HIV-ASSOCIATED WASTING REMAINS AN UNDERAPPRECIATED COMORBIDITY IN PEOPLE LIVING WITH HIV IN THE ERA OF MODERN ART

Javeed Siddiqui,[1] Brooke Hayward,[2] Kelly A. Wirka,[2] Amy Phillips,[2] Kathleen L Deering,[3] Qing Harshaw,[3] Michael Harbour[2]

[1]TeleMed2U, [2]EMD Serono, Inc., Rockland, MA, USA, a business of Merck KGaA, Darmstadt, Germany, Inc., [3]EPI-Q, Inc.

Miami Center for AIDS Research (CFAR) – HIV & Aging In The Era Of ART And COVID-19, February 8-9th, 2021 (Virtual)

EMD SERONO

Background

Advances in antiretroviral therapy (ART) and the care of people living with HIV have tremendously improved AIDS associated morbidity and mortality[1,2]

As people living with HIV are living longer, they remain at a **higher risk of age-associated comorbidities** including HIV-associated Wasting[2,3]

HIV-associated Wasting increases morbidity and mortality[4,5] but has received little attention in the era of modern antiretroviral therapy

Given the changing profile of people living with HIV, these **retrospective analyses evaluated the prevalence and comorbidity burden** of HIV-associated Wasting (2012-2018) using medical and pharmacy claims databases.

Methods: Selection Criteria And Study Design

Retrospective medical and pharmacy claims study using the IBM® MarketScan® Commercial and Medicare Supplemental Database and Medicaid Database

Selection Criteria For HIV+ Study Population

- **INCLUDES:** ≥2 outpatient claims (>30 days apart) or ≥1 inpatient claim for HIV (ICD-9/10: 042, V08, B20, Z21), **N=153,903**
- **INCLUDES:** ≥18 years old on the index date, **N=152,256**
- **EXCLUDES:** Patients with any malignancies, **N=146,966**
- **INCLUDES:** Patients continuously enrolled ≥6 months pre- and post-index, **N=42,587**

1 Defined as first date that all criteria were met between July 1, 2012 and September 30, 2018.
2 2012-2013 includes Medicaid only; 2019 includes Commercial/Medicare through March only

Methods: Statistical Analysis

Prevalence of HIV-associated Wasting

- Cumulative prevalence was estimated for the study period (2012-2018) and reported in terms of frequencies and percentages

Unadjusted bivariate analyses compared demographic and clinical characteristics

- Student's t-tests or Wilcoxon rank-sum tests were used for continuous variables and reported in terms of means, standard deviations (SD), medians, and ranges
- Chi-square tests were used for categorical variables and reported in terms of frequencies and percentages

