**Supplemental File**

***Description of development of weights***

Inverse probability of treatment weights (IPTW) were used to account for potential channeling-in bias in receipt of an efavirenz prescription by measured covariates. IPTW were estimated as the probability of initiating efavirenz-containing ART, conditional on baseline gender, suicidal thoughts and depressive symptoms, panic disorder, drug use, antidepressant use, CD4 count (<350 or > 350) and year of ART initiation.[34](#_ENREF_34) Two-way interactions between year of ART initiation with antidepressant use and CD4 count, gender with suicidal thoughts /depressive symptoms and antidepressant use were included. IPTWs were stabilized by the marginal probability of initiating efavirenz-containing ART. We evaluated associations between all covariates included in the IPTW weight model and efavirenz prescription in the observed and IPT weighted data to assess whether the weights sufficiently balanced the data (Table S1).

To account for possible bias due to loss to follow-up, we used inverse probability of censoring weights (IPCW).[35](#_ENREF_35) IPCW were estimated as the probability of not being lost to follow-up at a given visit, conditional on baseline factors (initial ART regimen, site, age, gender, race/ethnicity, HIV acquisition risk group, prior mental health or medical diagnosis, depressive symptoms/suicidal thoughts status) and time-varying factors at the previous visit (panic disorder, drug use, alcohol use, depressive symptoms score, antidepressant prescription, viral load suppression, ART adherence, CD4 count), calendar year and time since ART initiation (measured in days). Age, CD4 count, and depression symptoms scores were modeled using restricted cubic splines. IPCW were stabilized by baseline covariate values and multiplied across a participant’s visits over time.[35](#_ENREF_35) We did not develop IPCW for efavirenz discontinuation to account for channeling-out bias due to the limited number of people who discontinued during the follow-up period.

Participants in CNICS typically present for care every 4-6 months, although this varies. Measurement of PROs varies based on clinical follow-up and for logistical reasons. To account for this variation, we used inverse probability of observation weights (IPOW), under the assumption that participants should complete a PRO at least once every 6 months.[36](#_ENREF_36) Time-varying covariates were carried forward for up to 6 months (182 days). After 182 days with no reported depressive symptom, alcohol use, drug use, panic disorder or ART adherence measures, participants were considered to be missing a PRO assessment. For observed PRO assessments, multiple imputation (n=20 imputations) was used to fill in individual missing covariate values. IPOW were estimated as the inverse probability of having an observed PRO in each 6-month interval, conditional on baseline ART regimen, site, gender, race/ethnicity, HIV acquisition risk group, age, prior mental health or medical diagnosis, depressive symptoms/suicidal thoughts, and time-varying history of having a PRO in the last 6-months, depressive symptoms score, alcohol use, drug use, panic disorder, being on an antidepressant, ART adherence, CD4 count and viral load suppression at the previous visit, calendar year and time since ART initiation. Age, depressive symptom scores, and CD4 count were modeled using restricted cubic splines. IPTW, IPCW and IPOW were multiplied together to create a single combined set of weights for the weighted analysis.

**Table S1. Associations between baseline clinical and demographic characteristics with efavirenz initiation, before and after applying inverse probability of treatment weights to the data.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Observed Data** |  | **Weighted Data** |
|  | **EFV-free ART** | **EFV-containing ART** | **P-value** |  | **EFV-free ART** | **EFV-containing ART** | **P-value** |
| **Baseline Characteristics** | **N(%) or Mean (SD)** | **N(%) or Mean (SD)** |   |  | **N(%) or Mean (SD)** | **N(%) or Mean (SD)** |   |
| Year initiated cART | 2013 (1.0) | 2012 (0.9) | <0.01 |  | 2012 (1.1) | 2012 (1.1) | 0.84 |
| Gender |  |  | 0.02 |  |  |  | 0.20 |
| Male | 396 (88.0) | 139 (94.6) |  |  | 403 (89.6) | 134 (93.2) |  |
| Female | 54 (12.0) | 8 (5.4) |  |  | 47 (10.4) | 10 (6.8) |  |
| Depression and suicidal ideation |  |  | 0.05 |  |  |  | 0.98 |
| No depression of suicidal ideation | 268 (59.6) | 102 (69.4) |  |  | 278 (62.0) | 90 (62.7) |  |
| Depression | 90 (20.0) | 27 (18.4) |  |  | 88 (19.7) | 27 (18.9) |  |
| Suicidal ideation and/or depression | 92 (20.4) | 18 (12.2) |  |  | 82 (18.3) | 26 (18.4) |  |
| Antidepressant use |  |  | 0.03 |  |  |  | 0.86 |
| Not on antidepressants | 390 (87.4) | 136 (93.8) |  |  | 399 (88.9) | 127 (88.4) |  |
| On antidepressants | 56 (12.6) | 9 (6.2) |  |  | 50 (11.1) | 17 (11.6) |  |
| Panic Disorder |  |  | <0.01 |  |  |  | 0.59 |
| No symptoms | 279 (62.3) | 116 (80.6) |  |  | 399 (66.5) | 98 (68.0) |  |
| Some symptoms | 93 (20.7) | 16 (11.1) |  |  | 83 (18.4) | 22 (15.0) |  |
| Panic disorder | 76 (17.0) | 12 (8.3) |  |  | 68 (15.1) | 25 (17.0) |  |
| Drug use |  |  | 0.11 |  |  |  | 0.23 |
| No use | 166 (42.7) | 72 (50.7) |  |  | 195 (43.3) | 69 (48.2) |  |
| Current use | 113 (29.0) | 29 (20.4) |  |  | 133 (29.6) | 46 (31.9) |  |
| Past use | 110 (28.3) | 41 (28.9) |  |  | 122 (27.1) | 29 (19.9) |  |
| CD4 count, cells/mm3 |  |  | 0.17 |  |  |  | 0.93 |
| < 350 | 188 (41.8) | 52 (35.4) |  |  | 181 (40.2) | 57 (39.8) |  |
| >350 | 262 (58.2) | 95 (64.6) |   |   | 269 (59.8) | 87 (60.2) |   |
| EFV: efavirenz |  |  |  |  |  |  |  |

