# Characterization of People with HIV Who Have Heavy Treatment Experience, in a USA Real-world Database

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### Conclusions

- This study presents criteria to identify and characterize people with HIV who have heavy treatment experience (PWH-HTE) using an electronic health record (EHR) plus claims-linked database; the four HTE-defining criteria were:
- Received antiretroviral therapy (ART) specifically indicated for HTE
- Received ART suggestive of HTE and evidence of viremia
- Had resistance to ≥3 ART classes
- Had a history of exposure to three core ART classes
- Resistance data availability was limited
- The demographic characteristics of this population of treatment-experienced PWH who met one or more HTE-defining criteria were generally aligned with prior studies<sup>1–5</sup>
- The HTE population in this study included a greater proportion of female individuals (36.4%)<sup>1–5</sup> and a slightly greater proportion of Black individuals (44.0%)<sup>1,2,5</sup> versus prior studies
- This HTE population also included more individuals with Medicaid insurance versus prior studies<sup>3,6</sup>
- PWH-HTE identified in this study had a high clinical burden: median HIV viral load at baseline was 2.4 log<sub>10</sub> copies/mL, mean (SD) Charlson Comorbidity Index was 6.5 (2.9), and one quarter of the PWH-HTE had AIDS-defining conditions, with the most common being candidiasis and pneumonia
- While only 6.2% of identified treatment-experienced PWH met one or more HTE-defining criteria, identification of these individuals is important due to the clinical challenges associated with this subgroup, which may be exacerbated by the higher age and increased comorbidities faced by these individuals<sup>5</sup>
- These HTE-defining criteria should be tested in other databases and settings to further validate their utility in observational research

## Plain Language Summary

- A small group of people with HIV have received many HIV treatments that have stopped working for them
- It is important to improve our understanding of how to identify these individuals, as their HIV is hard to treat and can lead to poor quality of life and more medical conditions
- In this study, we tested four different sets of criteria to identify people with HIV with heavy treatment experience from a database of electronic health records
- Criterion 1: people who received medications for HIV that are used specifically for people with heavy treatment experience
- Criterion 2: people who received medications for HIV that suggest they have heavy treatment experience, and also have detectable levels of HIV in their blood
- Criterion 3: people whose HIV infection does not respond to three or more of the main groups of HIV medications
- Criterion 4: people who had received HIV medications from three of the main groups of HIV medications
- Only a small number (6.2%) of treatment-experienced people with HIV in this database met at least one of the heavy treatment experience criteria
- The balance of sex, race, and age in these individuals was similar to previous studies in this population; people in this study were predominantly male, Black, aged 50–59 years, and using Medicaid
- Most of these people were identified using Criterion 4
- These criteria need to be tested in other databases to confirm that they are useful in identifying people with heavy treatment experience

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## Background

- While there is no universal consensus on PWH-HTE identification, prior studies estimate the prevalence ranges from 1–15% based on various criteria<sup>1,3,4,7</sup>
- PWH-HTE have limited ART options due to antiretroviral drug resistance and intolerance, and/or concomitant medication interactions<sup>7–9</sup>
- PWH-HTE are often associated with higher disease burden, mortality rates, healthcare utilization, and costs compared with PWH without HTE<sup>5</sup>
- These factors may contribute to a poorer quality of life for PWH-HTE compared with PWH without HTE
- of PWH

— Therefore, It is important to improve our understanding and identification of this subset

- Here, we present the characteristics of PWH-HTE identified in a linked EHR-claims dataset
- This EHR platform serves both small healthcare practices and medium to large multi-specialty practices
- As EHRs are patient care records from healthcare providers, they provide clinical value and detail that are not necessarily linked with reimbursement

## Objective

 To identify and describe demographic and clinical characteristics of PWH-HTE using a linked EHR-claims database and various HTE identification criteria

