HIV-ASSOCIATED WASTING PREVALENCE IN THE ERA OF MODERN ANTIRETROVIRAL THERAPY

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

[1]TeleMed2U, [2]EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, [3]EPI-Q, Inc.

AIDS (London, England)
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Reference: Siddiqui, J., Samuel, S. K., Hayward, B., Wirka, K. A., Deering, K. L., Harshaw, Q., Phillips, A., & Harbour, M. (2022). HIV-associated wasting prevalence in the era of modern antiretroviral therapy. AIDS (London, England), 36(1), 127–135.

What is Real World Evidence?

Real World Evidence is clinical evidence about the use and benefits, or risks of a treatment based on Real World Data— obtained through randomized trials, pragmatic trials, or observational studies.

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**

Why Real World Evidence?

Randomized Controlled Trials (RCTs)		Real World Evidence (RWE)
Prospective data collection		Prospective and/or retrospective data collection
Limited segment of the population is eligible for inclusion		Broader and more representative of the patient population
Good patient adherence and compliance		Real world patient adherence and compliance
Important for demonstrating efficacy and safety for drug licensing		Provides insights into the benefits and risks of a drug in everyday clinical practice

RWE is evidence obtained from RWD which are observational data obtained outside the context of RCTs and generated during **routine clinical practice**

- Generated by analyzing data such as electronic health records (EHR) and medical claims or billing databases
- It may be derived from retrospective or prospective observational studies

RWE becomes relevant:

- When clinical trials cannot really account for the entire patient population of a particular disease
- Patients suffering from comorbidities or belonging to a distant geographic region or age limit who did not participate in any clinical trial may not respond to the treatment in question as expected

RWE may provide clinical relevance to medical issues and as importantly, have the ability to analyze effects of drugs over a longer period of time

It is important to note that RWE does have limitations, including lack of randomization, less control over data collection, and less reliability/accuracy as compared to RCTs

Reference: How real-world evidence transforms the entire healthcare ecosystem. Retrieved December 13 2020 from https://www.dxc.technology/healthcare/insights/146938-how_real_world_evidence_transforms_the_entire_healthcare_ecosystem; What does real world evidence offer in comparison to conventional randomized controlled trials? Retrieved December 13 2020 from https://www.svmpharma.com/?attachment_id=1568

Real World Data *is* Patient Data

CLINICAL

- Demographics
- EHR data
- Lab test results
- Diagnoses
- Procedures
- Pathology/ histology data
- Microbiology data
- Radiology images
- Provider notes
- Admission/ discharge and progress reports
- Performance status
- Telemedicine

MEDICATION

- Medication orders
- Administration (dose, route, NDC/RxNorm codes)
- Concomitant therapies
- Point of sale data (prescription & OTC)
- Prescription refill
- Allergies

CLAIMS

- Medical claims
- Prescription drug claims
- Other drug and treatment use data

MOLECULAR PROFILING

- Genomic and genetic testing data (SNPs/panels)
- Pharmacogenetics
- Pharmacogenomics
- Artificial intelligence
- Multi-omics data (proteomics, transcriptomics, metabonomics, lipidomics)
- Other biomarker status

FAMILY HISTORY

- Historical data on health conditions and allergies relating to patient and extended family
- Smoking status
- Alcohol use

MOBILE HEALTH

- Fitness trackers
- Wearable devices
- Other health apps measuring activity and body function

ENVIRON-MENTAL

- Climate factors
- Pollutants
- Infections
- Lifestyle factors (diets, stress)
- Other environmental and occupational sources

PATIENT REPORTED

- Patient reported outcomes
- Surveys
- Diaries (diets, habits)
- Personal health records
- Adverse event reporting

SOCIAL MEDIA

- Patient communities
- Twitter
- Facebook
- Blogs

LITERATURE

- Disease burden
- Clinical characteristics
- Prevalence
- Incidence
- Rates of treatment
- Resource use and costs
- Disease control

Reference: Swift, B. et al (2018), Innovation at the Intersection of Clinical Trials and Real-World Data Science to Advance Patient Care. Clinical And Translational Science, 11: 450-460; How real-world evidence transforms the entire healthcare ecosystem. Retrieved December 13 2020 from https://www.dxc.technology/healthcare/insights/146938-how_real_world_evidence_transforms_the_entire_healthcare_ecosystem

