

Supplement

Methods

Patient Selection

PLWH ≥ 65 years old and HIV-negative individuals ≥ 65 years old were selected. The group of PLWH included individuals with (a) ≥ 2 non-diagnostic claims with an ICD-9-CM diagnosis of HIV (042, 795.71, V08, 079.53) in any position (primary or secondary) or (b) 1 non-diagnostic claim with an HIV diagnosis and ≥ 1 claim for ART between January 1, 2010 and September 30, 2015. A non-diagnostic claim is one that has a procedure code for a procedure other than a laboratory or radiology test, known as diagnostic claims. As all claims require a diagnosis, the suspected diagnosis may appear on a diagnostic claim, regardless of the results of the test. Therefore, diagnoses appearing on diagnostic claims are typically ignored when defining a patient population. The comparator group comprised individuals with no claims with HIV diagnosis and no claims for ART from January 1, 2009 to September 30, 2015 (referred to as “HIV-negative individuals”).

The service date on a patient’s most recent claim with an HIV diagnosis was referred to as the index date. The most recent date with an HIV diagnosis was chosen as the index date in order to evaluate non-HIV health conditions and non-ART medication use at an individual’s oldest age in the database to maximize the sample size among the upper distribution of age (e.g., someone who is 65 years old in 2010 but has data that with an HIV ICD-9-CM diagnosis code through 2014 would be analyzed as a 70-year old using the most recent year of data). A pseudo-index date for HIV-negative individuals was randomly assigned based on the distribution of calendar year for index dates among selected PLWH. The index date for HIV-negative individuals was not tied to any diagnosis or healthcare encounter.

Individuals with an HIV diagnosis on only one non-diagnostic claim and no ART medication claims during the patient selection period were excluded from the analysis, because it is unclear whether or not these individuals had HIV.

PLWH and HIV-negative individuals were required to have 12 months of continuous enrollment in the Medicare Supplemental database prior to their index date to evaluate the study outcomes (evaluation period). This requirement was made to ensure that if the enrollee saw a healthcare provider or filled a prescription which generated a healthcare claim, the diagnosis and medications would appear in the database. Patients were required to be ≥ 65 years old at the start of the evaluation period.

Exposure

The primary exposure of interest was HIV status.

Outcomes

The outcomes were: (a) the most common non-HIV 3-digit ICD-9-CM diagnoses codes appearing in the two groups, (b) the most common non-ART therapeutic medication classes for pharmacy claims in the two groups, (c) prevalence of non-HIV conditions in the two groups, (d) the number of non-HIV health conditions diagnosed in individuals, and (e) the number of daily non-ART medications by individuals. All outcomes were based on healthcare claims with service dates in the 12 months prior to and including the index date.

ICD-9-CM diagnosis codes range from 3 to 5 digits in length and are organized in a hierarchical structure. To evaluate the most non-HIV health conditions present, the diagnoses codes on each non-diagnostic inpatient or outpatient claim were rolled up to the 3-digit level to combine similar conditions. On outpatient pharmacy claims, therapeutic class was based on Redbook™,

a database containing drug product information. All unique 3-digit ICD-9-CM diagnosis codes present/unique therapeutic classes filled among the PLWH group were identified and the number and proportion of individuals with each diagnosis/therapeutic class was captured. This process was repeated for the men with HIV, women with HIV, the overall HIV-negative group, HIV-negative men and HIV-negative women.