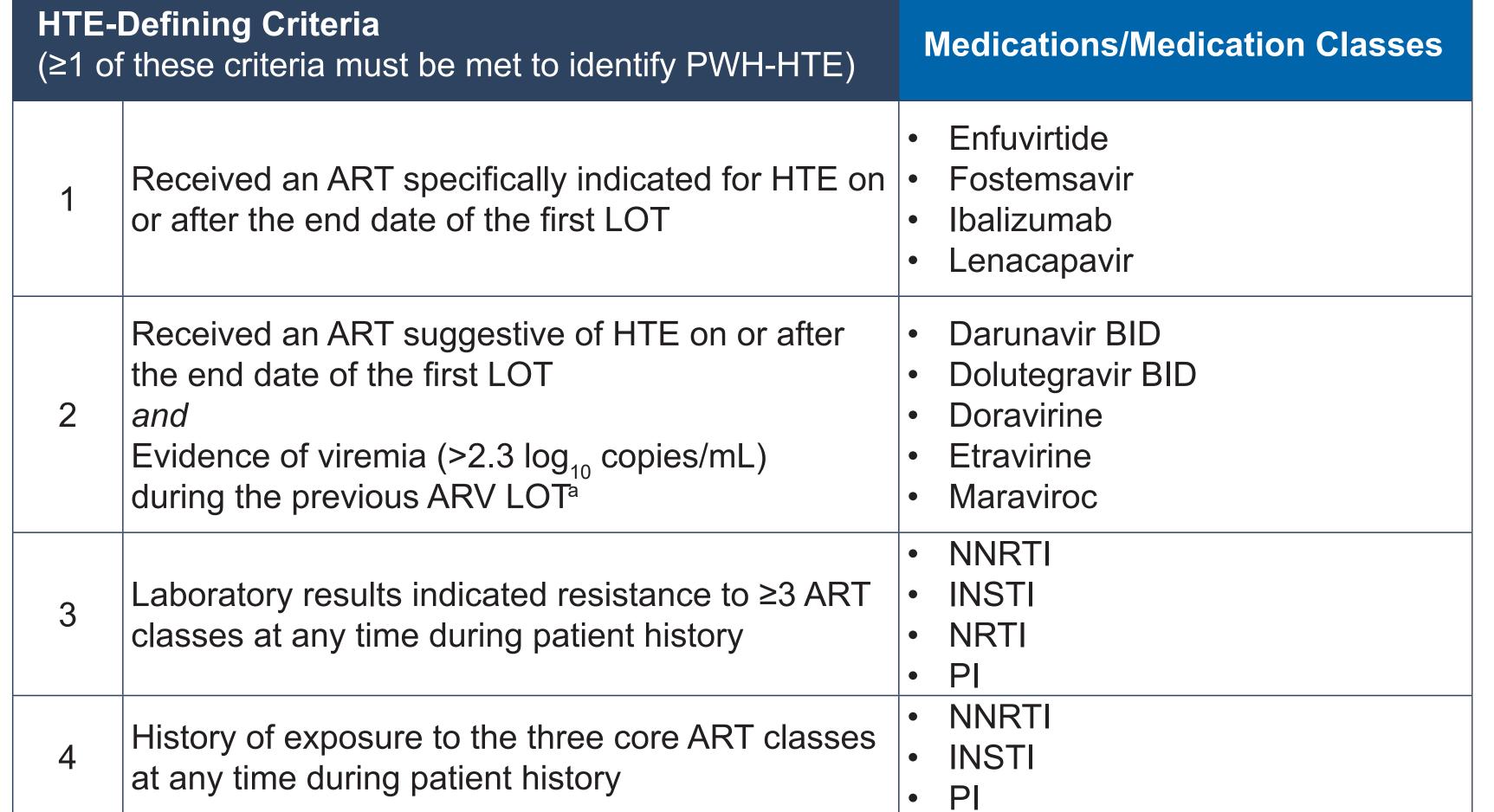
### Methods

- In this retrospective, observational study, HTE individuals were identified from the Veradigm Network EHR-linked claims database during the study period, January 2015–December 2022
- Firstly, HIV treatment-experienced individuals were identified based on claims for ≥2 ART lines of therapy (LOTs)
- Out of these treatment-experienced individuals, PWH-HTE were then identified through ≥1 of four HTE-defining criteria (Table 1), which were based on criteria from prior HTE studies and expert opinion<sup>1,7,9</sup>
- For inclusion in the analysis, individuals must have met ≥1 HTE-defining criteria and all of the following eligibility criteria:
- Aged ≥18 years on the index date
- HIV diagnosis at any time prior to/on the index date
- Continuous enrollment in medical and pharmacy claims and activity in the EHR
   ≥6 months before and after the index date
- For LOTs, antiretroviral (ARV) combinations were identified by a minimum overlap of 45 days in prescription fills for each ARV
- Index date was defined as the most recent date on which one of the HTE-defining criteria was met
- The baseline period was the 6-month period before the index date
- The follow-up period was the variable (minimum 6-month) period after (and including) the index date
- This follow-up period allows for assessment of the change in PWH-HTE clinical characteristics shortly after they have met HTE criteria and have potentially reoptimized their medication regimen
- Capture rates from the four HTE-defining criteria and findings from the descriptive analyses were reported

#### Results

- Among the 308,088 identified HIV treatment-experienced individuals, 19,056 (6.2%) met ≥1 HTE-defining criterion, and 2911 (0.9%) were eligible for analysis, having met all eligibility criteria (Figure 1)
- Most PWH-HTE (97.6%) were identified based on exposure to three core ART classes (non-nucleoside reverse transcriptase inhibitors, integrase strand transfer inhibitors, and protease inhibitors; Criterion 4)
- Data on resistance to ART classes (Criterion 3) were available for only two individuals
- PWH-HTE were predominantly: male, Black, aged 50–59 years, and used Medicaid (Table 2)