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Background

Advances in antiretroviral therapy (ART) and the care of people living with HIV have improved AIDS associated morbidity and mortality

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

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

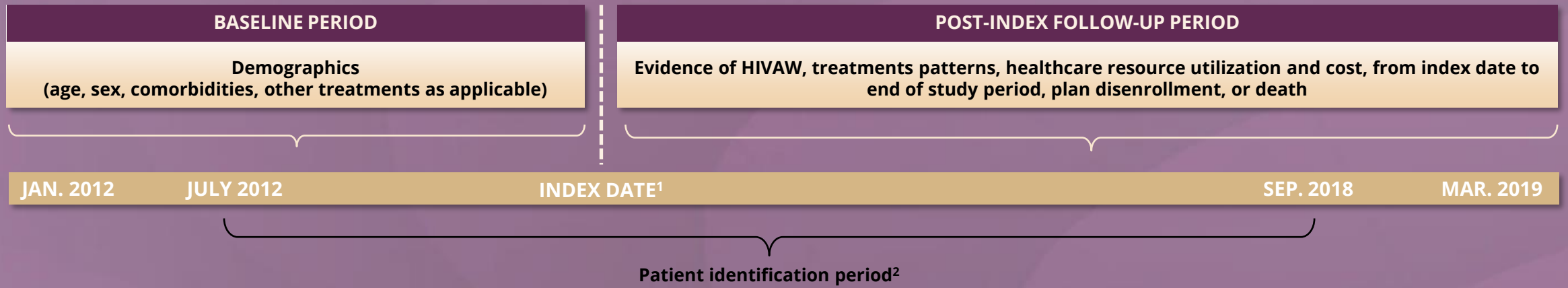
Given the changing profile of people living with HIV, these **retrospective analyses evaluated the prevalence and comorbidity burden** of HIV-associated Wasting (2012-2018) using medical and pharmacy claims databases.

Reference: Siddiqui, J., Samuel, S. K., Hayward, B., Wirka, K. A., Deering, K. L., Harshaw, Q., Phillips, A., & Harbour, M. (2022). HIV-associated wasting prevalence in the era of modern antiretroviral therapy. AIDS (London, England), 36(1), 127–135.

Methods: Selection Criteria And Study Design

Retrospective medical and pharmacy claims study using the IBM® MarketScan® Commercial, Medicare Supplemental and Multi-State Medicaid Research Databases

Selection Criteria of the HIV+ Study Population



HIV Population: Total Patients with HIV diagnosis between July 1, 2012 – Sept 30, 2018, **N=196,297**

- **INCLUDED:** ≥2 outpatient claims (>30 days apart) or ≥1 inpatient claim for HIV (ICD-9/10: 042, B20), **N=153,903**
- **INCLUDED:** ≥18 years old on the index date, **N=152,256**
- **EXCLUDED:** Patients with any malignancies, **N=146,966**
- **INCLUDED:** 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

Reference: Siddiqui, J., Samuel, S. K., Hayward, B., Wirka, K. A., Deering, K. L., Harshaw, Q., Phillips, A., & Harbour, M. (2022). HIV-associated wasting prevalence in the era of modern antiretroviral therapy. AIDS (London, England), 36(1), 127–135.

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 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

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Methods: Identification of HIV-associated Wasting Cohort

Cohort: HIV-associated Wasting* ***Patients in the HIV-associated Wasting cohort met at least one of A, B, C, or D criteria.***		**HIV+ Study Population N=42,587 n (%)**
A. ≥1 inpatient claim or ≥2 outpatient claims (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	**6,873 (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)	**1,644 (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, amino acid injections/solutions (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		**7,804 (18.3)**