The prevalence of the following conditions were evaluated: ischemic heart disease (including myocardial infarction, angina, and atherosclerosis), congestive heart failure, cardiac dysrhythmia, hypertension, dyslipidemia, non-rheumatic heart valve disorders, peripheral vascular disease, dementia, cerebrovascular disease, rheumatologic disease, osteoarthritis, osteoporosis, peptic ulcer disease/esophageal reflux, liver disease, hepatitis C, diabetes, hemiplegia/paraplegia, kidney disease, non-AIDS defining cancer (cancers other than Kaposi's sarcoma, cervical cancer, and non-Hodgkin's lymphoma), benign prostate hyperplasia, anemia, unspecified acquired hypothyroidism, glaucoma, cataract, retinal disorders (including non-diabetic retinopathy, and retinal or macular degeneration), anxiety, depression, schizophrenia, bipolar disorder, substance abuse, and tobacco use disorder. The list was based on conditions included in the Deyo Charlson Comorbidity Index (20), which is a claims-based comorbidity score commonly used in the claims-based analyses consisting of 15 health conditions in addition to HIV, the most common diagnoses in both PLWH and HIV-negative individuals in this dataset, and conditions including in other analyses of comorbidities (4,5,7,21-23). We also captured AIDS-defining cancers (Kaposi's sarcoma, cervical cancer, and non-Hodgkin's lymphoma). An individual was considered to have a condition if he or she had ≥ 1 non-diagnostic claims with the relevant diagnosis or procedure code during the 12-month evaluation period. For each HIV+ and HIV-negative individual, the number of aforementioned non-HIV conditions of interest present was calculated (minimum of 0 and maximum of 32) as was the number of daily non-ART medications. AIDS-defining cancer did not contribute to the number of non-HIV

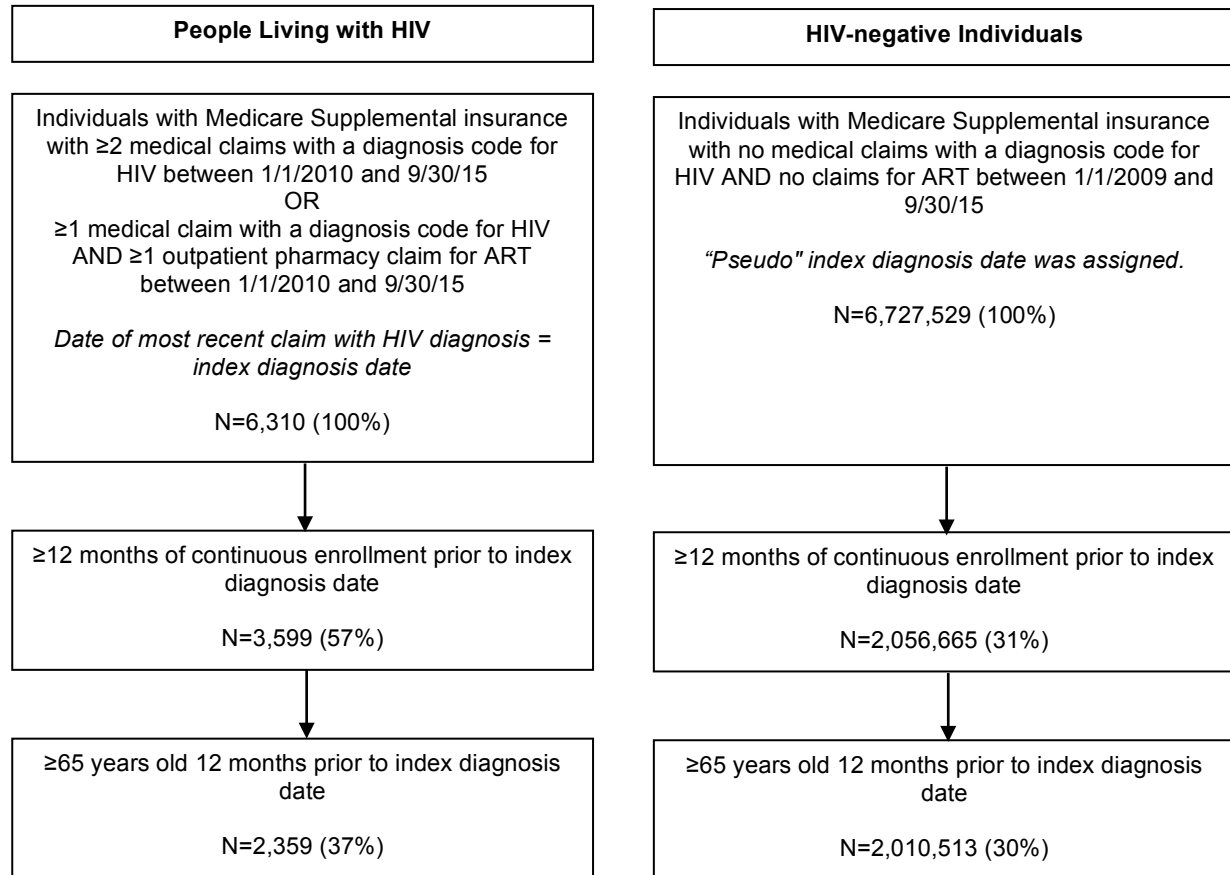
conditions. To calculate the number of daily medications, the days' supplies of all outpatient pharmacy claims during the 12-month evaluation period were summed and the sum was divided by 366 days, in a method similar to the calculation for medication possession ratio (24).