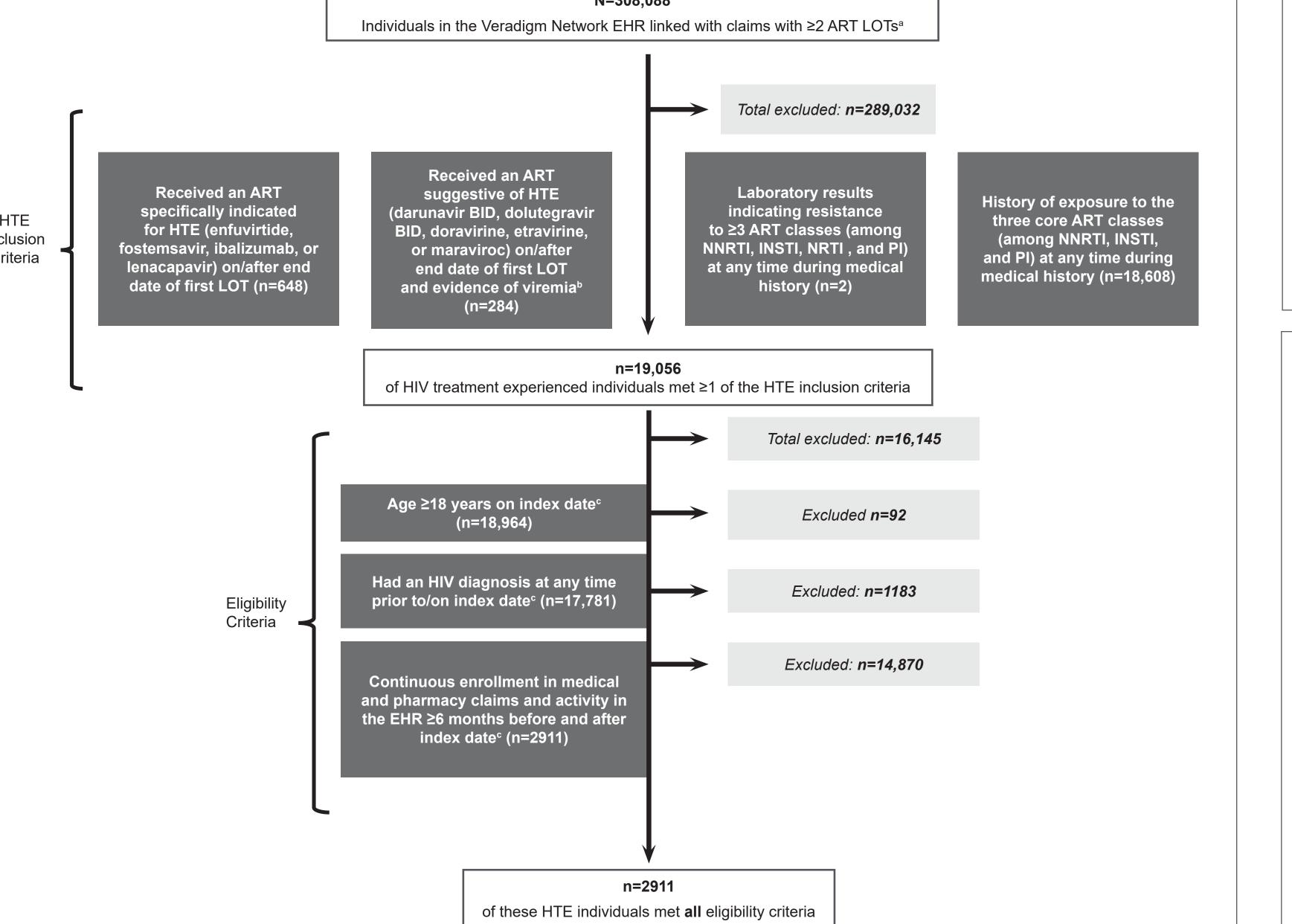
#### Table 1. HTE-Defining Criteria



Or during the 90 days prior to the start of the LOT, if the HTE-indicative medication was observed during the first LOT.

ART, antiretroviral therapy; ARV, antiretroviral; BID, twice daily; HTE, heavy treatment experience; INSTI, integrase strand transfer inhibitor; LOT, line of therapy; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; PWH-HTE, people with HIV who have heavy treatment experience.