Correlates of HIV-associated Wasting

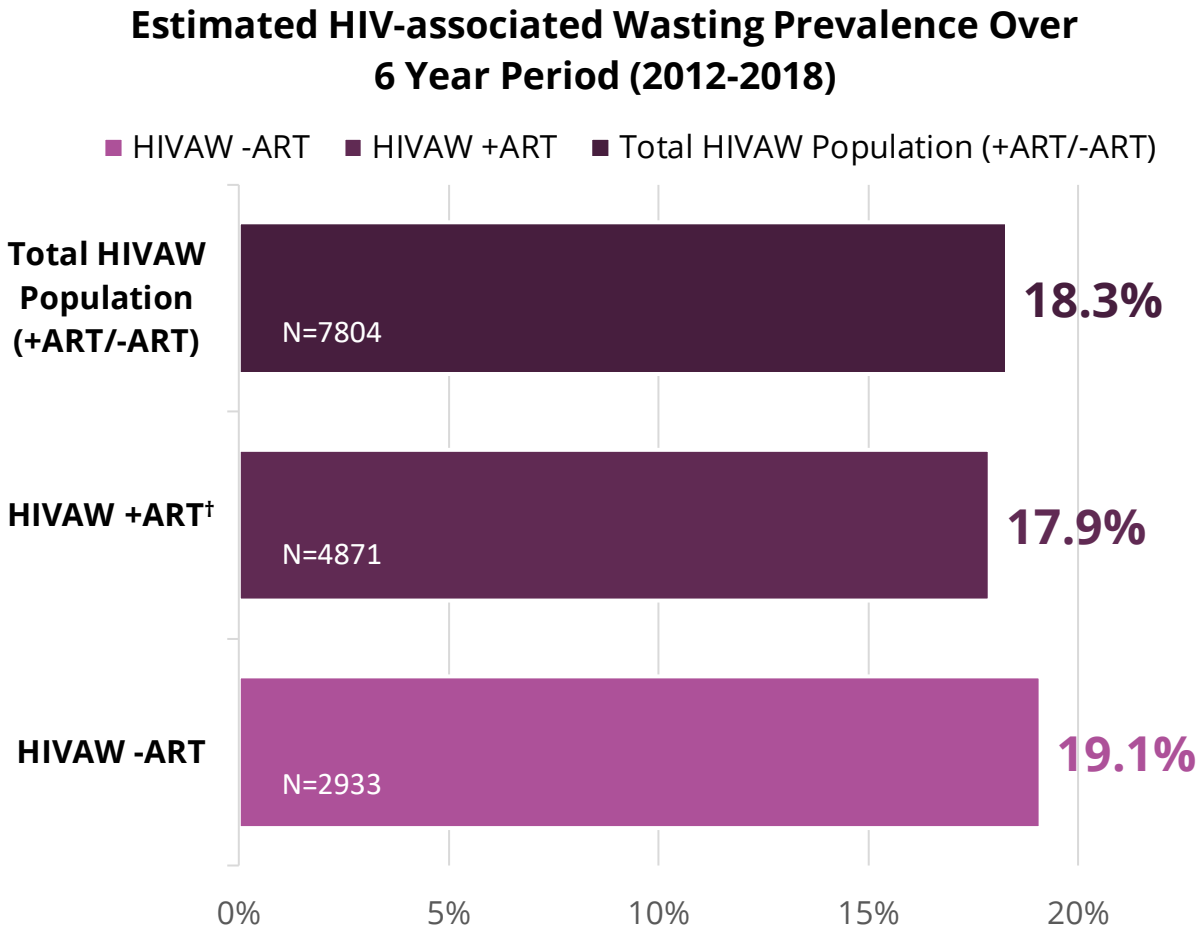
- Multivariate logistic regression analyses were conducted to assess demographic and clinical correlates of HIV-associated Wasting

Methods: Identification of HIV-Associated Wasting Cohort

Cohort: HIV-associated Wasting* ***Patients in the HIV-associated Wasting cohort must meet at least one of A, B, C, or D criteria***		**HIV+ Study Population N=42,587 n (%)**
A. ≥1 inpatient claim or ≥2 outpatient claim (with same diagnosis code on different service date or combination of any diagnosis below on different dates) with a diagnosis for weight loss	Nutritional marasmus, Other protein-calorie malnutrition, Anorexia nervosa, Abnormal loss of weight and underweight (unintentional weight loss), Feeding difficulties and mismanagement, Failure to thrive, Cachexia, Effects of hunger, Adult neglect (nutritional), Body Mass Index (BMI) <19, adult	**6873 (16.1)**
B. A claim for appetite stimulant or non-testosterone anabolic agent	Appetite stimulants (dronabinol, megestrol) and Anabolic agents (oxandrolone, nandrolone, oxymetholone, dehydroepiandrosterone [DHEA], 7-oxo-DHEA, androstenedione)	**1644 (3.9)**
C. Evidence of enteral or parenteral nutrition	Enteral infusion of nutritional substances, Enteral nutrition home therapy, Enteral feeding supplies, Enteral nutrition formula/additives, Enteral nutrition infusion pump, Total parenteral nutrition home therapy, Parenteral nutrition solution/additives, Parenteral nutrition supplies, Parenteral nutrition infusion pump, Aminosyn, Freamine, Procalamine, Travasol	**776 (1.8)**
D. At least two of the following:	Presence of only one medical claim for weight loss or wasting in the primary or secondary position; Anorexia (≥1 inpatient claim or ≥ 2 outpatient claims at least 30 days apart); A claim for testosterone (and derivatives), growth hormone, thalidomide, or high-calorie nutritional supplements	**122 (0.3)**
Total HIV-associated Wasting Cohort		**7804 (18.3)**