In a sensitivity analysis, the following conditions were not included when summing the number of non-HIV conditions because of their potential to be adverse events of ART (25):

hypertension, osteoporosis, ischemic heart disease, dyslipidemia, liver disease, depression, kidney disease and anemia.

Supplemental Figure 1. Selection of cohorts of people living with HIV and HIV-negative

individuals



Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus.

Supplemental Table 1. Demographic characteristics of PLWH and HIV-negative individuals, stratified by sex

	PLWH: Men		HIV-negative Individuals: Men		PLWH: Women		HIV-negative Individuals: Women	
	N=1,909		N=895,123		N=450		N=1,115,390	
	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD	N/Mean	%/SD
Individual-Level Characteristics								
Age (Mean, SD)	71.26	4.91	75.36	7.19	72.12	6.20	76.53	7.82
Age group (N, %)								
65-69	884	46.31%	237,894	26.58%	200	44.44%	260,794	23.38%
70-74	628	32.90%	234,994	26.25%	142	31.56%	266,145	23.86%
75-79	253	13.25%	172,087	19.22%	48	10.67%	211,801	18.99%
80-84	92	4.82%	132,202	14.77%	30	6.67%	174,149	15.61%
85+	52	2.72%	117,946	13.18%	30	6.67%	202,501	18.16%
Region (N, %)								
Northeast	503	26.35%	199,799	22.32%	150	33.33%	261,067	23.41%
North Central	287	15.03%	286,399	32.00%	63	14.00%	354,504	31.78%
West	543	28.44%	267,311	29.86%	177	39.33%	331,299	29.70%
South	560	29.33%	136,947	15.30%	55	12.22%	163,814	14.69%
Unknown	16	0.84%	4,667	0.52%	5	1.11%	4,706	0.42%
Urbanicity (N, %)								
Urban	1,793	93.92%	746,056	83.35%	406	90.22%	945,535	84.77%
Rural	104	5.45%	144,891	16.19%	39	8.67%	165,621	14.85%
Unknown	12	0.63%	4,176	0.47%	5	1.11%	4,234	0.38%

Abbreviations: HIV, human immunodeficiency syndrome; PLWH, people living with HIV.

Supplemental Table 2. Rank and prevalence of 3-digit diagnoses and therapeutic classes present in ≥15% of HIV+ men or HIV+ women