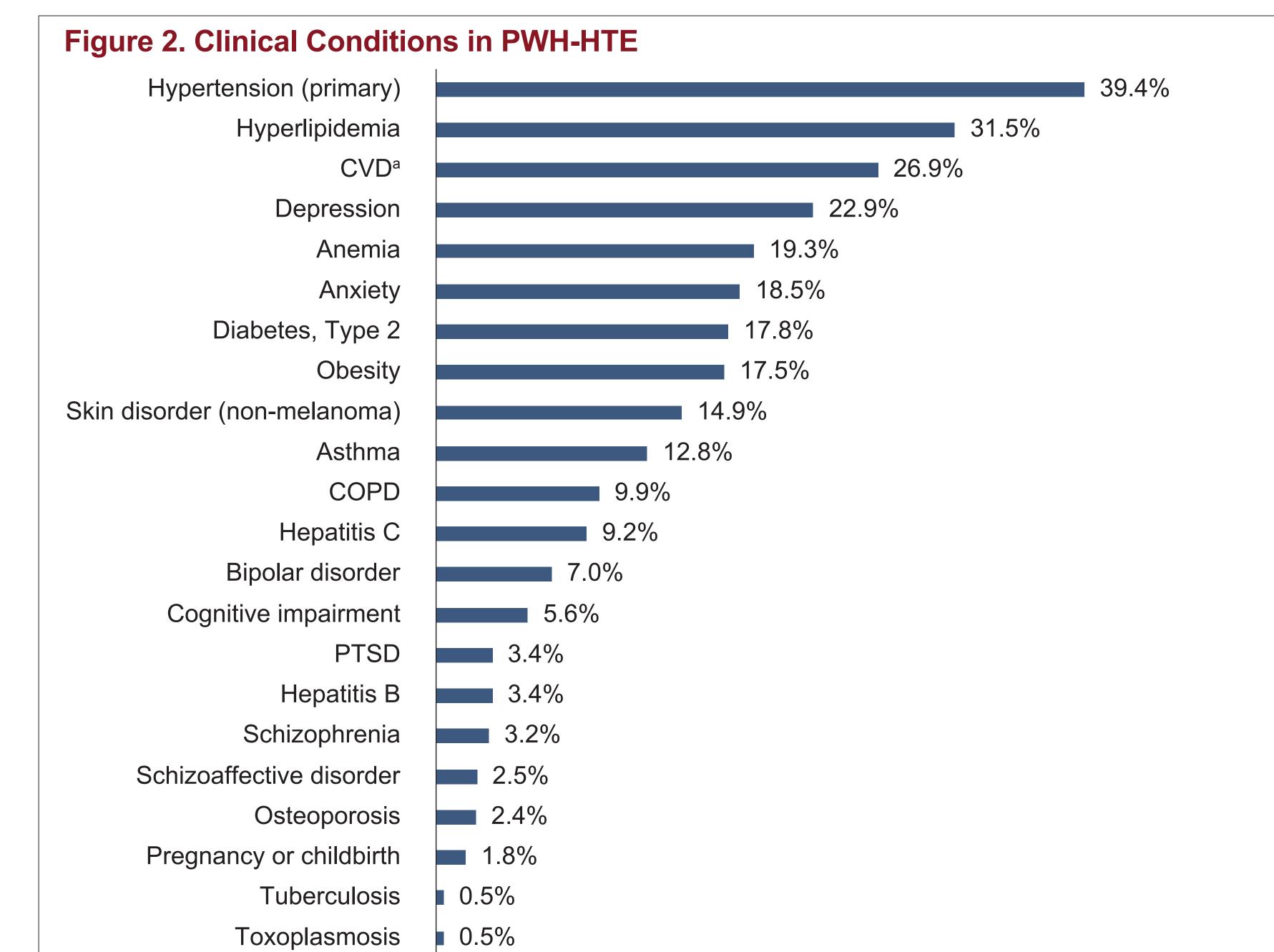
#### Figure 1. PWH-HTE Study Attrition Diagram



aldentified within the study period of January 01, 2015 to December 31, 2022. bViremia was defined as viral load >2.3 log<sub>10</sub> copies/mL. Laboratory result indicating viremia was required to occur during the immediately prior ARV LOT (or during the 90 days prior to the start of the LOT if the HTE-indicative medication was observed during the first LOT). cIndex date was defined as the most recent date on which one of the HTE-defining criteria was met.

- ART, antiretroviral therapy; ARV, antiretroviral; BID, twice daily; EHR, electronic health record; HTE, heavy treatment experience; INSTI, integrase strand transfer inhibitor; LOT, line of therapy; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; PWH-HTE, people with HIV who have heavy treatment experience.
- Mean (SD) Charlson Comorbidity Index was 6.5 (2.9)
- The most common comorbidities (≥10% of PWH-HTE) included: chronic pulmonary disease (n=694; 23.8%); diabetes (n=556; 19.1%); renal disease (n=521; 17.9%); mild liver disease<sup>10</sup> (n=400; 13.7%)
- The most common clinical conditions in PWH-HTE included: primary hypertension (n=1147; 39.4%), hyperlipidemia (n=918; 31.5%), and cardiovascular disease (n=782; 26.9%) (Figure 2)
- Approximately one quarter (25.9%) of these individuals were reported as having a
  psychoactive substance use disorder (identified through ICD-10 diagnosis codes) (Figure 3)
- HIV-related clinical characteristics of the eligible HTE population are summarized in Table 3
- Median HIV viral load at baseline was 2.4 log<sub>10</sub> copies/mL
- After 6-months follow-up, median HIV viral load was 1.9 log<sub>10</sub> copies/mL