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

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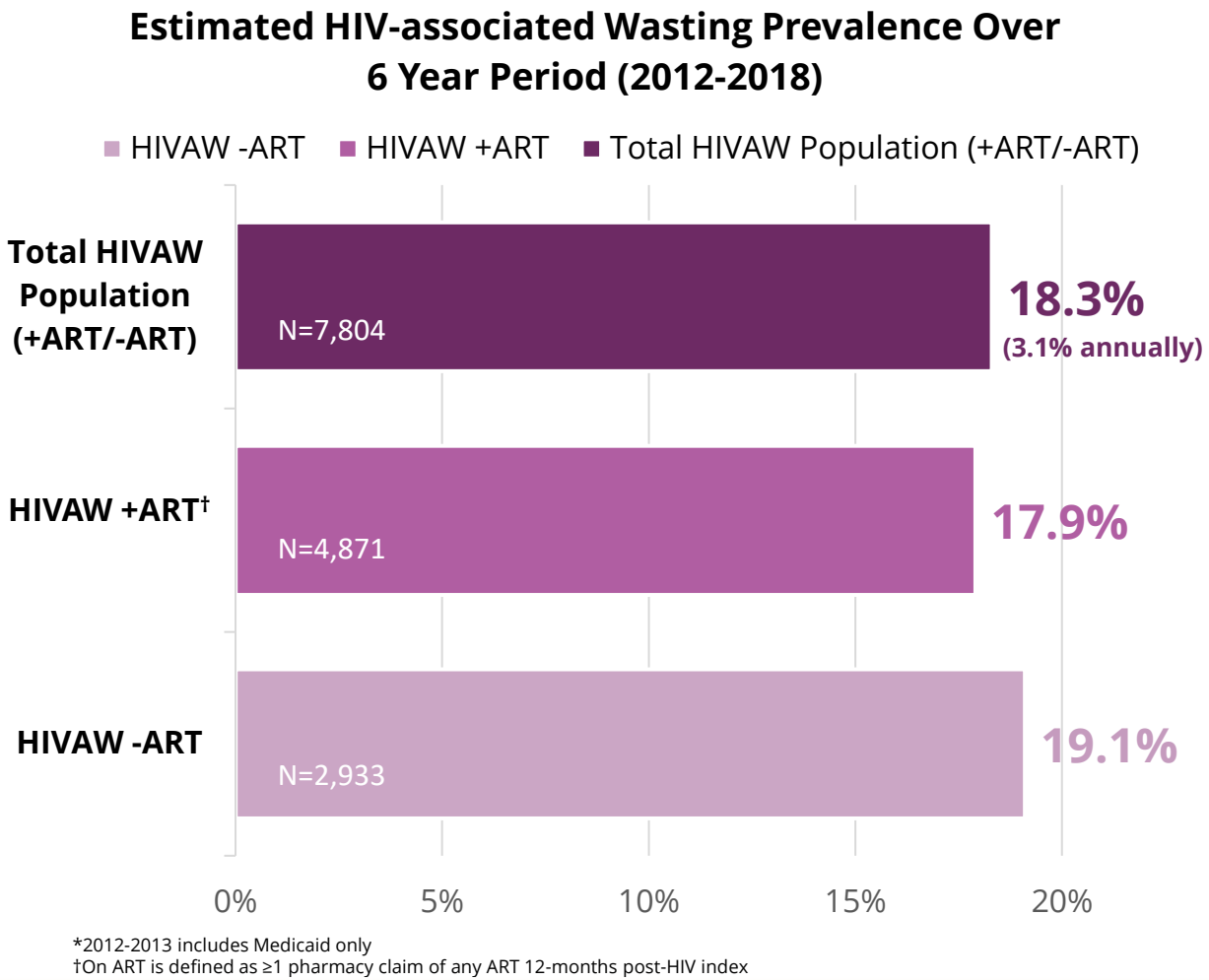
Results: Estimated HIV-associated Wasting Prevalence During a 6 Year Period (2012-2018)



*2012-2013 includes Medicaid only
†On ART is defined as ≥1 pharmacy claim of any ART 12-months post-HIV index

63.9% Among the HIV+ Study Population (N=42,587), 63.9% were on ART (n=27,223), 36.1% were not on ART (n=15,364)

18.3%
(3.1% annually) Across the span of the 6 year Retrospective Medical and Pharmacy Claims analysis (2012-2018*), it was estimated that 18.3% of HIV-positive patients were identified as having HIV-associated Wasting (~ 3.1% annually)

17.9% of HIV-associated Wasting patients were on antiretroviral therapy

19.1% of HIV-associated Wasting were not on antiretroviral therapy

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Results: Baseline Demographics