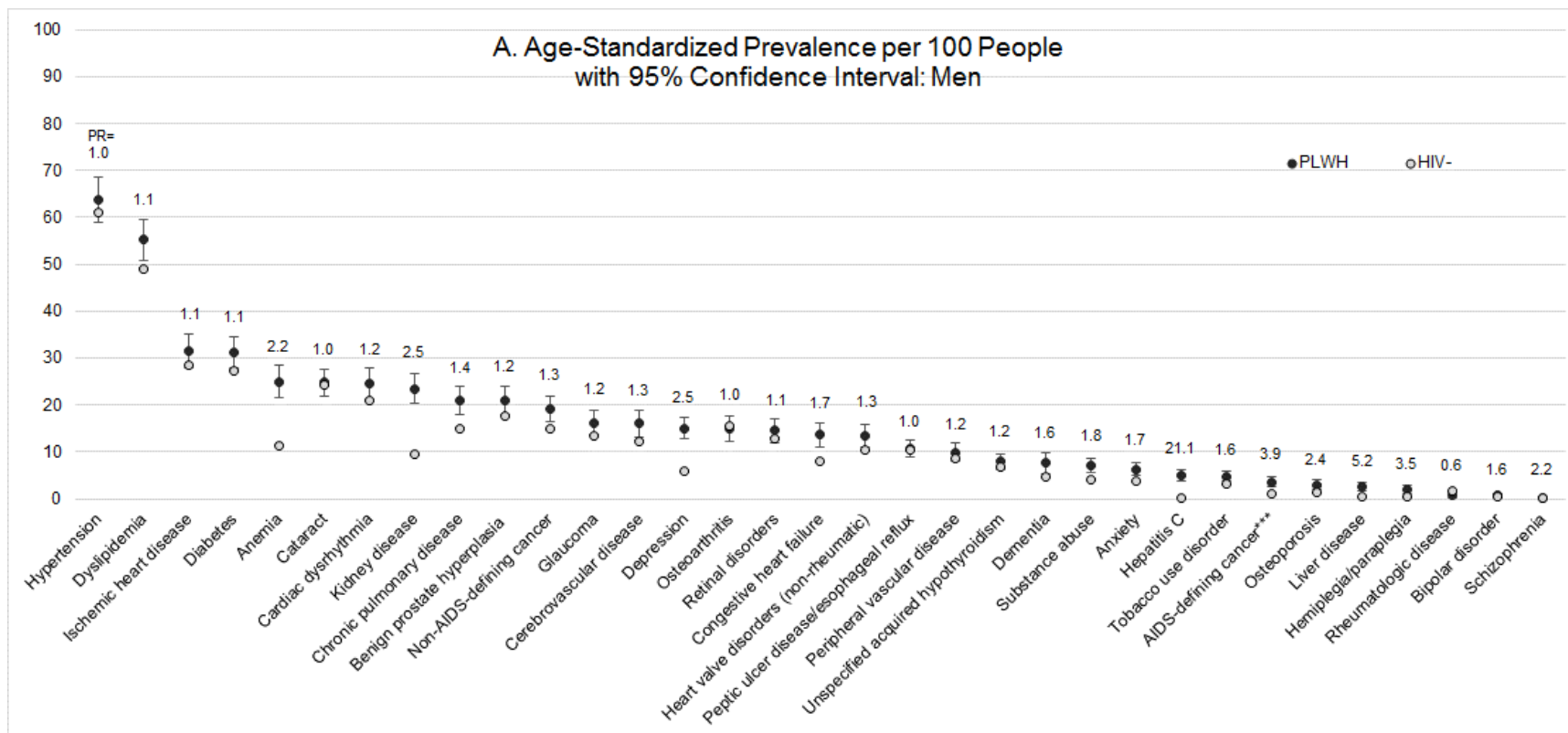
	PLWH: Men			PLWH: Women		
	Rank	N	%	Rank	N	%
Most Common 3-Digit ICD-9-CM Diagnosis Codes (N, %)						
401 Essential hypertension	1	870	45.6%	1	259	57.6%
272 Disorders of lipid metabolism	2	669	35.0%	2	173	38.4%
786 Symptoms involving respiratory system and other chest symptoms	3	584	30.6%	3	154	34.2%
780 General symptoms	4	561	29.4%	4	150	33.3%
250 Diabetes mellitus	5	495	25.9%	6	116	25.8%
414 Other forms of chronic ischemic heart disease	6	422	22.1%	20/21	71	15.8%
366 Cataract	7	421	22.1%	8	102	22.7%
702 Other dermatoses	8	399	20.9%	41	24	5.3%
729 Other disorders of soft tissues	9	383	20.1%	7	113	25.1%
427 Cardiac dysrhythmias	10	357	18.7%	16	76	16.9%
719 Other and unspecified disorder of joint	11	353	18.5%	5	126	28.0%
V04 Need for prophylactic vaccination and inoculation against certain viral diseases	12	352	18.4%	13	80	17.8%
600 Hyperplasia of prostate	13	319	16.7%	N/A		
V58 Other and unspecified aftercare	14	316	16.6%	19	73	16.2%
788 Symptoms involving urinary system	15	316	16.6%	31	50	11.1%
724 Other and unspecified disorders of back	16	286	15.0%	12	84	18.7%
787 Symptoms involving digestive system	17	285	14.9%	14	79	17.6%
782 Symptoms involving skin and other integumentary tissue	19	261	13.7%	22/23	69	15.3%
285 Other and unspecified anemias	20	249	13.0%	10/11	88	19.6%
