Comparison of HIV-Associated Wasting Definitions in the OPERA® Cohort

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OPERA®
The Longitudinal Cohort

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BACKGROUND

- HIV-associated wasting (HIVAW) is defined as progressive, involuntary weight loss with both fat and lean muscle tissue loss
- Multiple criteria are often used to define HIVAW in observational research, with no consensus:
  - Claims data analyses have focused on medical and pharmacy claims related to diagnoses and treatments for wasting (e.g., appetite stimulants, enteral or parenteral nutrition)[1,2]
  - Cohort studies have included body mass index (BMI) measurements and weight loss trajectories, in addition to wasting diagnoses, as part of their HIVAW definitions[3,4]

OBJECTIVE

Compare predictors of incident HIVAW/low weight between two approaches to defining HIVAW using electronic health records in the United States.

METHODS

Study Population

- OPERA® observational cohort
  - Prospectively captured, routine clinical data from electronic health records
  - >140,000 PWH as of November 2021, representing ~13% of people living with diagnosed HIV infection in the US[5]
- Baseline: First date between 01JAN2016 and 31DEC2020 eligibility criteria were met
- Inclusion criteria
  - People with HIV (PWH), 18 years of age or older
  - In care: ≥ 1 visit in OPERA® from 2016 - 2020
  - No malignancy within 3 years (except basal and squamous cell carcinoma or *in situ* cancer) or AIDS-defining opportunistic infection within 12 months prior to baseline
  - No prior HIVAW/low weight (as described by **definition 1**; **Table 1**)
  - Antiretroviral therapy (ART)-experienced at baseline

HIVAW/Low Weight Definitions

Table 1. Criteria for HIVAW/low weight in OPERA®

HIVAW/Low Weight Criterion	Definition 1	Definition 2
Wasting diagnosis (ICD codes, title search)	☑	☑
Low BMI/underweight diagnosis (ICD codes, title search)	☑	☑
BMI vitals measurement < 20 kg/m²	☑	
Two consecutive BMI vitals measurements < 18.5 kg/m²		☑
Loss of ≥ 10% of baseline body weight within 12 months		☑

BMI, body mass index; HIVAW, HIV-associated wasting; ICD, International Classification of Disease; kg, kilograms; m, meters

Analyses

- Incident HIVAW/low weight was defined as the first occurrence over follow-up when ≥1 criterion for **definition 1** or **definition 2** (Table 1) was met; study end was 31OCT2021
- Predictors of HIVAW/low weight at baseline were selected *a priori* based on scientific literature and expert opinion and assessed with multivariable logistic regression models

RESULTS

Table 2. Predictors of incident HIVAW/low weight among 52,087 ART-experienced PWH[a]

