Association Between Weight Gain and the Incidence of Cardiometabolic Conditions Among People Living With HIV-1 at High Risk of Weight Gain Initiated on Antiretroviral Therapy

Grace A. McComsey,[1] Bruno Emond,[2] Aditi Shah,[2] Brahim K. Bookhart,[3] Carmine Rossi,[2] Katherine Milbers,[2] Marie-Hélène Lafeuille,[2] Prina Donga[3,*]

*Presenting author.

[1]Case Western Reserve University, Cleveland, OH, USA; [2]Analysis Group, Inc., Montréal, QC, Canada; [3]Janssen Scientific Affairs, LLC, Titusville, NJ, USA.

INTRODUCTION

- Antiretroviral therapy (ART) effectively reduces transmission[1] and improves clinical outcomes[2,3] and quality of life[4] among people living with human immunodeficiency virus (HIV; PLWH)
- However, ART has also been associated with weight gain in PLWH; in particular, female, Black, or Hispanic PLWH are at higher risk of ART-related weight gain, regardless of the regimen being used[5,6]
- While previous research has shown that ART use is associated with a higher risk of diabetes[6–8] and that weight gain is associated with a higher risk of developing cardiometabolic conditions and death,[9,10] there are few studies that have assessed the risk of metabolic, cardiovascular, and cardiometabolic outcomes associated with ART-related weight gain

OBJECTIVE

- To evaluate the incidence of metabolic and cardiovascular conditions among treatment-naïve PLWH who are at high risk of weight gain and experiencing a ≥5% versus <5% weight or body mass index (BMI) increase following ART initiation

METHODS

Data Source

- Electronic medical records (EMR) and administrative claims data from the Symphony Health, an ICON plc company, IDV® database (October 1, 2014–March 31, 2021) were used to identify the population of interest and conduct the analysis
- The database links health care data for the US population from 3 basic sources: pharmacy point-of-service; switch/network transactions; and additional direct prescription, medical, and hospital claims data
- The data comprise claimant demographics, medical and procedure claims, as well as historical clinical information from linked EMR data, including medications prescribed, laboratory results, vital signs, height and weight measurements, and diagnoses
- Data are de-identified and comply with the patient requirements of the Health Insurance Portability and Accountability Act (HIPAA)

Study Design

- A retrospective longitudinal cohort study design was used for this study (**Figure 1**)
- The index date was identified in the EMR and defined as the date of initiation of the first ART regimen with a recommended protease inhibitor (PI)–based, integrase strand transfer inhibitor (INSTI)–based, or non-nucleoside reverse transcriptase inhibitor (NNRTI)–based regimen per the Department of Health and Human Services (DHHS) guidelines[11]
- The baseline period was defined as the 12-month period before the index date
- The 6-month period following the index date was defined as the landmark period and was used to assess weight/BMI changes following ART initiation relative to the baseline period
- The observation period to evaluate cardiometabolic outcomes started after the 6-month landmark period and ended at the end of continuous clinical activity or end of data availability (i.e., March 31, 2021), whichever occurred first
- PLWH were assigned to 1 of 2 cohorts based on the change in weight/BMI observed between the baseline period and the landmark period:
  - ≥5% weight/BMI increase
  - <5% weight/BMI increase

Study Population

- Treatment-naïve female, Black, or Hispanic PLWH initiating an ART regimen were identified for inclusion in the study
- The sample selection criteria are presented in **Figure 2**

Figure 1. Study design scheme.

Abbreviations: ART=antiretroviral therapy; BMI=body mass index; DHHS=Department of Health and Human Services; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; PI=protease inhibitor.
*Baseline laboratory and weight/BMI values were obtained from the baseline period measurement prior to and closest to the index date.
†All weight/BMI values observed during the landmark period were assessed to determine if there was a weight/BMI gain ≥5% relative to the baseline value.

Figure 2. Study population selection.

Abbreviations: ART=antiretroviral therapy; BMI=body mass index; CKD=chronic kidney disease; ESRD=end-stage renal disease; HIV=human immunodeficiency virus; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; PLWH=people living with human immunodeficiency virus.