599 Other disorders of urethra and urinary tract	23/24	240	12.6%	18	74	16.4%
365 Glaucoma	23/24	240	12.6%	22/23	69	15.3%
276 Disorders of fluid, electrolyte, and acid-base balance	25/26	234	12.3%	10/11	88	19.6%
789 Other symptoms involving abdomen and pelvis	29	223	11.7%	17	75	16.7%
V72 Special investigations and examinations	33	205	10.7%	20/21	71	15.8%
715 Osteoarthritis and allied disorders	34	202	10.6%	15	77	17.1%
V76 Special screening for malignant neoplasms	38	174	9.1%	9	102	22.7%
Most Common Medication Therapeutic Classes (N, %)						
Antihyperlipidemic Drugs: Not Elsewhere Classified	1	1,074	56.3%	1	235	52.2%
Cardiac, Beta Blockers	2	620	32.5%	2	148	32.9%
Analgesics/Antipyretics: Opiate Agonists	3	610	32.0%	3	135	30.0%
Cardiac: ACE Inhibitors	4	573	30.0%	6	123	27.3%
Unclassified Agents: Not Elsewhere Classified*	5	458	24.0%	33	23	5.1%
Psychotherapeutic Agents: Antidepressants	6	451	23.6%	5	124	27.6%
Cardiac: Calcium Channel	7	445	23.3%	4	131	29.1%
Gastrointestinal Drugs Miscellaneous: Not Elsewhere Classified	8	441	23.1%	7	118	26.2%
Quinolones: Not Elsewhere Classified	9	385	20.2%	11	83	18.4%
Antivirals: Not Elsewhere Classified*	10	384	20.1%	26	53	11.8%
Antibiotics: Penicillins	11	354	18.5%	12	83	18.4%
Anxiolytics, Sedatives, and Hypnotics: Benzodiazepines	12	332	17.4%	14	81	18.0%