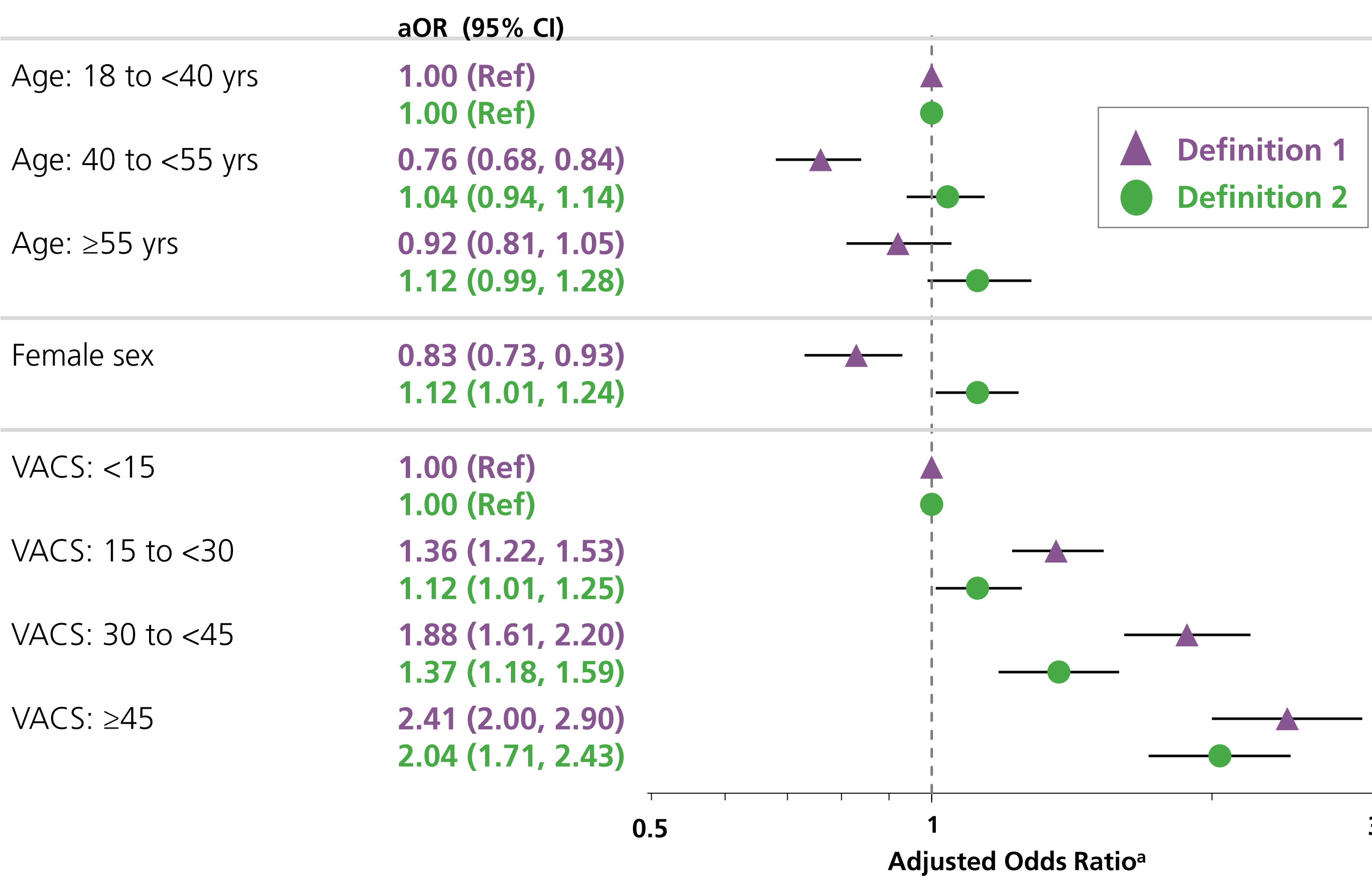| Predictor of Incident HIVAW/Low Weight	Definition 1 aOR[b] (95% CI)	Definition 2 aOR[b] (95% CI)
Age, years		
18 to < 40	Reference	Reference
40 to < 55	**0.76 (0.68, 0.84)**	1.04 (0.94, 1.14)
≥ 55	0.92 (0.81, 1.05)	1.12 (0.99, 1.27)
Female sex	**0.83 (0.73, 0.93)**	1.11 (1.00, 1.23)
Black race	0.98 (0.89, 1.08)	0.93 (0.85, 1.02)
Hispanic ethnicity	**0.78 (0.69, 0.88)**	**0.79 (0.71, 0.89)**
Medicaid	**1.22 (1.11, 1.34)**	**1.25 (1.15, 1.37)**
History of AIDS	0.96 (0.86, 1.07)	0.96 (0.87, 1.07)
VACS Mortality Index Score[c]		
0 to < 15	Reference	Reference
15 to < 30	**1.36 (1.22, 1.53)**	1.12 (1.00, 1.25)
30 to < 45	**1.88 (1.61, 2.20)**	**1.38 (1.18, 1.60)**
≥ 45	**2.41 (2.00, 2.90)**	**2.04 (1.71, 2.43)**
CD4 cell count, cells/µL		
≥ 500	Reference	Reference
200 to < 500	0.95 (0.86, 1.06)	0.93 (0.84, 1.03)
0 to < 200	1.07 (0.90, 1.27)	1.02 (0.87, 1.21)
Calendar year of ART initiation		
≤ 2015	Reference	Reference
2016 – 2020	1.05 (0.94, 1.18)	1.01 (0.91, 1.12)
Ever used INSTI	0.97 (0.88, 1.06)	0.98 (0.90, 1.07)
Ever used PI	1.10 (1.00, 1.21)	**1.13 (1.03, 1.23)**
Ever used TAF	**0.81 (0.72, 0.92)**	**0.78 (0.69, 0.88)**

aOR, adjusted odds ratio; ART, antiretroviral therapy; CI, confidence interval; HIVAW, HIV-associated wasting; INSTI, integrase strand transfer inhibitor; µl, microliter; n, number; PI, protease inhibitor; PWH, people with HIV; TAF, tenofovir alafenamide; VACS, Veterans Aging Cohort Study
[a] 3,343 (6%) and 3,469 (7%) ART-experienced PWH experienced incident HIVAW/low weight over follow-up according to **definition 1** and **definition 2**, respectively
[b] Adjusted for all variables in the table
[c] The VACS Mortality Index score is a composite score used to estimate a 5-year risk of all-cause mortality; a higher VACS score is associated with a higher risk of mortality[6]