*Patients might have more than one criterion
Criteria requiring ≥2 outpatient diagnosis claims were required to be on separate service dates

Results: Estimated HIV-Associated Wasting Prevalence During a 6 Year Period (2012-2018)



64.0% Among the HIV+ Study Population (N=42,587), 64.0% were on ART (n=27,242)#

Across the span of the 6-year respective medical and pharmacy claims analysis (2012-2018*):

18.3% 18.3% of HIV-positive patients were identified as having HIV-associated Wasting

17.9% **17.9% of patients were on antiretroviral therapy**

19.1% **19.1% were not on antiretroviral therapy**

#Updated Analysis
*2012-2013 includes Medicaid only; 2019 includes Commercial/Medicare through March only
†On ART is defined as ≥1 pharmacy claim of any ART 12-months post-HIV index

Results: Baseline Demographics

	non-HIVAW N=34,783	Total HIVAW N=7804	HIVAW +ART N= 4871	HIVAW -ART N= 2933
Male, n (%)	22,700 (65.3)	4816 (61.7)	2972 (61.0)	1844 (62.9)
Age on HIV index date				
Mean (SD)	43.5 (12.5)	46.4 (12.0)	44.6 (11.6)	49.4 (12.3)
18 - 39 years of age, n (%)	12,805 (36.8)	2100 (26.9)	1521 (31.2)	579 (19.7)
40 - 64 years of age, n (%)	20,908 (60.1)	5330 (68.3)	3295 (67.7)	2035 (69.4)
65+ years of age, n (%)	1070 (3.1)	374 (4.8)	55 (1.1)	319 (10.9)
Age at first evidence of HIV-associated Wasting				
Mean (SD)		48.1 (12.2)	46.2 (11.7)	51.4 (12.4)
18 - 39 years of age, n (%)		1856 (23.8)	1365 (28.0)	491 (16.7)
40 - 64 years of age, n (%)		5451 (69.9)	3384 (69.5)	2067 (70.5)
65+ years of age, n (%)		497 (6.4)	122 (2.5)	375 (12.8)

The majority of people living with HIV in this study were male

The HIV-associated Wasting cohort was older at HIV index compared to non-HIV-associated Wasting