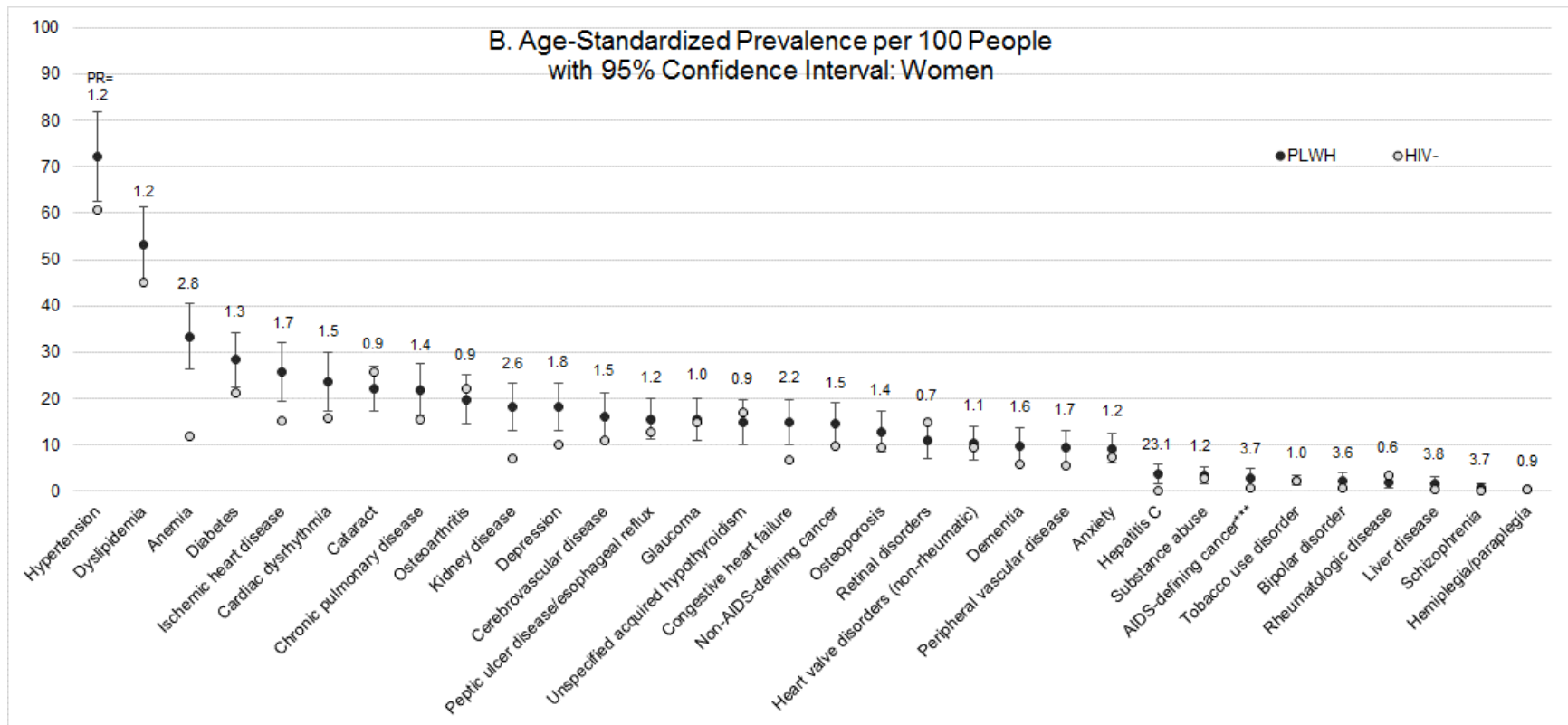
Analgesics/Antipyretics: Non-steroid/Anti-inflammatory	13	316	16.6%	8	92	20.4%
Adrenals & Combinations: Not Elsewhere Classified*	14	313	16.4%	9	89	19.8%
Antibiotics: Erythromycin & Macrolide	15	309	16.2%	13	83	18.4%
Anti-inflammatory Skin/Mucous Membrane Agents & Combinations: Miscellaneous	16	304	15.9%	19	65	14.4%
Cardiac Drugs: Not Elsewhere Classified	17	298	15.6%	10	89	19.8%
Anti-inflammatory Agents Eye, Ear, Nose, and Throat: Not Elsewhere Classified	18	296	15.5%	18	68	15.1%
Sulfonamides & Combinations: Not Elsewhere Classified	19	274	14.4%	15	76	16.9%
Anticonvulsants, Miscellaneous	23	252	13.2%	16	75	16.7%
Sympathomimetic Agents: Not Elsewhere Classified	24	239	12.5%	17	73	16.2%