**Table S2. Baseline Characteristics comparing all new ART initiators (2011-2014), those with a valid patient reported outcome (PRO)\*, and the final study population.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Baseline Characteristics** | **New ART Initiators** |   | **Valid PRO** |   | **Study Population** |
| N=2,729 |  | N=875 |  | N=597 |
| **N(%) or Median (IQR)** |   | **N(%) or Median (IQR)** |   | **N(%) or Median (IQR)** |
| Initial ART regimen |  |  |  |  |  |
| Efavirenz-free ART | 1,963 (71.9) |  | 655 (74.9) |  | 450 (75.4) |
| Efavirenz-containing ART | 766 (28.1) |  | 220 (25.1) |  | 147 (24.6) |
| Year initiated ART |  |  |  |  |  |
| 2011 | 562 (20.6) |  | 193 (22.1) |  | 155 (26.0) |
| 2012 | 712 (26.1) |  | 204 (23.3) |  | 160 (26.8) |
| 2013 | 827 (30.3) |  | 275 (31.4) |  | 163 (27.3) |
| 2014 | 628 (23.0) |  | 203 (23.2) |  | 119 (19.9) |
| Age | 36 (28, 46) |  | 37 (30, 46) |  | 35 (28, 44) |
| Gender |  |  |  |  |  |
| Male | 2,372 (86.9) |  | 770 (88.0) |  | 535 (89.6) |
| Female | 357 (13.1) |  | 105 (12.0) |  | 62 (10.4) |
| Race/ethnicity |  |  |  |  |  |
| White, non-Hispanic  | 1,287 (47.7) |  | 449 (51.6) |  | 294 (49.6) |
| Black, non-Hispanic | 861 (31.9) |  | 211 (24.3) |  | 135 (22.8) |
| Hispanic | 396 (14.7) |  | 158 (18.2) |  | 121 (20.4) |
| Other | 155 (5.7) |  | 52 (6.0) |  | 43 (7.3) |
| HIV risk group |  |  |  |  |  |
| MSM  | 1,827 (67.5) |  | 594 (68.0) |  | 418 (70.1) |
| IDU | 296 (10.9) |  | 101 (11.6) |  | 69 (11.6) |
| Heterosexual | 529 (19.5) |  | 152 (17.4) |  | 88 (14.8) |
| Other | 56 (2.0) |  | 26 (3.0) |  | 21 (3.5) |
| Antidepressant use |  |  |  |  |  |
| Not on an antidepressant | 2,294 (85.5) |  | 761 (87.0) |  | 526 (89.0) |
| On an antidepressant | 390 (14.5) |  | 114 (13.0) |  | 65 (11.0) |
| History of mental health disorder |  |  |  |  |  |
| No  | 2,053 (75.2) |  | 601 (68.7) |  | 412 (69.0) |
| Yes | 676 (24.8) |  | 274 (31.3) |  | 185 (31.0) |
| History of a co-morbid medical disorder |  |  |  |  |  |
| No  | 2,365 (86.7) |  | 737 (84.2) |  | 515 (86.3) |
| Yes | 365 (13.3) |  | 138 (15.8) |  | 82 (13.7) |
| CD4 count, cells/mm3 | 396 (237, 569) |   | 442 (286, 615) |   | 396 (246, 542) |
| \*Valid PRO defined as having a PRO measurement within 6 months prior, or one week after, initiating ART. |

**Table S3. Description of initial ART regimen among 597 new ART users in CNICS.**

|  |  |  |
| --- | --- | --- |
| **Initial Regimen** | **Efavirenz-free**  | **Efavirenz-containing**  |
| TDF + FTC + EVG | 110 (24.4) | -- |
| TDF + FTC + DRV + RTV | 108 (24.0) | -- |
| TDF + FTC + RLR | 98 (21.8) | -- |
| TDF + FTC + RGV | 39 (8.7) | -- |
| TDF + FTC + ATZ + RTV | 33 (7.3) | -- |
| 3TC + ABC + DTG | 13 (2.9) | -- |
| TDF + FTC + DTG | 10 (2.2) | -- |
| TDF + FTC + EFV | -- | 142 (96.6) |
| Other | 39 (8.9) | 5 (3.4) |
| Total | 450 | 147 |
| TDF = tenofovir, FTC = emtricitabine, EVG = elvitegravir, DRV = darunavir, RTV = ritonavir (boosted and unboosted), RLR = rilpivirine, RGV = raltegravir, ATZ = zidovudine, 3TC = lamivudine, ABC = abacavir, DTG = dolutegravir, EFV = efavirenz |