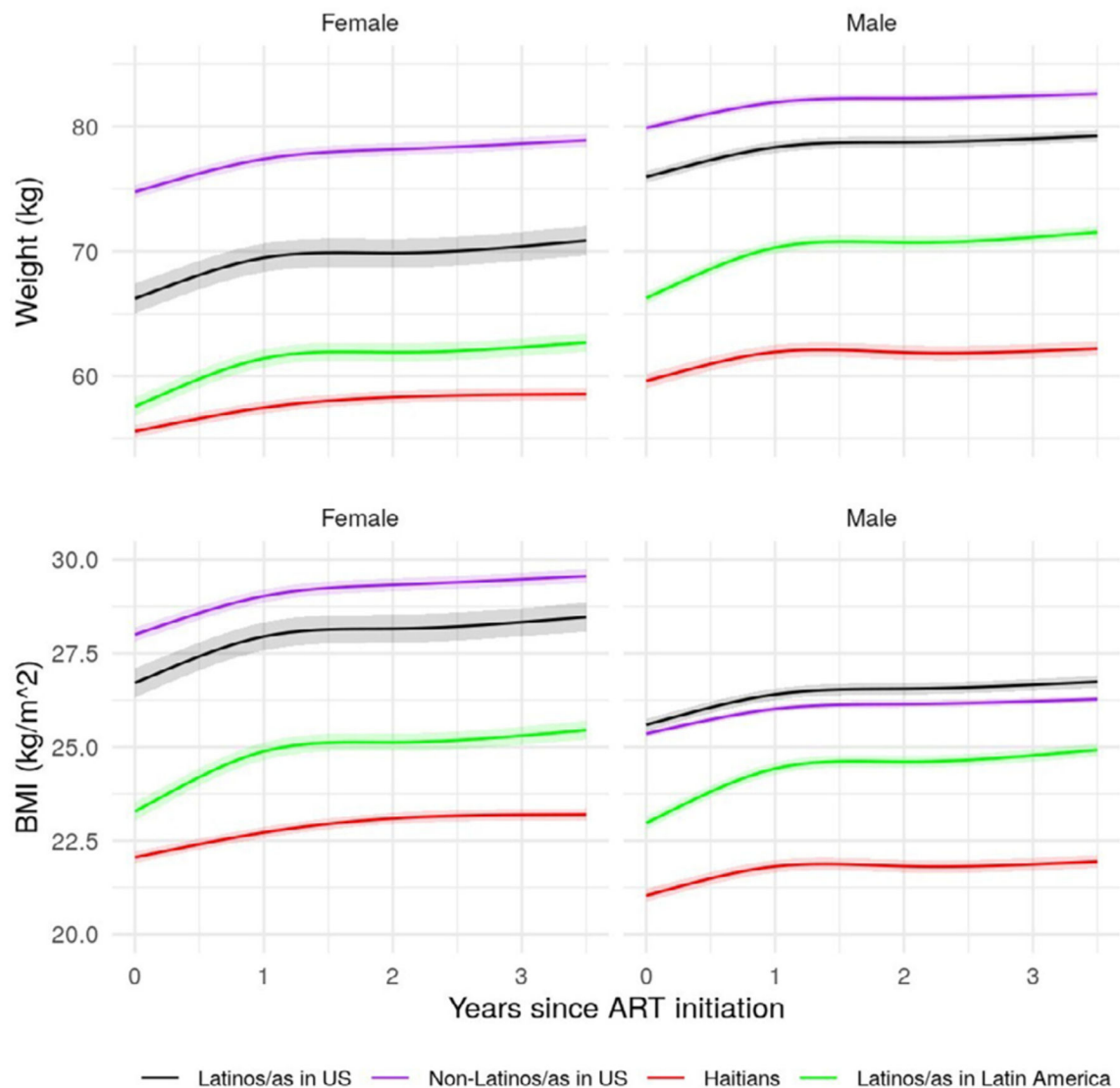
Figure 1.
Estimated changes in weight and BMI after ART initiation summarized by birth sex according to site/ethnicity