Abbreviations: HIV, human immunodeficiency virus; ICD-9-CM, International Classification of Diseases, Ninth Edition, Clinical Modification; PLWH, people living with HIV.

**Unclassified agents includes medications for benign prostate hyperplasia. Antivirals includes medications for hepatitis, influenza, cytomegalovirus, and herpes. Adrenals includes corticosteroids.*

Supplemental Figure 2A-B. Standardized prevalence of non-HIV conditions and AIDS-defining cancers per 100 people with 95% confidence intervals and prevalence ratios for PLWH versus HIV-negative individuals for (A) men and (b) women





Abbreviations: HIV, human immunodeficiency virus; PLWH, people living with HIV; PR, prevalence ratio.

Supplemental Table 3. Number of non-HIV conditions of interest and number of daily non-ART medications

	PLWH		HIV-negative Individuals		PLWH: Men		PLWH: Women		HIV-negative Individuals: Men		HIV-negative Individuals: Women	
	N=2,359		N=2,010,513		N=1,909		N=450		N=895,123		N=1,115,390	
	N/Mean/ Median	%/SD/IQR	N/Mean/ Median	%/SD/IQR	N/Mean/ Median	%/SD/IQR	N/Mean/ Median	%/SD/IQR	N/Mean/ Median	%/SD/IQR	N/Mean/ Median	%/SD/IQR
Number of non-HIV conditions of interest (Mean, SD)	4.61	3.06	3.94	2.79	4.59	3.09	4.68	2.96	4.04	2.85	3.85	2.74
Median, IQR	4	2-6	4	2-6	4	2-6	4	2-6	4	2-6	4	2-5
≥2 non-HIV conditions of interest (N, %)	2,036	86.31%	1,598,853	79.52%	1,640	85.91%	396	88.00%	715,424	79.92%	883,429	79.20%
Number of daily non-ART medications (Mean, SD)	3.79	3.09	3.41	2.76	3.86	3.13	3.49	2.90	3.42	2.79	3.40	2.74
Median, IQR	3.16	1.38-5.48	2.95	1.21-5.01	3.24	1.42-5.53	2.72	1.29-5.08	2.96	1.17-5.05	2.94	1.23-4.98
≥5 non-ART medications per day (N, %)	680	28.83%	504,692	25.10%	567	29.70%	113	25.11%	227,760	25.44%	276,932	24.83%

Note. p-values comparing means and proportions among PLWH with HIV-negative individuals were all <0.001. p-values comparing mean number of non-HIV conditions between men and women with HIV was 0.575, comparing proportions of individuals with ≥2 non-HIV conditions was 0.246, comparing number of daily non-ART medications was 0.022, and comparing proportions of individuals with ≥5 non-ART medications per day was 0.053.

Supplemental Table 4A. Complete modeling results for number of non-HIV conditions

	Adjusted				Sensitivity Analysis ¹			
	Men		Women		Men		Women	
	Ratio for Number of Non-HIV Conditions (95% CI)	p-value	Ratio for Number of Non-HIV Conditions (95% CI)	p-value	Ratio for Number of Non-HIV Conditions (95% CI)	p-value	Ratio for Number of Non-HIV Conditions (95% CI)	p-value
PLWH vs. HIV-negative²	1.272 (1.233-1.312)	<0.001	1.326 (1.245-1.413)	<0.001	1.243 (1.199-1.288)	<0.001	1.221 (1.134-1.315)	<0.001
Age, years								
70-74 vs. 65-69	1.205 (1.200-1.210)	<0.001	1.179 (1.174-1.183)	<0.001	1.250 (1.244-1.256)	<0.001	1.195 (1.189-1.201)	<0.001
75-59 vs. 65-69	1.387 (1.381-1.393)	<0.001	1.332 (1.326-1.338)	<0.001	1.479 (1.471-1.487)	<0.001	1.359 (1.352-1.366)	<0.001
80-84 vs. 65-69	1.515 (1.508-1.523)	<0.001	1.422 (1.416-1.429)	<0.001	1.646 (1.637-1.655)	<0.001	1.457 (1.449-1.464)	<0.001
85+ vs 65-69	1.591 (1.583-1.599)	<0.001	1.474 (1.468-1.480)	<0.001	1.753 (1.744-1.763)	<0.001	1.532 (1.525-1.540)	<0.001
Region								
North Central vs. Northeast	0.950 (0.946-0.954)	<0.001	0.977 (0.973-0.980)	<0.001	0.930 (0.926-0.934)	<0.001	0.962 (0.958-0.966)	<0.001
West vs. Northeast	0.917 (0.914-0.921)	<0.001	0.926 (0.922-0.929)	<0.001	0.895 (0.891-0.899)	<0.001	0.907 (0.903-0.911)	<0.001
South vs. Northeast	0.828 (0.824-0.832)	<0.001	0.860 (0.856-0.864)	<0.001	0.804 (0.799-0.808)	<0.001	0.842 (0.838-0.847)	<0.001
Unknown vs. Northeast	0.533 (0.495-0.573)	<0.001	0.558 (0.517-0.602)	<0.001	0.521 (0.478-0.568)	<0.001	0.552 (0.505-0.605)	<0.001
Urbanicity								
Rural vs. Urban	0.964 (0.960-0.968)	<0.001	0.957 (0.954-0.961)	<0.001	0.962 (0.958-0.967)	<0.001	0.958 (0.953-0.962)	<0.001
Unknown vs. Urban	1.514 (1.403-1.634)	<0.001	1.407 (1.301-1.523)	<0.001	1.480 (1.352-1.621)	<0.001	1.356 (1.234-1.490)	<0.001

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; PLWH, people living with HIV.