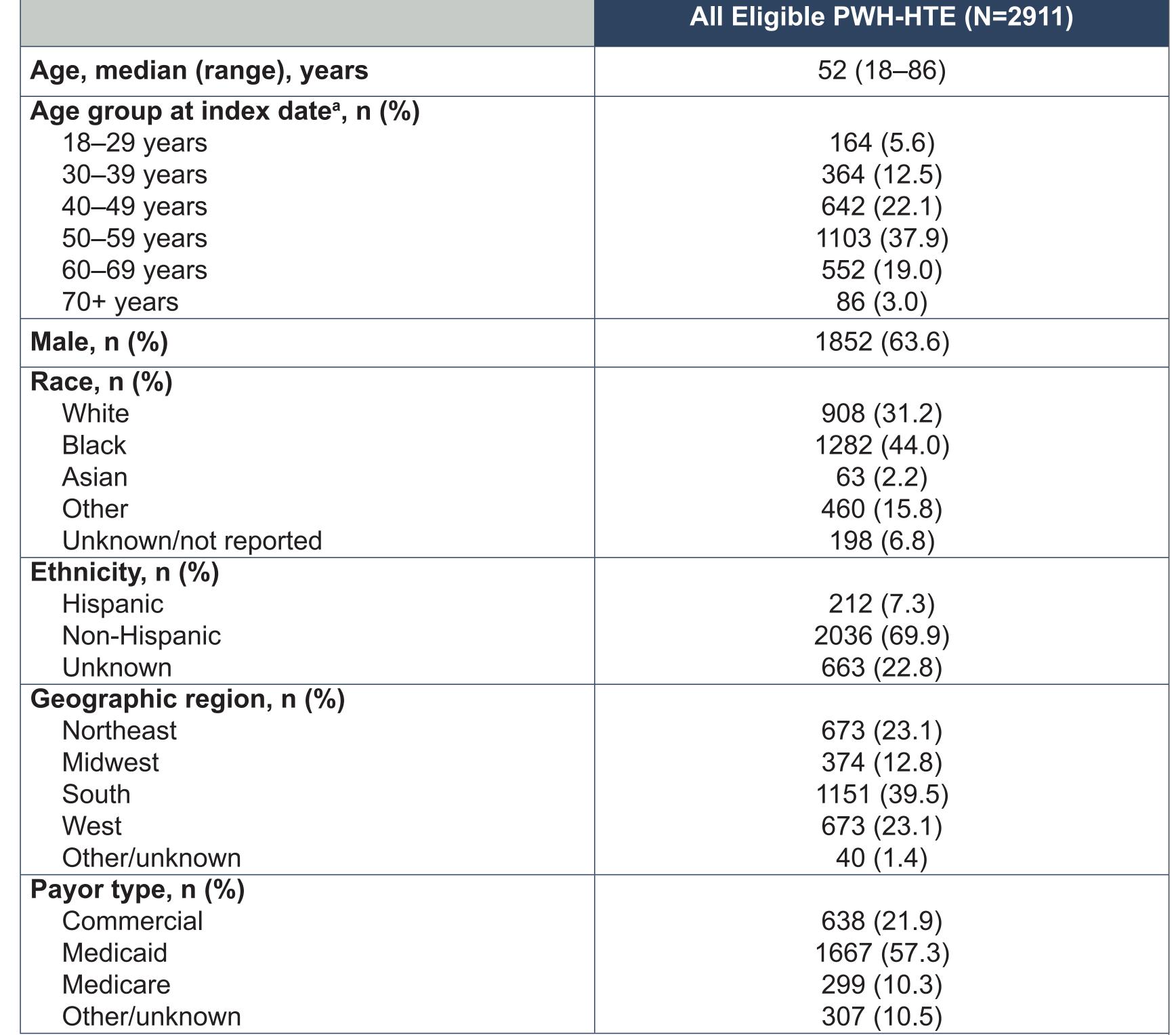
- Mean CD4+ T lymphocyte count at baseline was 484.0 cells/mm<sup>3</sup>
- After 6-months follow up, mean CD4+ T lymphocyte count was 506.0 cells/mm³
   One quarter of the PWH-HTE had AIDS-defining conditions, with the most common being candidiasis (6.8% at baseline) and pneumonia (6.6% at baseline)