	Non-HIVAW cohort N=34,783	HIVAW cohort N=7,804
Male, n (%)	22,700 (65.3)	4,816 (61.7)
Age on HIV index date		
Mean (SD)	43.5 (12.5)	46.4 (12.0)
18 - 39 years of age, n (%)	12,805 (36.8)	2,100 (26.9)
40 - 64 years of age, n (%)	20,908 (60.1)	5,330 (68.3)
65+ years of age, n (%)	1,070 (3.1)	374 (4.8)

A 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

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Results: Insurance Status

	Non-HIVAW cohort N=34,783	HIVAW cohort N=7,804
Commercial, n (%)	12,806 (36.8)	1,040 (13.3)
Commercial and Medicare supplement Population Region, n (%)[a]	n=12,806	n=1,040
Northeast	2,367 (18.5)	166 (16.0)
North Central	1,530 (11.9)	127 (12.2)
South	7,184 (56.1)	612 (58.8)
West	1,706 (13.3)	133 (12.8)
Unknown	19 (0.2)	2 (0.2)
Medicaid, n (%)	21,977 (63.8)	6,764 (86.7)
Medicare Dual eligible[b], n (%)	9,090 (41.4)	2,597 (38.4)
Race for Medicaid Population, n (%)[a]	n=19,248	n=5,960
White	4,701 (24.4)	1,576 (26.4)
Black	14,066 (73.1)	4,274 (71.7)
Hispanic	286 (1.5)	61 (1.0)
Other	195 (1.0)	49 (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
[a]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
[b]People who are dual eligible qualify for both Medicare and Medicaid benefits

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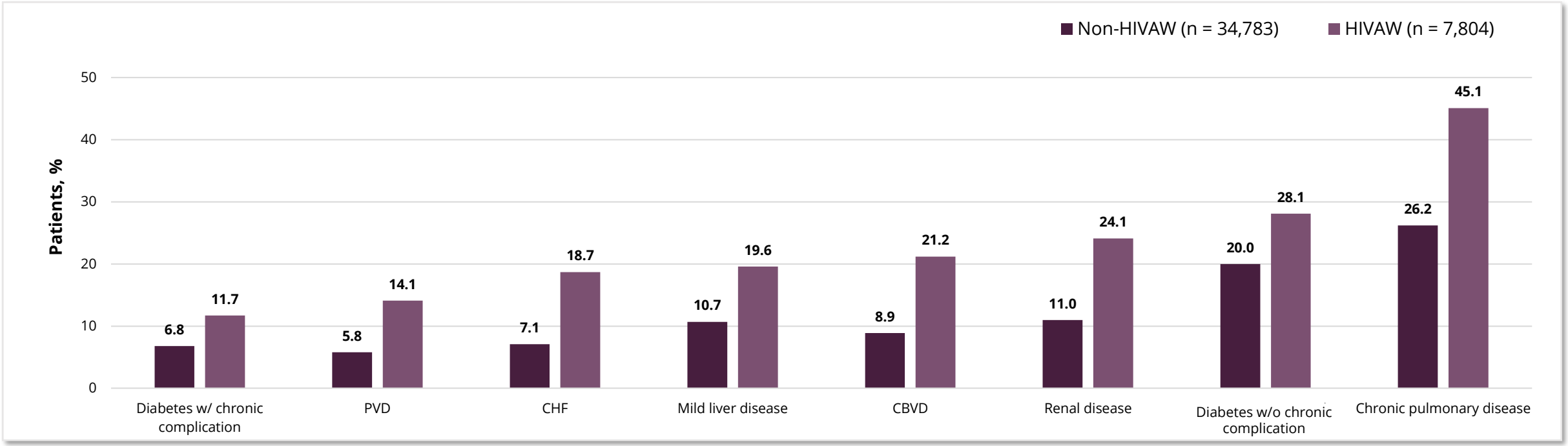
Results: Comorbidities

- 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



* 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).