Results: Insurance Status

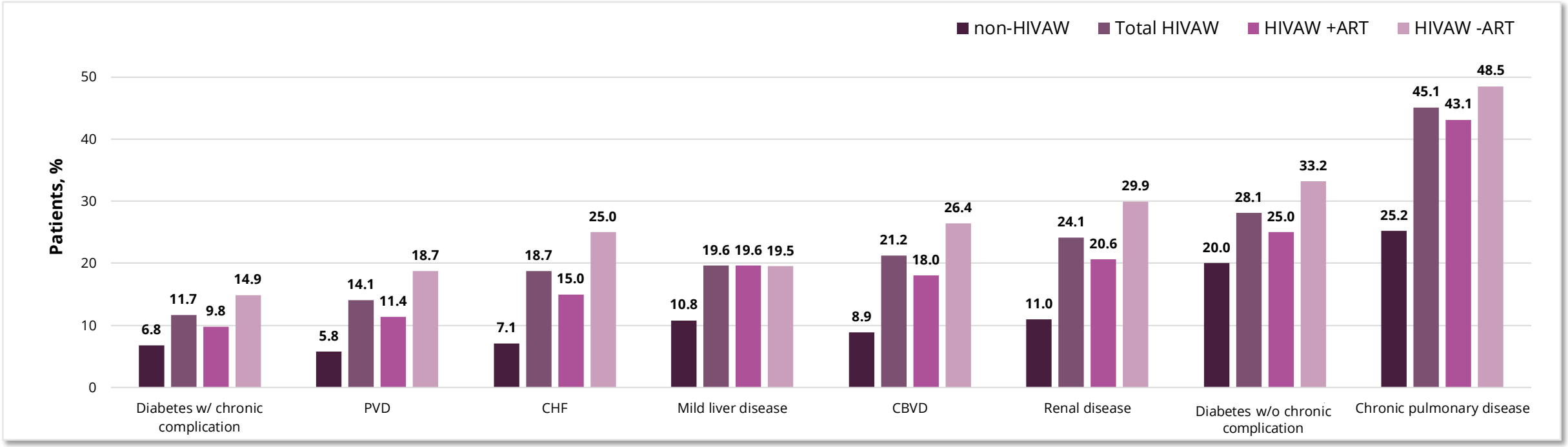
	non-HIVAW N=34,783	Total HIVAW N=7804	HIVAW +ART N= 4871	HIVAW -ART N= 2933
Commercial, n (%)	12,806 (36.8)	1040 (13.3)	836 (17.2)	204 (7.0)
Medicare Supplementation, n(%)	353 (1.0)	44 (0.6)	24 (0.5)	20 (0.7)
Commercial and Medicare supplement Population Region, n (%)*	n=12,806	n=1040	n=836	n=204
Northeast	2367 (18.5)	166 (16.0)	112 (13.4)	54 (26.5)
North Central	1530 (12.0)	127 (12.2)	97 (11.6)	30 (14.7)
South	7184 (56.1)	612 (58.8)	505 (60.4)	107 (52.5)
West	1706 (12.8)	133 (12.8)	120 (14.4)	13 (6.4)
Unknown	19 (0.2)	2 (0.2)	2 (0.2)	0 (0)
Medicaid, n (%)	21,977 (63.8)	6764 (86.7)	4035 (82.8)	2729 (93.0)
Medicare Dual eligible, n (%)	9090 (41.4)	2597 (38.4)	536 (13.3)	2061 (70.3)
Race for Medicaid Population, n (%)*	n=19,248	n=5960	n=3468	n=2492
White	4701 (24.4)	1576 (26.4)	913 (26.3)	663 (26.6)
Black	14,066 (73.1)	4274 (71.7)	2477 (71.4)	1797 (72.1)
Hispanic	286 (1.5)	61 (1.0)	49 (1.4)	12 (0.5)
Other	195 (1.0)	49 (0.8)	29 (0.8)	20 (0.8)

A greater number of people living with HIV-associated Wasting were insured by Medicaid

P-values for non-HIVAW versus HIVAW were all <0.0001
*There were missing values in each group, region was only available in the Commercial and Medicare Supplemental databases and race was only available in the Medicaid database