Study Measures

- Demographic and clinical characteristics were evaluated during the baseline period
- Following the landmark period, the incidence of each of the following conditions was evaluated: metabolic conditions (i.e., type 2 diabetes mellitus [T2DM], hypertension, lipid disorders, lipodystrophy, and metabolic syndrome) and cardiovascular conditions (i.e., coronary artery disease, congestive heart failure, stroke/transient ischemic attack, and myocardial infarction)
  - PLWH were eligible for the analysis of each incident outcome, separately, if they did not have ≥1 diagnosis for this condition or use ≥1 medication related to the condition (e.g., antidiabetic medication as a proxy for T2DM) during the baseline or landmark periods
- Furthermore, a composite outcome was evaluated and was defined as having an incident outcome with any of the above conditions
  - Patients with the presence of a specific condition during the baseline or landmark periods could not develop that same condition during the observation period, but they could develop another cardiometabolic outcome that they did not have during the baseline or landmark periods

Statistical Analysis

- Baseline characteristics were balanced between patients with weight/BMI increase ≥5% or <5% using inverse probability treatment weighting (IPTW)
  - Weights were calculated based on propensity scores obtained from a logistic regression model adjusting for the following variables: age, sex, race, geographic region, insurance plan type, year of index date, Quan-Charlson Comorbidity Index (excluding HIV symptoms), weight loss, weight gain medications, weight loss medications, antihypertensives, antihyperlipidemics, antidiabetics, time between HIV onset and the index date (in months), and use of a PI, INSTI, NNRTI, tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) as part of the index regimen
- Comparison of baseline characteristics after applying IPTW was made using standardized differences, with differences of <10% considered balanced[12]
- Weighted multivariate Cox regression models were used to obtain hazard ratios (HRs) comparing the time to incident cardiometabolic outcomes between patients with weight/BMI increase ≥5% or <5%
- Nonparametric bootstrap procedures with 500 resamples were used to calculate 95% confidence intervals and p-values

RESULTS

Patient Characteristics

- A total of 1,252 PLWH met the study inclusion criteria; during the landmark period, 366 (29.2%) experienced a weight/BMI increase ≥5% and the remaining 886 (70.8%) experienced a weight/BMI increase <5% (**Figure 2**)
- After IPTW, the weighted sample size was 620 for PLWH with weight/BMI increase ≥5% and 632 for PLWH with weight/BMI increase <5%; the baseline characteristics were well balanced between the 2 cohorts (**Table 1**)
- The mean age in both cohorts was 47.8 years, ~60% were female, ~49% were Black, and ~17% were Hispanic (**Table 1**)
- INSTI-based regimens were the most frequently observed ART regimens in both cohorts (~78%; **Table 1**)
- The mean change in weight observed between the baseline period and the landmark period was +6.7 kg (+14.8 lbs) for patients with weight/BMI increase ≥5% and –0.1 kg (–0.2 lbs) for patients with weight/BMI increase <5%; mean changes in BMI measurements are shown in **Table 2**

Comparison of Incident Cardiometabolic Outcomes

- The mean (standard deviation) length of the observation period post-landmark was 2.0 (1.3) years for both cohorts
- PLWH with weight/BMI increase ≥5% were significantly and substantially more likely to develop T2DM (HR=2.19; p=0.044) compared to PLWH with weight/BMI increase <5% (**Figure 3**)
- There was no statistically significant difference in the likelihood of experiencing ≥1 cardiometabolic outcome between the 2 cohorts (HR=1.09; p=0.248; **Figure 3**)
- Differences for the other individual cardiometabolic outcomes also did not reach statistical significance; HRs ranged from 0.44 for congestive heart failure (p=0.220) to 1.07 for lipid disorders (p=0.820; **Figure 3**)