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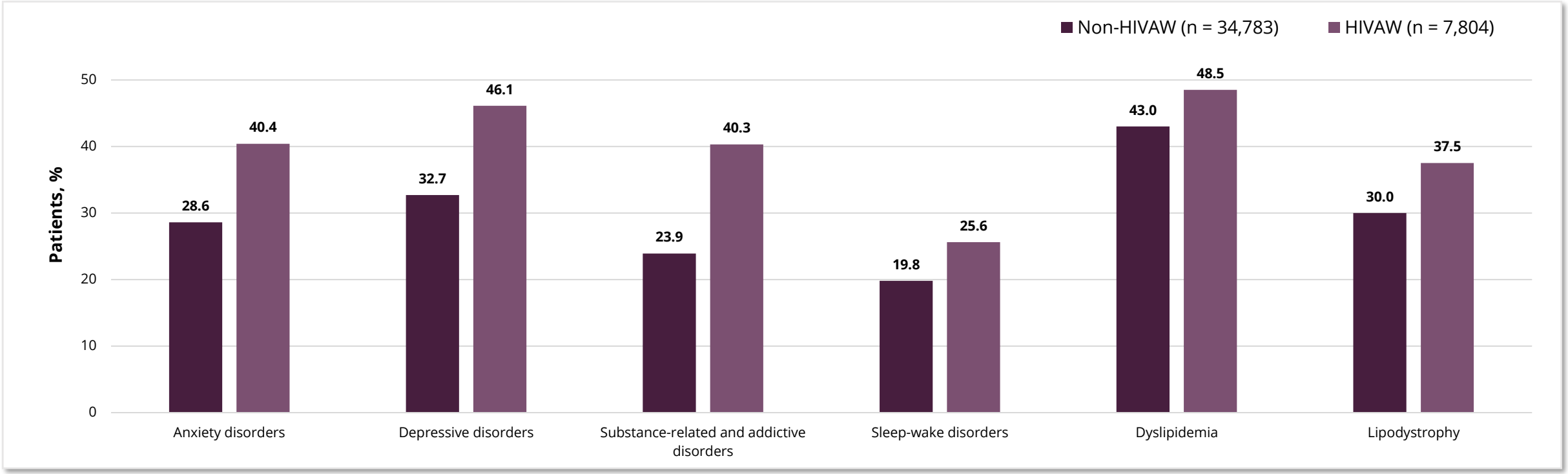
Results: Other Comorbidities

- The HIV-associated Wasting cohort had significantly higher comorbidity burden in many other morbidities
- People living with HIV within the HIV-associated Wasting cohort had higher proportions of metabolic disorders
    - The metabolic disorders were frequent in the HIVAW cohort with lipodystrophy (37.5%) and dyslipidemia (48.5%)
- Over 40% of the HIVAW cohort had psychiatric medical claims



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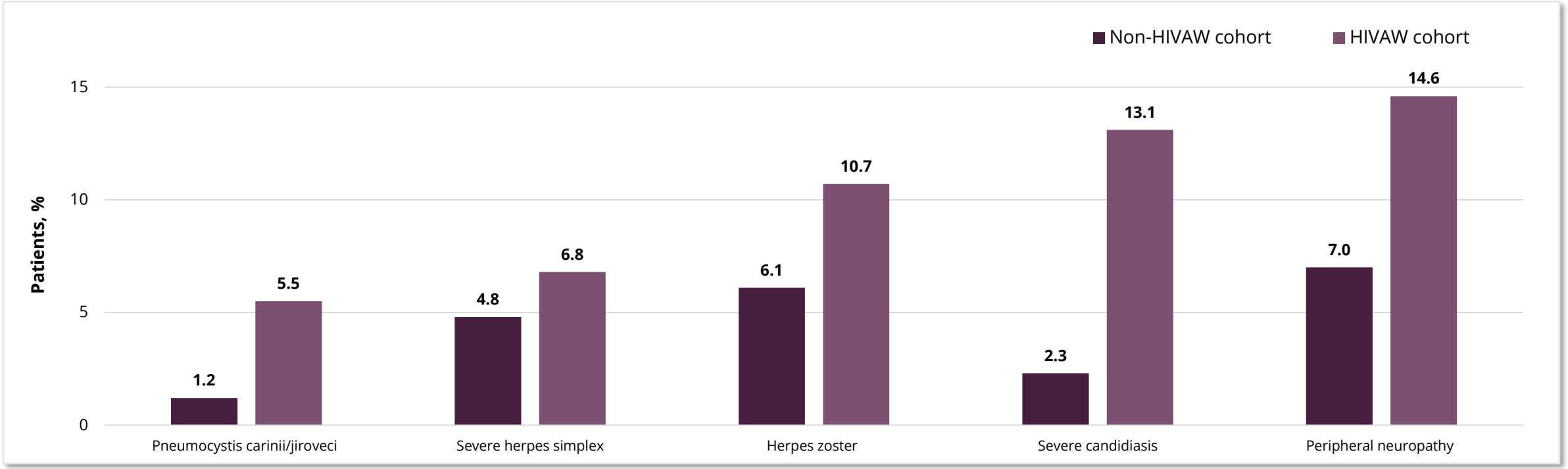
Results: Opportunistic Infections And Select HIV/AIDS Conditions