Average weight (upper left and right panels) and BMI (lower left and right panels) and 95% confidence intervals were estimated from adjusted models. Covariates included in the models were time since ART initiation, the initial antiretroviral class regimen, birth sex, year of ART initiation, and baseline age, CD4 count and HIV viral load. Time was interacted with baseline weight or BMI, sex, and ethnicity. An interaction between sex and ethnicity was also included.
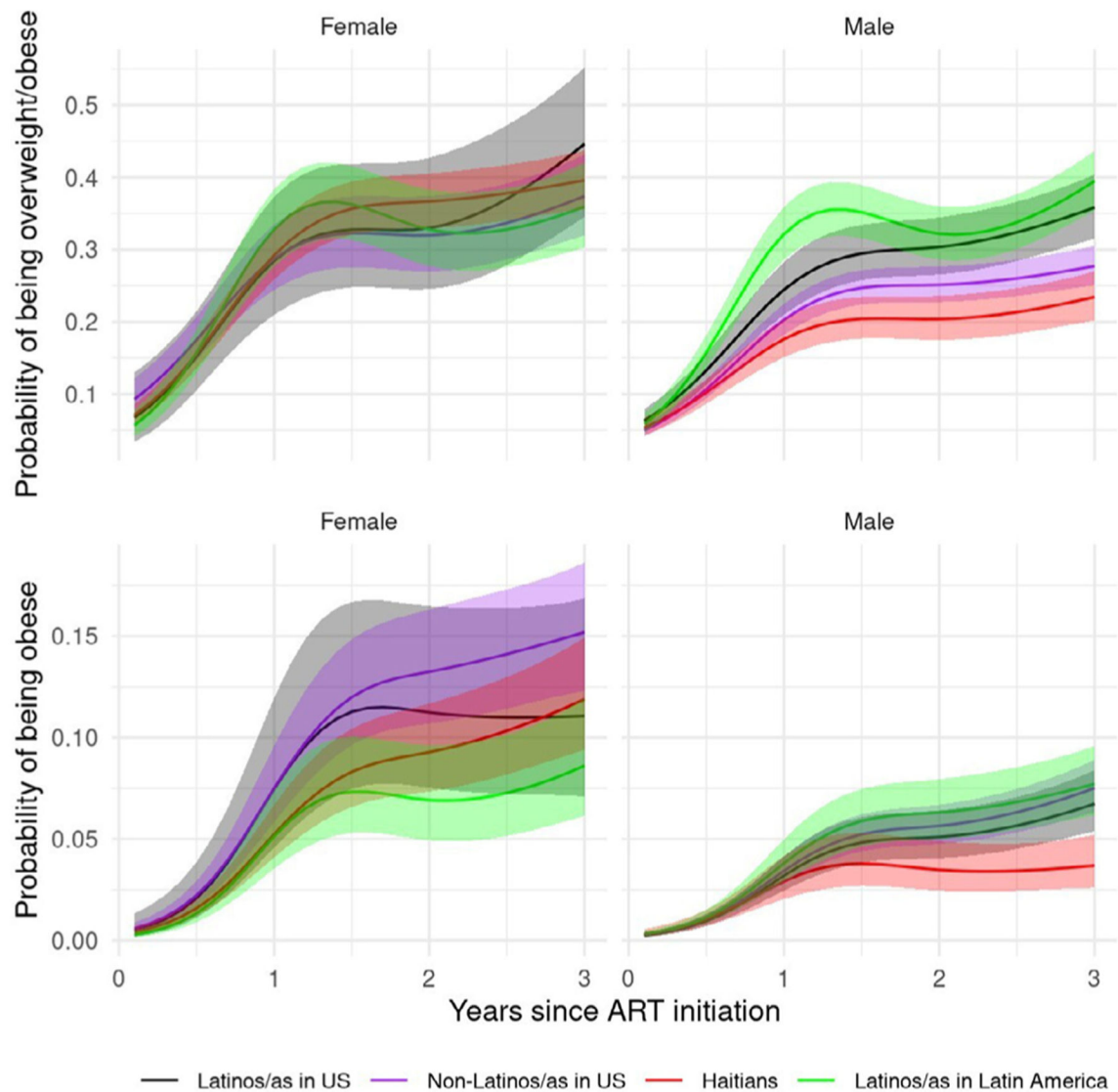
Figure 2.
Probabilities of becoming overweight or obese (subset of PWH with BMI <25 kg/m^2 at ART initiation) and probabilities of becoming obese (subset of PWH with BMI <30 kg/m^2 at ART initiation) among males and females according to site/ethnicity

Probabilities and 95% confidence intervals. Covariates included in the models were time since ART initiation, the initial antiretroviral class regimen, birth sex, year of ART initiation, and baseline age, CD4 count and HIV viral load. Time was interacted with baseline weight or BMI, sex, and ethnicity. An interaction between sex and ethnicity was also included.