Table 1. Patient Baseline Characteristics

	Weighted population*		
	Weight/BMI gain ≥5% N=620	Weight/BMI gain <5% N=632	Standardized difference
Demographic characteristics			
Age at index date (years), mean ± SD [median]	47.8 ± 13.0 [49.0]	47.8 ± 13.0 [49.0]	0.2%
Female, n (%)	372 (59.9)	368 (58.2)	3.5%
Race/ethnicity, n (%)			
Black	305 (49.2)	312 (49.3)	0.2%
Hispanic	101 (16.3)	109 (17.2)	2.6%
White	97 (15.6)	95 (15.0)	1.6%
Other	4 (0.6)	5 (0.8)	2.6%
Unknown	113 (18.3)	111 (17.6)	1.9%
US geographic region, n (%)			
South	427 (68.9)	435 (68.9)	0.1%
Northeast	71 (11.5)	68 (10.8)	2.1%
Midwest	65 (10.5)	66 (10.4)	0.4%
West	56 (9.1)	61 (9.7)	2.1%
Unknown	0	1 (0.2)	6.4%
Insurance plan type, n (%)			
Insurance plan information available (in claims)	568 (91.6)	577 (91.2)	1.3%
Commercial	372 (60.0)	377 (59.6)	0.9%
Medicare	97 (15.7)	105 (16.5)	2.3%
Medicaid	86 (13.9)	82 (12.9)	2.9%
Other	4 (0.6)	4 (0.7)	1.2%
Unknown	8 (1.4)	9 (1.5)	0.9%
Year of index date, n (%)			
2015	39 (6.2)	38 (6.0)	0.9%
2016	155 (25.0)	166 (26.2)	2.8%
2017	146 (23.6)	150 (23.7)	0.2%
2018	122 (19.6)	119 (18.9)	1.9%
2019	125 (20.2)	126 (19.9)	0.8%
2020	33 (5.4)	34 (5.3)	0.1%
Clinical characteristics			
Time between HIV disease onset and index date, n (%)			
≤12 months	37 (6.0)	35 (5.5)	1.9%
>12 to ≤24 months	28 (4.5)	27 (4.3)	0.8%
>24 to ≤36 months	17 (2.8)	17 (2.7)	0.6%
>36 to ≤48 months	17 (2.7)	20 (3.1)	2.1%
>48 to ≤60 months	21 (3.4)	20 (3.2)	1.2%
>60 months	74 (11.9)	74 (11.7)	0.8%
Unknown	426 (68.7)	439 (69.5)	1.7%
Quan-CCI (excluding HIV symptoms), mean ± SD [median]	1.1 ± 1.4 [1.0]	1.1 ± 1.6 [0.0]	0.8%
Weight loss, n (%)	42 (6.8)	39 (6.2)	2.7%
Medications associated with weight gain, n (%)	159 (25.6)	154 (24.3)	2.9%
Medications associated with weight loss, n (%)	44 (7.1)	43 (6.8)	1.1%
Antihypertensives, n (%)	117 (18.9)	127 (20.1)	3.2%
Antihyperlipidemics, n (%)	52 (8.4)	52 (8.3)	0.5%
Antidiabetics, n (%)	39 (6.3)	37 (5.8)	2.1%
Index regimen characteristics			
Patients treated with specific regimens, n (%)			
INSTI-based	483 (78.0)	488 (77.1)	2.0%
NNRTI-based	123 (19.8)	131 (20.7)	2.1%
PI-based	24 (3.9)	25 (3.9)	0.0%
NRTI agents			
TAF	278 (44.8)	273 (43.2)	3.1%
TDF	169 (27.3)	184 (29.1)	4.0%

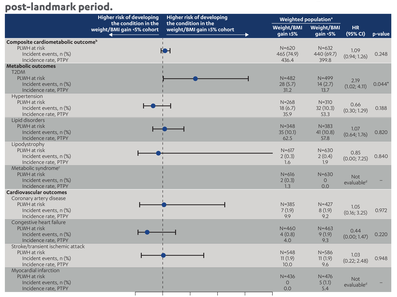
Abbreviations: BMI=body mass index; CCI=Charlson Comorbidity Index; HIV=human immunodeficiency virus; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; SD=standard deviation; TAF=tenofovir alafenamide; TDF=tenofovir disoproxil fumarate; US=United States.
*Of note, the number of patients reported in this weighted population represents the sum of weights for the corresponding patients, rounded to the nearest integer. The proportions displayed were calculated prior to the rounding and may be slightly different than if they were calculated based on rounded numbers.