- 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
  - 64.2% 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



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

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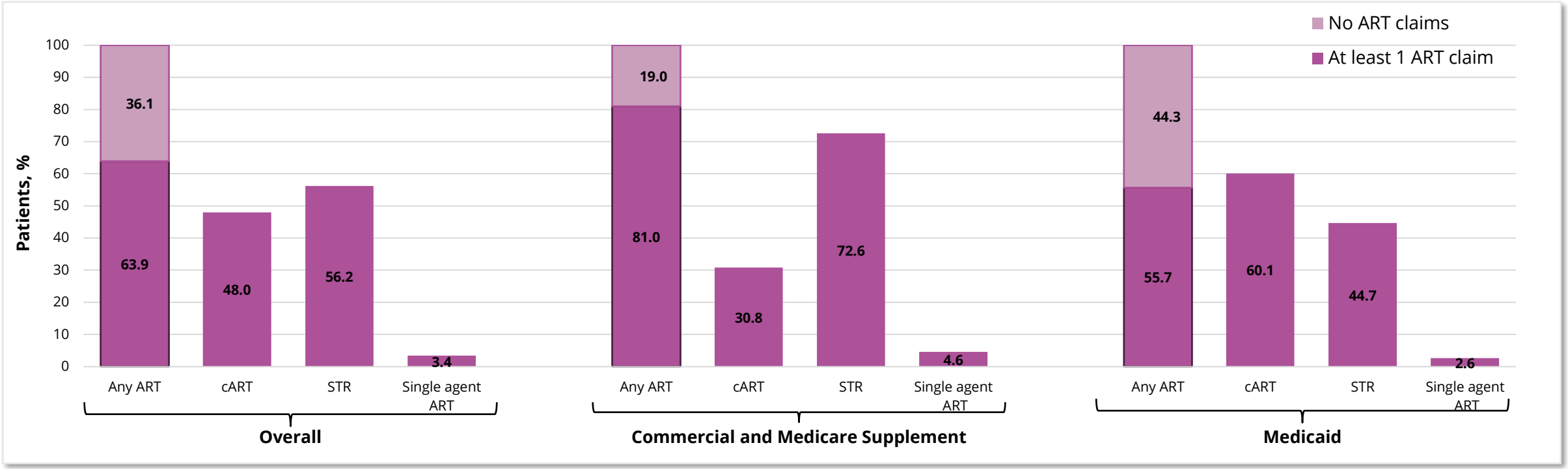
Results: Antiretroviral Therapy Utilization at HIV Index

- At HIV-index* date, >35% of people living with HIV had no evidence of a pharmacy claim and >40% of people living with HIV in the Medicaid population had no evidence of a pharmacy claim for ART
- cART was the most common treatment within the Medicaid population; whereas STR was most common overall and in the Commercial and Medicare Supplement population.