Results: Comorbidities

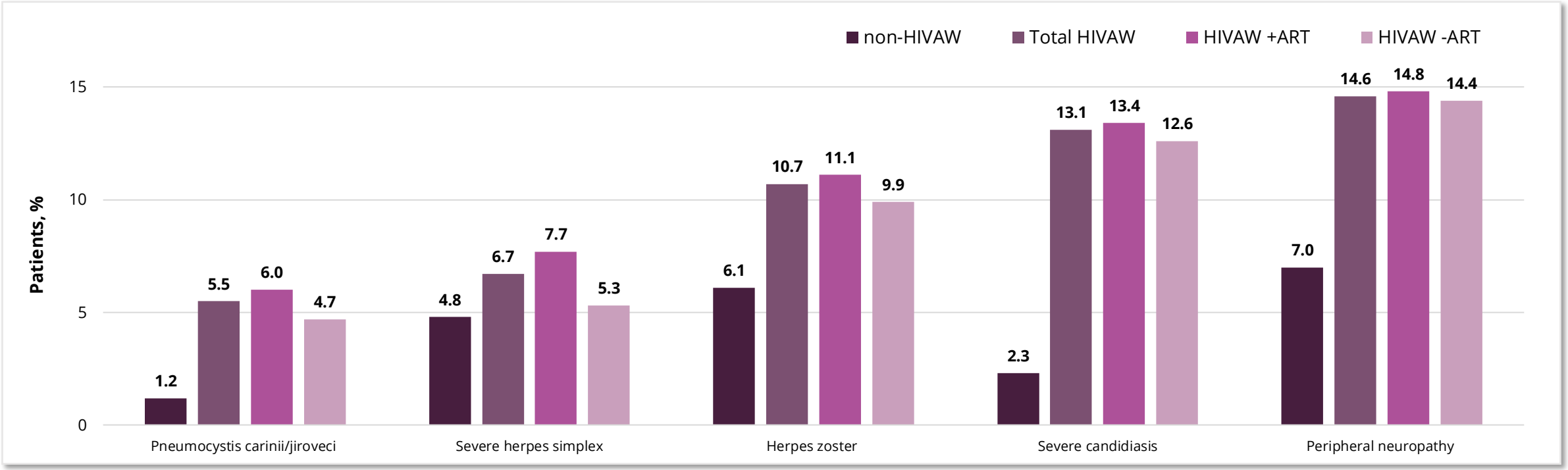
- The HIV-associated Wasting cohort had significantly higher comorbidity burden with Charlson Comorbidity Index (CCI)* mean (SD) compared to non-HIV-associated Wasting: 3.6 (3.0) vs. 2.0 (2.2)
  - Nearly all Charlson comorbidities were more common in the HIV-associated Wasting cohort compared with the non-HIV-associated Wasting cohort
- People living with HIV within the HIV-associated Wasting cohort had higher proportions of metabolic disorders



* Only those Charlson comorbidities with frequency >10% are presented in the bar chart; P-value <0.0001 for all comparisons
CCI=Charlson Comorbidity Index; PVD=Peripheral vascular disease; CHF=Chronic heart failure; CBVD=Cerebrovascular disease
The Charlson Comorbidities Index is a validated health status assessment based on summary score of 17 comorbidities (rated from 1 to 6 for mortality risk and disease severity).

Results: Opportunistic Infections And Select HIV/AIDS Conditions

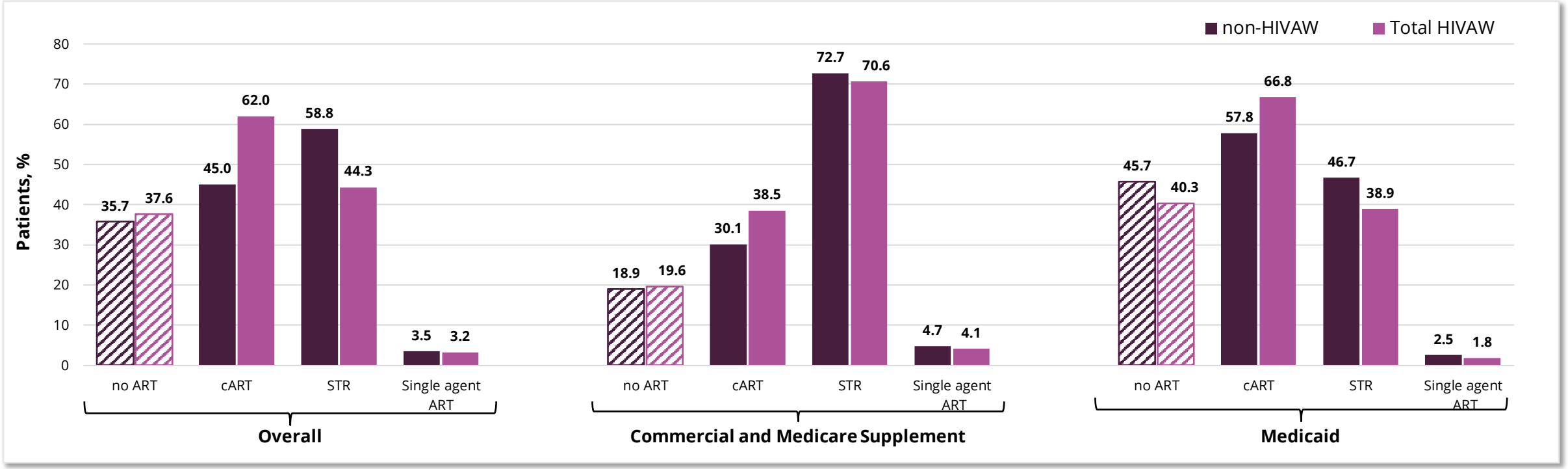
- The HIV-associated Wasting cohort had higher proportions of opportunistic infections (OI) and HIV/AIDS-related conditions compared to the non-HIV-associated Wasting cohort
  - 64.3% of the HIV-associated Wasting cohort had ≥1 diagnosis of an OI vs. 38.6% in the non-HIV-associated Wasting cohort, p<0.0001
- Within the HIV-associated Wasting cohort, the HIV-associated Wasting +ART cohort were more likely to have ≥1 diagnosis of an OI compared to the HIV-associated Wasting –ART cohort (66.0% vs. 61.3%, respectively)