Table 2. Weight, BMI, and Cardiometabolic Comorbidities During the Baseline and Landmark Periods

	Weighted population*	
	Weight/BMI gain ≥5% N=620	Weight/BMI gain <5% N=632
During the baseline period		
Patients with a BMI measurement,† n (%)	469 (75.7)	469 (74.3)
BMI (kg/m²),‡ mean ± SD [median]	30.2 ± 8.0 [28.8]	29.2 ± 6.8 [28.4]
BMI categories (kg/m²), n (%)		
<25	142 (30.2)	145 (31.0)
25 to 29	128 (27.3)	136 (29.0)
30 to 34	79 (16.8)	95 (20.3)
≥35	121 (25.7)	92 (19.7)
Patients with a weight measurement,† n (%)	615 (99.2)	626 (99.1)
Weight (kg),‡ mean ± SD [median]	87.3 ± 27.7 [81.2]	84.5 ± 21.6 [81.2]
Cardiometabolic comorbidities, n (%)		
Composite cardiometabolic outcome	395 (63.7)	364 (57.6)
T2DM	116 (18.7)	125 (19.8)
Hypertension	301 (48.6)	282 (44.7)
Lipid disorders	226 (36.4)	207 (32.8)
Lipodystrophy	3 (0.5)	2 (0.3)
Metabolic syndrome	3 (0.5)	2 (0.3)
Congestive heart failure	104 (16.7)	121 (19.2)
Coronary artery disease	163 (26.3)	151 (23.9)
Myocardial infarction	125 (20.2)	111 (17.6)
Stroke/ischemic attack	59 (9.6)	33 (5.2)
During the landmark period		
Patients with a BMI measurement,† n (%)	469 (75.7)	469 (74.3)
BMI (kg/m²),‡ mean ± SD [median]	32.4 ± 7.7 [31.1]	29.1 ± 6.8 [28.3]
BMI categories (kg/m²), n (%)		
<25	96 (20.4)	149 (31.7)
25 to 29	110 (23.5)	134 (28.5)
30 to 34	97 (20.6)	94 (20.1)
≥35	167 (35.5)	92 (19.7)
Patients with a weight measurement,† n (%)	615 (99.2)	626 (99.1)
Weight (kg),‡ mean ± SD [median]	94.0 ± 28.0 [87.5]	84.4 ± 21.8 [81.6]
Cardiometabolic comorbidities, n (%)		
Composite cardiometabolic outcome	375 (60.4)	344 (54.4)
T2DM	128 (20.7)	114 (18.0)
Hypertension	296 (47.7)	270 (42.8)
Lipid disorders	211 (34.0)	184 (29.1)
Lipodystrophy	0	1 (0.2)
Metabolic syndrome	3 (0.4)	0
Congestive heart failure	107 (17.3)	100 (15.9)
Coronary artery disease	157 (25.4)	134 (21.2)
Myocardial infarction	121 (19.6)	85 (13.4)
Stroke/ischemic attack	47 (7.6)	26 (4.1)
BMI and weight-related changes between the baseline and landmark periods§		
Change in BMI (kg/m²) after the index date, mean ± SD [median]	2.2 ± 2.1 [1.9]	0.0 ± 1.2 [0.1]
Change in weight (kg) after the index date, mean ± SD [median]	6.7 ± 6.9 [5.2]	–0.1 ± 3.3 [0.4]

Abbreviations: BMI=body mass index; HIV=human immunodeficiency virus; SD=standard deviation; T2DM=type 2 diabetes mellitus; TAF=tenofovir alafenamide; TDF=tenofovir disoproxil fumarate.
*Of note, the number of patients reported in this weighted population represents the sum of weights for the corresponding patients, rounded to the nearest integer.
†The proportions displayed were calculated prior to the rounding and may be slightly different than if they were calculated based on rounded numbers.
‡Evaluated based on the most recent measurement before the end of the 12-month pre-index (baseline) period among patients with a measurement in both the baseline and 6-month post-index (landmark) period.
§Evaluated as the difference between the highest measured value in the 6-month post-index (landmark) period among patients with a measurement in both the baseline and 6-month post-index (landmark) period.
¶Evaluated as the difference between the most recent baseline weight value and the highest measured value in the 6-month post-index (landmark) period.

Figure 3. Comparison of incident cardiometabolic outcomes during the post-landmark period.