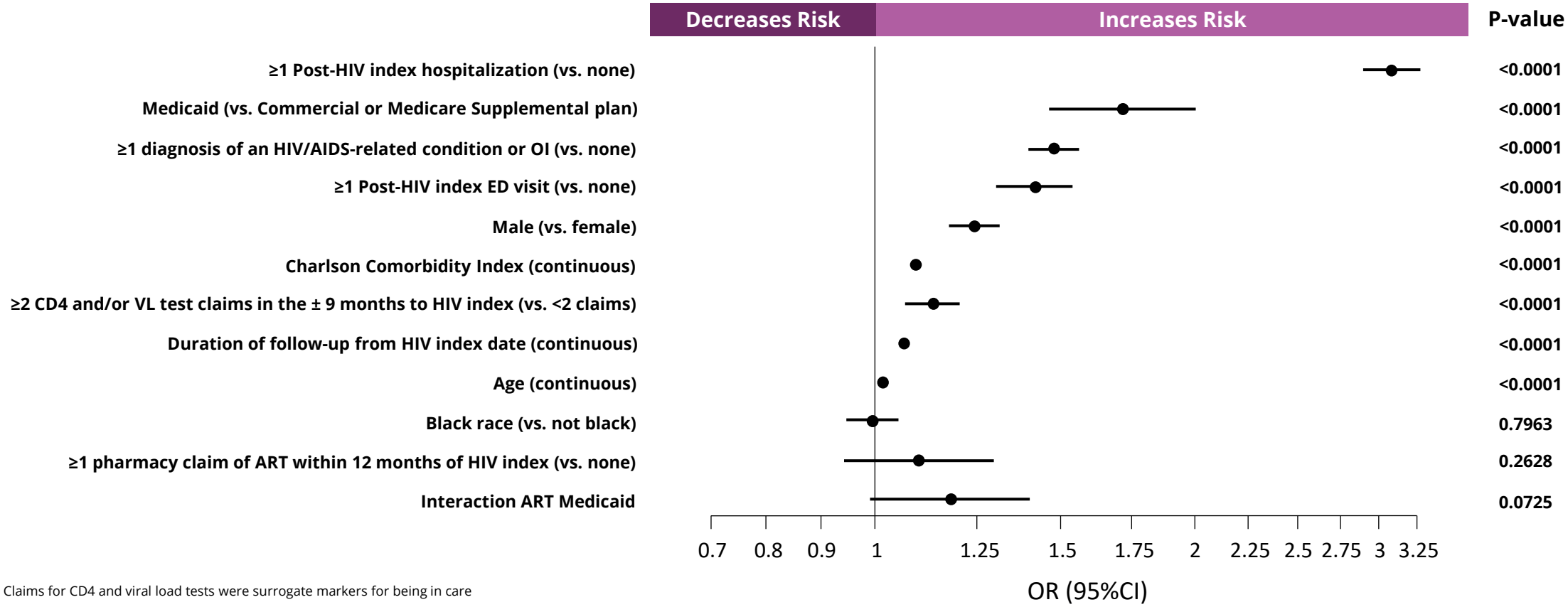


*At index includes medications used 12-months post-HIV index; cART is defined as any fixed-dose combinations (FDC) OR >2 single agents
cART - Combination Anti-Retroviral Therapy; STR – single tablet regimen

Reference: Siddiqui, J., Samuel, S. K., Hayward, B., Wirka, K. A., Deering, K. L., Harshaw, Q., Phillips, A., & Harbour, M. (2022). HIV-associated wasting prevalence in the era of modern antiretroviral therapy. AIDS (London, England), 36(1), 127–135.

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 with Medicaid insurance and hospitalization(s) post-HIV index



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

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Conclusions

Findings suggest HIVAW remains prevalent in people living with HIV. ART use was not found to be associated with HIVAW. HIVAW was highest among those with Medicaid coverage or any hospitalization(s). Further research is needed to better understand additional factors associated with and contributing to HIVAW.

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Key Observations

1. The data from this study suggests that ***HIV-associated Wasting remains an underappreciated comorbidity*** in people living with HIV in the era of modern antiretroviral therapy.

2. Across the span of the 6 year Retrospective Medical and Pharmacy Claims analysis (2012-2018*), it was estimated that ***18.3% of people living with HIV*** (~ 3.1% annually) in medical care had a medical and/or pharmacy ***claim of HIV-associated Wasting*** or cachexia.

3. The HIV-associated Wasting cohort had ***significantly higher comorbidity burden*** with Charlson Comorbidity Index mean compared to non-HIV-associated Wasting.

4. The HIV-associated Wasting cohort had ***higher proportions of opportunistic infections and HIV/AIDS-related conditions*** compared to the non-HIV-associated Wasting cohort.

5. Numerous factors were found to be correlates of HIV-associated Wasting, the strongest associations being ***Medicaid insurance*** and ***hospitalization(s) post-HIV index.***

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