Only those conditions with proportion >5% are presented in the bar chart; P-value <0.0001 for all comparisons

Results: Antiretroviral Therapy Utilization at HIV Index

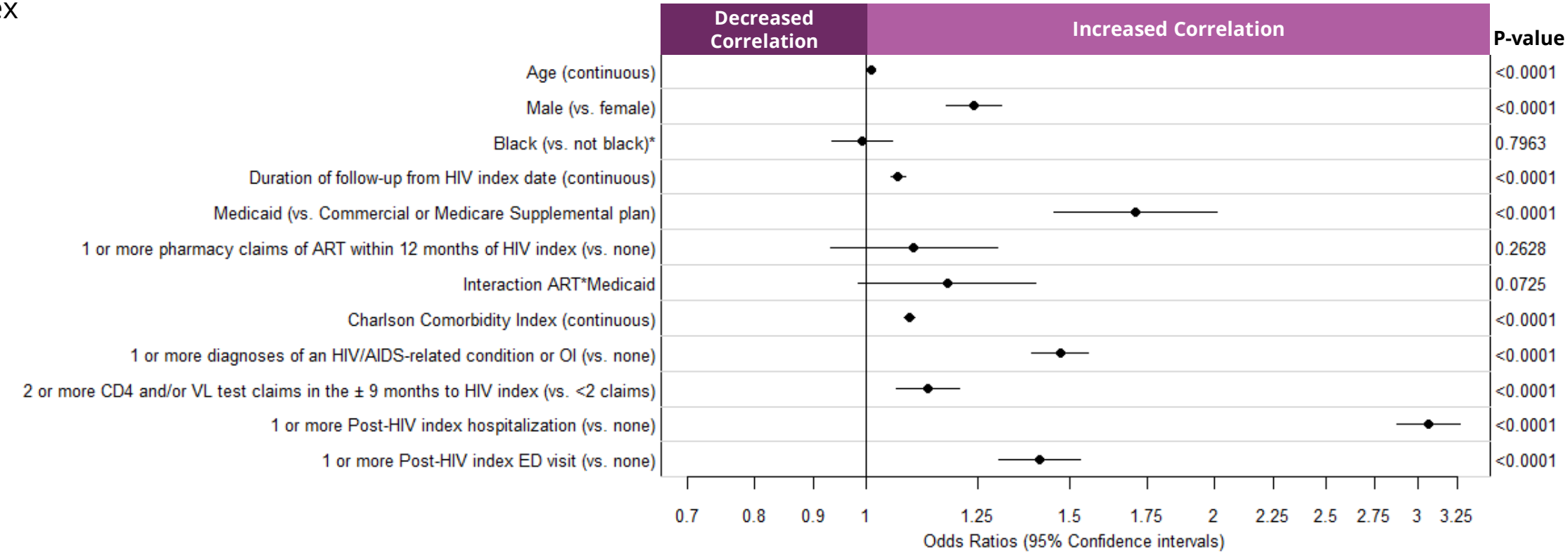
- At HIV-index* date, >35% of people living with HIV had no evidence of a pharmacy claim for ART and >45% of people living with HIV in the Medicaid population had no evidence of a pharmacy claim for ART
- cART was the most common treatment overall, within the Medicaid population and HIV-associated Wasting cohort; whereas STR was most common in the Commercial and Medicare Supplement population and non-HIV-associated Wasting cohort