## who have heavy treatment experience

0% 5% 10% 15% 20% 25% 30% 35% 40% 45%

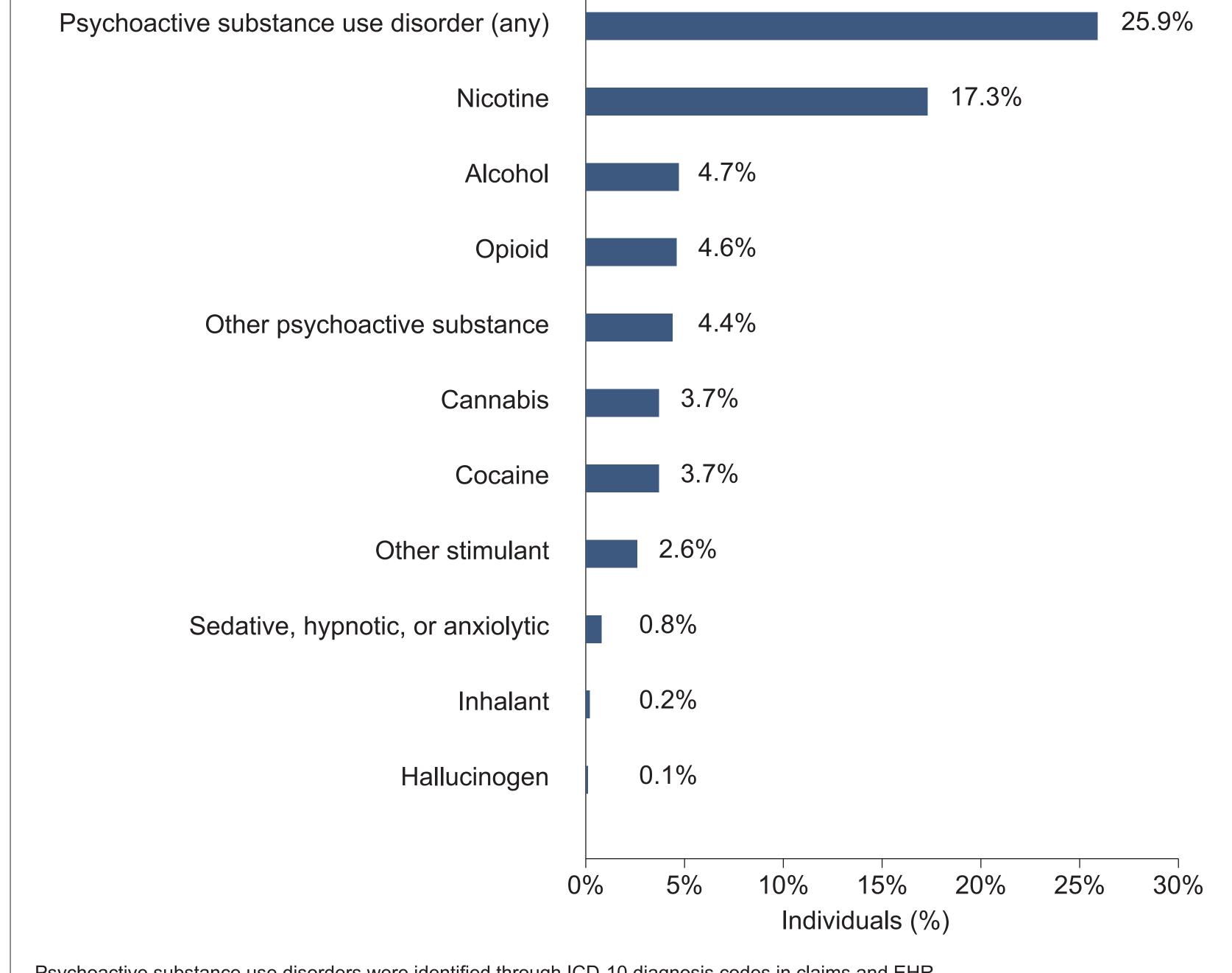
#### Table 2. PWH-HTE Baseline Demographics



<sup>a</sup>Index date was defined as the most recent date on which one of the HTE-defining criteria was met.