Abbreviations: BMI=body mass index; CI=confidence interval; HR=hazard ratio; ICD-9-CM/ICD-10-CM=International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification; PTPY=per 100 person-years; T2DM=type 2 diabetes mellitus; vs=versus.
*Of note, the number of patients reported in this weighted population represents the sum of weights for the corresponding patients, rounded to the nearest integer. The proportions displayed were calculated prior to the rounding and may be slightly different than if they were calculated based on rounded numbers.
†Either T2DM, hypertension, lipid disorders, lipodystrophy, metabolic syndrome, coronary artery disease, congestive heart failure, stroke/transient ischemic attack, or myocardial infarction.
‡The incidence of metabolic syndrome may have been underestimated in the current analysis, as it was identified solely based on ICD-9-CM/ICD-10-CM codes and information such as waist circumference was not available.
#HR was not available due to there being no incident events in 1 of the cohorts.
*Significant at the 5% level.

LIMITATIONS

- Claims and EMR data may contain inaccuracies or omissions in diagnoses, billing, and other variables; information on family or social history was not available
- The Symphony Health, an ICON plc company, IDV® database is a provider-based data source that will not capture the services patients received from a provider outside of the network
- Since the study population was PLWH at high risk of weight gain who were treatment naïve and had ≥1 weight/BMI measurement in the baseline and landmark periods, results may not be generalizable to the entire HIV population
- This study used an intention-to-treat approach where patients were observed until the end of follow-up regardless of switching or discontinuation of the ART regimen initiated at index
- Imposing 6 months of clinical activity after the index date (i.e., the landmark period) may have resulted in survival bias and the selection of more healthy patients
- The incidence of metabolic syndrome may have been underestimated in the current analysis, as waist circumference was not available

CONCLUSIONS

- **Despite a short follow-up of 2 years, female, Black, or Hispanic PLWH experiencing ≥5% weight/BMI increase within 6 months of initiation of ART more than doubled their risk of incident T2DM**
- **No difference in cardiovascular outcomes was noted, likely due to the short follow-up period**
- **Further research with longer follow-up is warranted to examine the impact of ART-related weight gain on long-term clinical outcomes, but these data suggest that, at least for some conditions, the implications of early weight gain after ART initiation are significant**

REFERENCES

1. Baxmeier BR, et al. Lancet HIV. 2018;5(8):e438–e447.
2. Petoletta P, et al. N Engl J Med. 1998;338(13):853–860.
3. Lundgren JD, et al. N Engl J Med. 2015;373(9):795–807.
4. Farham PC, et al. J Acquir Immune Defic Syndr. 2013;64(2):183–189.
5. Chen YM, et al. J Health Econ Outcomes Res. 2020;7(2):102–110.
6. Koumi A, et al. Open Forum Infect Dis. 2020;7(suppl 1):S501–S506.
7. Nansseu JR, et al. Epidemiology. 2018;29(3):431–441.
8. Yu Y, et al. Front Endocrinol (Lausanne). 2020;11:559401.
9. Bae YS, et al. J Am Heart Assoc. 2019;8(17):e013025.
10. Narayan KMV, et al. Diabetes Care. 2007;30(6):1562–1566.
11. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. 2021. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/AdultAndAdolescentGL_2021_08_16.pdf. Accessed April 6, 2022.
12. Austin PC. Commun Stat Simul Comput. 2009;38(6):1228–1234.

ACKNOWLEDGMENT

Editorial support was provided by Melanie Chen, PharmD, of Cello Health Communications/Medthings, and was funded by Janssen Scientific Affairs, LLC.

DISCLOSURES

This study was funded by Janssen Scientific Affairs, LLC. GAM is an employee of Case Western Reserve University and has received consulting fees from Janssen Scientific Affairs, LLC; BE, SR, KM, and M-HL are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC; BKB and PD are employees of Janssen Scientific Affairs, LLC, and shareholders of Johnson & Johnson. All authors participated in the design of the study, interpretation of the results, and preparation of the poster.

If you have any additional questions or would like to request a copy of this poster, call +1-800-JANSSEN (+1-800-526-7736) or go to www.janssen-MD.com.

An electronic version of the poster can be viewed by scanning the QR code. The QR code is intended to provide scientific information for individual reference. The PDF should not be altered or reproduced in any way.