*At index includes medications used 12-months post-HIV index; cART is defined as any fixed-dose combinations (FDC) OR >2 single agents
cART - Combination Anti-Retroviral Therapy; STR – single tablet regimen

Results: Correlates of HIV-associated Wasting

- In logistic regression analysis, race and ART status were not found to be correlates of HIV-associated Wasting
- The strongest associations with HIV-associated Wasting were having Medicaid insurance and hospitalization(s) post-HIV index



Claims for CD4 and viral load tests were surrogate markers for being in care

Conclusions

- **Modern antiretroviral therapy does not have an impact** on the prevalence of HIV-associated Wasting
- **Greater than one in six people** living with HIV in medical care had evidence of HIV-associated Wasting
- The evidence suggests the **need for continuous assessment of people living with HIV for weight loss** and the need to better differentiate HIV-associated Wasting by ART status, comorbidities, and payer type

Strengths and Limitations

Strengths

Claims databases allow for analysis of large numbers of patients over time and are generally representative of the US patient population

Pharmacy claims provide an understanding of a patient's intent to take a prescribed medication; whereas a medication order would only show what medication a prescriber is proposing to treat a patient

Ability to better understand underserved populations which were not available in previous clinical studies with traditional design

Limitations

Claims data are not specifically collected for research purposes, and diagnostic and drug-use information are not always validated. As such, there can be missing information that limits the inferences that can be made from the data

As an analysis of administrative health care claims data, it **does not take into account all clinical information**

References

1. Teeraananchai S, Kerr SJ, Amin J, Ruxrungtham K, Law MG. Life expectancy of HIV-positive people after starting combination antiretroviral therapy: a meta-analysis. *HIV Med*. 2017;18(4):256-266.
2. Marcus JL, Leyden WA, Alexeeff SE, et al. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000-2016. *JAMA Netw Open*. 2020;3(6):e207954.
3. Other health issues of special concern for people living with HIV. HIV.gov. https://www.hiv.gov/hiv-basics/staying-in-hiv-care/other-related-health-issues/other-health-issues-of-special-concern-for-people-living-with-hiv. Updated May 01, 2019. Accessed January 27, 2021.
4. Erlandson KM, Li X, Abraham AG, et al. Long-term impact of HIV wasting on physical function. *AIDS*. 2016;30(3):445-454.
5. Tang AM, Forrester J, Spiegelman D, Knox TA, Tchetgen E, Gorbach SL. Weight loss and survival in HIV-positive patients in the era of highly active antiretroviral therapy. *J Acq Immuno Defic Syndr*.2002;31(2):230-236.

Disclosures & Acknowledgements

This study was sponsored by EMD Serono, Inc., Rockland, MA, USA, a business of Merck KGaA, Darmstadt, Germany, Inc.

- **JS** has received consulting and speaking fees from AbbVie, Merck, EMD Serono, Inc., Rockland, MA, USA, a business of Merck KGaA, Darmstadt, Germany, Inc., Cumberland, and BioFire
- **BH, KAW, AP, and MH** are employees of EMD Serono, Inc., Rockland, MA, USA, a business of Merck KGaA, Darmstadt, Germany, Inc.
- **KLD and QH** are employees of EPI-Q, Inc., which received payment from EMD Serono, Inc. for the development and execution of this study