¹Doesn't include hypertension, osteoporosis, ischemic heart disease, dyslipidemia, liver disease, depression, kidney disease, and anemia.

²Ns for models were: men with HIV=1,909; HIV-negative men=895,123; women with HIV=450; and HIV-negative women=1,115,390.

Supplemental Table 4B. Complete modeling results for having no non-ART medications

	Adjusted			
	Men		Women	
	Odds Ratio for Having No Non-ART Medications (95% CI)	p-value	Odds Ratio for Having No Non-ART Medications (95% CI)	p-value
PLWH vs. HIV-negative¹	0.523 (0.427-0.642)	<0.001	0.840 (0.586-1.203)	0.341
Age, years				
70-74 vs. 65-69	0.777 (0.762-0.792)	<0.001	0.857 (0.841-0.874)	<0.001
75-59 vs. 65-69	0.645 (0.630-0.659)	<0.001	0.762 (0.746-0.779)	<0.001
80-84 vs. 65-69	0.636 (0.620-0.652)	<0.001	0.787 (0.770-0.805)	<0.001
85+ vs 65-69	0.750 (0.732-0.769)	<0.001	0.954 (0.935-0.974)	<0.001
Region				
North Central vs. Northeast	1.160 (1.136-1.185)	<0.001	1.197 (1.175-1.220)	<0.001
West vs. Northeast	1.050 (1.028-1.073)	<0.001	1.071 (1.051-1.092)	<0.001
South vs. Northeast	1.232 (1.202-1.262)	<0.001	1.142 (1.117-1.169)	<0.001
Unknown vs. Northeast	5.428 (4.479-6.577)	<0.001	4.973 (4.070-6.078)	<0.001
Urbanicity				
Rural vs. Urban	0.916 (0.942-0.982)	<0.001	0.979 (0.960-0.998)	0.028
Unknown vs. Urban	0.438 (0.356-0.538)	<0.001	0.572 (0.462-0.709)	<0.001

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; PLWH, people living with HIV.

¹Ns for models were: men with HIV=1,909; HIV-negative men=895,123; women with HIV=450; and HIV-negative women=1,115,390.

Supplemental Table 4C. Complete modeling results for number of daily non-ART medications among people with non-ART medication use

	Adjusted			
	Men		Women	
	Ratio for Number of Non-ART Medications per Day (95% CI)	p-value	Ratio for Number of Non-ART Medications per Day (95% CI)	p-value
PLWH vs. HIV-negative¹	1.178 (1.133-1.226)	<0.001	1.086 (1.003-1.176)	0.043
Age, years				
70-74 vs. 65-69	1.133 (1.128-1.139)	<0.001	1.118 (1.113-1.123)	<0.001
75-59 vs. 65-69	1.242 (1.235-1.249)	<0.001	1.224 (1.218-1.230)	<0.001
80-84 vs. 65-69	1.305 (1.297-1.313)	<0.001	1.302 (1.295-1.309)	<0.001
85+ vs 65-69	1.318 (1.309-1.326)	<0.001	1.330 (1.323-1.336)	<0.001
Region				
North Central vs. Northeast	0.993 (0.988-0.998)	0.005	1.048 (1.044-1.053)	<0.001
West vs. Northeast	1.045 (1.040-1.050)	<0.001	1.116 (1.111-1.121)	<0.001
South vs. Northeast	0.941 (0.935-0.947)	<0.001	0.996 (0.990-1.001)	0.107
Unknown vs. Northeast	0.835 (0.763-0.914)	<0.001	0.931 (0.852-1.017)	0.114
Urbanicity				
Rural vs. Urban	0.996 (0.991-1.001)	0.086	1.019 (1.015-1.024)	<0.001
Unknown vs. Urban	1.127 (1.025-1.238)	0.013	1.051 (0.958-1.154)	0.293

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; PLWH, people living with HIV.

¹Ns for models were: men with HIV=1,811; HIV-negative men=818,618; women with HIV=418; and HIV-negative women=1,023,855.