Figure 1. Select predictors of incident HIVAW/low weight among 52,087 ART-experienced PWH

	aOR (95% CI)
Age: 18 to <40 yrs	**1.00 (Ref)** (Definition 1) / **1.00 (Ref)** (Definition 2)
Age: 40 to <55 yrs	**0.76 (0.68, 0.84)** (Definition 1) / **1.04 (0.94, 1.14)** (Definition 2)
Age: ≥55 yrs	**0.92 (0.81, 1.05)** (Definition 1) / **1.12 (0.99, 1.28)** (Definition 2)
Female sex	**0.83 (0.73, 0.93)** (Definition 1) / **1.12 (1.01, 1.24)** (Definition 2)
VACS: <15	**1.00 (Ref)** (Definition 1) / **1.00 (Ref)** (Definition 2)
VACS: 15 to <30	**1.36 (1.22, 1.53)** (Definition 1) / **1.12 (1.01, 1.25)** (Definition 2)
VACS: 30 to <45	**1.88 (1.61, 2.20)** (Definition 1) / **1.37 (1.18, 1.59)** (Definition 2)
VACS: ≥45	**2.41 (2.00, 2.90)** (Definition 1) / **2.04 (1.71, 2.43)** (Definition 2)

▲ Definition 1 ● Definition 2

Adjusted Odds Ratio[a] (0.5 – 1 – 3)

aOR, adjusted odds ratio; CI, confidence interval; VACS, Veterans Aging Cohort Study; yrs, years
[a] Adjusted for all variables in the forest plot as well as Black race, Hispanic ethnicity, Medicaid, history of AIDS, baseline CD4 cell count, calendar year of ART initiation, ever use of integrase strand transfer inhibitor, ever use of protease inhibitor, and ever use of tenofovir alafenamide (Table 2)

Table 3. Baseline distribution of select predictors of incident HIVAW/low weight among 52,087 ART-experienced PWH

Predictor at baseline, n (%)	Definition 1 N = 2,306 with outcome	Definition 1 N = 36,860 without outcome	Definition 2 N = 2,551 with outcome	Definition 2 N = 36,632 without outcome
Age, years				
18 to < 40	947 (41)	15,414 (42)	913 (36)	15,459 (42)
40 to < 55	790 (34)	14,560 (40)	1,021 (40)	14,333 (39)
≥ 55	569 (25)	6,886 (19)	617 (24)	6,840 (19)
Female sex	443 (19)	6,823 (19)	583 (23)	6,683 (18)
VACS Mortality Index Score[a]				
0 to < 15	960 (42)	19,713 (53)	1,126 (44)	19,561 (53)
15 to < 30	705 (31)	10,890 (30)	760 (30)	10,838 (30)
30 to < 45	343 (15)	3,768 (10)	335 (13)	3,776 (10)
≥ 45	298 (13)	2,489 (7)	330 (13)	2,457 (7)

HIVAW, HIV-associated wasting; n, number; PWH, people with HIV; VACS, Veterans Aging Cohort Study
[a] The VACS Mortality Index score is a composite score used to estimate a 5-year risk of all-cause mortality; a higher VACS score is associated with a higher risk of mortality[6]

DISCUSSION

- Both definitions of HIVAW/low weight likely overrepresented **younger** PWH, who may still be growing and have a higher metabolism
- Because HIVAW is not limited to underweight bodies:
  - **Definition 1** could potentially have underrepresented **female** PWH, who tend to have higher BMI
  - **Definition 2** identified excessive weight loss over a short period, allowing PWH of all body sizes to be identified as potentially experiencing HIVAW
- The **VACS Mortality Index** was the strongest predictor of HIVAW/low weight, regardless of the HIVAW/low weight definition used
  - This association highlights the relationship between advanced HIV and comorbidities with wasting
- The proportion of PWH experiencing incident HIVAW/low weight and the association with most predictors were otherwise consistent between **definition 1** and **definition 2**
- The pattern of results described above was similar among 15,032 ART-naïve PWH (data not shown)

KEY FINDINGS

In the absence of objective measures or a standard definition of HIVAW, it is important to consider multiple avenues through which HIVAW may be identified in observational research.

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ACKNOWLEDGEMENTS

SUPPORT

Epividian®