PWH-HTE, people with HIV who have heavy treatment experience.

#### Figure 3. Psychoactive Substance Use Disorders in PWH-HTE



EHR, electronic health record; PWH-HTE, people with HIV who have heavy treatment experience.

#### Table 3. HIV-Related Clinical Characteristics

|  | All Eligible PWH-HTE (N=2911) |                        |
|--|-------------------------------|------------------------|
|  | Baseline <sup>a</sup>         | Follow-up <sup>a</sup> |
| HIV viral load, median (IQR), log <sub>10</sub> copies/mL <sup>b</sup> | 2.4 (1.5–4.0)                 | 1.9 (1.3–2.8)          |
| CD4+ cell count, mean (SD), cells/mm <sup>c</sup>                      | 484.0 (369.5)                 | 506.0 (363.3)          |
| AIDS-defining conditions <sup>d</sup> (≥2% of individuals), n (%)      |                               |                        |
| Total  | 729 (25.0)                    | 756 (26.0)             |
| Candidiasise   | 198 (6.8)                     | 194 (6.7)              |
| Pneumonia  | 192 (6.6)                     | 206 (7.1)              |
| Herpes simplex virus   | 60 (2.1)                      | 59 (2.0)               |
| Wasting syndrome due to HIV  | 58 (2.0)                      | 53 (1.8)               |
| Adverse events <sup>f</sup> , n (%)                                    |                               |                        |
| Nausea   | 230 (7.9)                     | 262 (9.0)              |
| Diarrhea   | 221 (7.6)                     | 256 (8.8)              |
| Fatigue  | 220 (7.6)                     | 233 (8.0)              |
| Vomiting   | 187 (6.4)                     | 199 (6.8)              |
| Loss of appetite   | 35 (1.2)                      | 40 (1.4)               |
| Lipodystrophy  | 37 (1.3)                      | 42 (1.4)               |

<sup>a</sup>Index date was defined as the most recent date that one of the HTE-defining criteria was met. The baseline period is the 6-month period before the index date. The follow-up period is the variable (minimum 6-month) period after (and including) the index date. Baseline period: the value closest to, but before the index date is reported; follow-up period: the value closest to the end of the follow-up period is reported. <sup>b</sup>A total of 764 PWH-HTE had vir load results available. <sup>c</sup>A total of 645 PWH-HTE had CD4+ T lymphocyte results available. <sup>d</sup>All AIDS-defining conditions were defined based on ICD-10 diagnosis codes or SNOMED codes found in claims or the electronic medical record. <sup>e</sup>Candidiasis of any site was included; however, only candidiasis of the esophagus, bronchi, trachea, or lungs are considered AIDS-defining conditions. <sup>f</sup>Adverse events are not specified as treatment relate PWH-HTE, people with HIV who have heavy treatment experience.

### Limitations

- Limited resistance data may lead to missed identification and under-reporting of the PWH-HTE population size
- However, minimal impact is estimated as most individuals with resistance likely met and were identified through the other study criteria
- Viral suppression results can vary over time and may not be uniformly collected regularly in the real world; the number of PWH-HTE with viral load data available in this study was low
- It could not be fully confirmed in the EHR or claims data if regimen changes were due to changes in viral load
- This study focused on USA PWH only and results may vary in other countries
- It was not possible to confirm if all conditions included as AIDS-defining conditions were related to HIV or due to other circumstances

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