Table 1:

Characteristics of the PWH included in the study by site/ethnicity categories.

	Haitians	Latinos in Latin America	Latinos in US	Non-Latinos in US	Total	P-value
	N=8393	N= 5450	N=5081	N = 40283	N = 59207	
Sex						< 0.001
Male	37% (3114)	72% (3907)	90% (4577)	88% (35481)	80% (47079)	
Female	63% (5279)	28% (1543)	10% (504)	12% (4802)	20% (12128)	
Age at ART initiation (years)	37 (30, 45)	35 (29, 42)	40 (32, 49)	45 (36, 53)	42 (33, 51)	< 0.001
BMI at ART initiation (kg/m^2)	21 (19, 24)	22 (20, 25)	25 (23, 28)	25 (22, 28)	24 (21, 28)	< 0.001
<18.5	18% (1206)	12% (475)	3% (117)	4% (1069)	7% (2867)	
18.5–24.9	62% (4054)	62% (2523)	44% (1612)	46% (12561)	50% (20750)	
25.0–29.9	13% (865)	21% (860)	38% (1380)	32% (8693)	29% (11798)	
30.0	6% (423)	5% (210)	15% (553)	18% (4777)	14% (5963)	
BMI at 1 year (kg/m^2)						< 0.001
<18.5	12% (403)	4% (79)	2% (30)	2% (372)	4% (884)	
18.5–24.9	63% (2030)	52% (1085)	37% (647)	40% (6098)	45% (9860)	
25.0–29.9	19% (600)	35% (740)	42% (729)	35% (5356)	34% (7425)	
30.0	6% (204)	9% (196)	19% (322)	22% (3264)	18% (3986)	
BMI at 3 years (kg/m^2)						< 0.001
<18.5	10% (195)	3% (52)	1% (18)	2% (312)	3% (577)	
18.5–24.9	59% (1206)	49% (895)	34% (561)	39% (5045)	42% (7707)	
25.0–29.9	22% (450)	36% (664)	43% (703)	36% (4627)	35% (6444)	
30.0	10% (198)	12% (229)	21% (347)	23% (3016)	20% (3790)	
CD4 at ART initiation (cells/mm^3)	239 (116, 352)	174 (64, 302)	305 (152, 491)	310 (157, 494)	287 (136, 459)	< 0.001
HIV viral load at ART initiation (copies/mL log10-transformed)	3.9 (3.1, 4.4)	4.9 (4.3, 5.4)	4.5 (3.3, 5.0)	4.4 (3.1, 5.0)	4.5 (3.3, 5.1)	< 0.001
Year of ART initiation	2012 (2009, 2014)	2009 (2006, 2011)	2009 (2005, 2012)	2009 (2004, 2012)	2009 (2005, 2012)	< 0.001
Regimen class at ART initiation						< 0.001
NNRTI-based	94% (7866)	83% (4520)	48% (2428)	51% (20412)	59% (35226)	
PI-based	6% (527)	15% (842)	36% (1854)	36% (14388)	30% (17611)	
INSTI-based	0% (0)	2% (88)	16% (799)	14% (5483)	11% (6370)	
Lost to follow-up						< 0.001

	Haitians	Latinos in Latin America	Latinos in US	Non-Latinos in US	Total	P-value
	N=8393	N= 5450	N=5081	N = 40283	N = 59207	
No	13% (1107)	12% (645)	30% (1530)	28% (11245)	25% (14527)	
Yes	87% (7286)	88% (4805)	70% (3551)	72% (29038)	75% (44680)	
Follow-up (Years)	2·7 (1·3, 3·4)	3·2 (2·2, 3·4)	3·1 (1·7, 3·4)	3·1 (1·9, 3·4)	3·1 (1·8, 3·4)	< 0·001

Results presented frequencies and proportions or as medians and interquartile ranges.

BMI: body mass index; ART: antiretroviral therapy; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; INSTI: integrase strand inhibitor.