

Supplementary Table 1: Cost impacts of patients' demographics, cardiometabolic diseases, antiretroviral therapy (ART) and AIDS-defining illnesses (ADIS) in HIV-infected population

<b>Estimation of annual direct medical cost</b>	
<b>Base-case cost (2017 USD)</b>	Yearly medical cost for the male patients without any occurrence of ADIs, comorbidities and cardiovascular diseases
	\$547 (95% CI: 532-563)
<b>Characteristics</b>	<b>Cost multipliers (95% CI)</b>
<b>Female (vs. male)</b>	1.05 (1.01-1.10)
<b>Age at HIV diagnosis (vs. ref.: 35-49 years)</b>	
≤ 24 years	0.99 (0.95-1.02)
25-34 years	0.98 (0.96-1.01)
50-64 years	1.06 (1.00-1.12)
≥ 65 years	1.19 (0.93-1.51)
<b>HIV duration (vs. ref.: first year)</b>	
Second year	0.69 (0.67-0.70)
Third year	0.70 (0.68-0.71)
Fourth year	0.72 (0.71-0.74)
Fifth year	0.78 (0.76-0.80)
<b>Occurrence of any ADIs (vs. ref.: none)</b>	1.91 (1.82-2.00)
<b>Every 10% increase of MPR of ART</b>	1.33 (1.32-1.34)
<b>Comorbidities (vs. ref.: none)</b>	

Renal diseases	2.44 (2.04-2.92)
Liver diseases	1.46 (1.43-1.50)
Cancer	1.75 (1.54-1.99)
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<b>Cardiometabolic diseases (vs. ref.: none)</b>	
Hypertension	1.28 (1.21-1.35)
Diabetes	1.40 (1.27-1.54)
Dyslipidemia	1.00 (0.97-1.03)
Cardiovascular diseases	1.96 (1.69-2.27)
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Abbreviations: MPR, medication possession ratio; ART, antiretroviral therapy; CI: confidence interval.

Supplementary Table 2: Operational definitions of cardiometabolic diseases, comorbidities, and AIDS-defining illnesses

Variable of interest		Operational definition
<b>Cardiometabolic diseases and comorbidities</b>		
Hypertension		Diagnosis record (ICD-9-CM: 401-405) in inpatient or outpatient file
Diabetes		Diagnosis record (ICD-9-CM: 250) in inpatient or outpatient file
Hyperlipidemia		Diagnosis record (ICD-9-CM: 272) in inpatient or outpatient file
Cardiovascular disease	Cerebrovascular disease	At least 1 diagnosis record (ICD-9-CM: 430-437) in inpatient file or 3 diagnosis records in outpatient file
	Myocardial infarction	At least 1 diagnosis record (ICD-9-CM: 410) in inpatient file or 3 diagnosis records in outpatient file
	Heart failure	At least 1 diagnosis record (ICD-9-CM: 428) in inpatient file or 3 diagnosis records in outpatient file
	Arrhythmia	At least 1 diagnosis record (ICD-9-CM: 426, 427) in inpatient file or 3 diagnosis records in outpatient file

	Ischemic heart disease	At least 1 diagnosis record (ICD-9-CM: 411, 413, 414) in inpatient file or 3 diagnosis records in outpatient file
	Cardiogenic shock	At least 1 diagnosis record (ICD-9-CM: 785.51) in inpatient file or 3 diagnosis records in outpatient file
Renal diseases		Diagnosis records (ICD-9-CM: 582, 583-583.7, 585, 586, 588) in inpatient or outpatient file
Liver diseases		Diagnosis records (ICD-9-CM: 571.2, 571.4, 571.5, 571.6, 572.2-572.8, 456.0-465.21) in inpatient or outpatient file
Cancer		Leukemia/lymphoma (exclude Kaposi's sarcoma, Hodgkin's lymphoma, Non-Hodgkin's lymphoma): diagnosis records (ICD-9-CM: 140-172, 174-195.8, 200-208.9; exclude 176, 200, 201, 202) in inpatient or outpatient file  Solid tumor: diagnosis records (ICD-9-CM: 196-199.1) in inpatient or outpatient file
<b>AIDS-defining illnesses (ADIs)</b>		
Candidiasis		Disease diagnosis and medication use confirmed in inpatient or outpatient file  • ICD-9-CM: 112

	<ul style="list-style-type: none"> <li>Medication use: fluconazole, voriconazole, posaconazole, caspofungin, micafungin, anidulafungin, amphotericin B</li> </ul>
Cryptococcosis	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>ICD-9-CM: 117.5</li> <li>Medication use: amphotericin B, flucytosine, fluconazole, itraconazole</li> </ul>
<i>Cytomegalovirus</i>	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>ICD-9-CM: 078.5</li> <li>Medication use: ganciclovir, valganciclovir</li> </ul>
Tuberculosis	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>ICD-9-CM: 010-018</li> <li>Medication use: isoniazid, ethambutol, rifampicin, pyrazinamide, streptomycin, thioacetazone, amikacin, kanamycin, ciprofloxacin, ofloxacin, moxifloxacin, levofloxacin, prothionamide, clarithromycin, ethionamide, para-aminosalicylic acid, cycloserine, rifabutin, clofazimine, thioridazine</li> </ul>

Varicella-zoster virus	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>• ICD-9-CM: 053</li> <li>• Medication use: aciclovir, valaciclovir</li> </ul>
<i>Pneumocystis jirovecii</i> pneumonia	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>• ICD-9-CM: 136.3</li> <li>• Medication use: sulfamethoxazole/trimethoprim, sulfamethoxazole, trimethoprim, caspofungin, micafungin, anidulafungin</li> </ul>
Penicilliosis	<p>Disease diagnosis and medication use confirmed in inpatient or outpatient file</p> <ul style="list-style-type: none"> <li>• ICD-9-CM: 117.9</li> <li>• Medication use: amphotericin B, fluconazole, voriconazole, itraconazole, caspofungin, micafungin, anidulafungin</li> </ul>
Kaposi's sarcoma	At least 3 diagnosis records (ICD-9-CM: 176) in inpatient or outpatient file
Hodgkin's lymphoma	At least 3 diagnosis records (ICD-9-CM: 201) in inpatient or outpatient file
Non-Hodgkin's lymphoma	At least 3 diagnosis records (ICD-9-CM: 200, 202) in inpatient or outpatient file

Supplementary Table 3: AIDS-defining illnesses in the overall study cohort, ART (low) & ADI (+) group, and ART (high) & ADI (+) group

AIDS-defining illnesses, ADIs (%)	Overall study cohort	Study group		<i>p</i> value*
		ART (low) & ADI (+)	ART (high) & ADI (+)	
Candidiasis	2.49%	11.73%	18.77%	0.0046
Cryptococcosis	0.30%	3.08%	1.23%	0.0859
<i>Cytomegalovirus</i>	0.28%	1.92%	3.38%	0.1843
Tuberculosis	1.99%	14.62%	23.08%	0.0018
Varicella-zoster virus	0.66%	1.54%	1.85%	0.7332
<i>Pneumocystis jirovecii</i> pneumonia	2.96%	12.12%	23.08%	<.0001
Penicilliosis	0.13%	0.96%	0.31%	0.4149
Kaposi's sarcoma	0.22%	1.54%	3.38%	0.0782
Hodgkin's lymphoma	0.02%	0.19%	0%	N/A
Non-Hodgkin's lymphoma	0.32%	3.27%	2.15%	0.3423

Abbreviations: ART, antiretroviral therapy; N/A, not applicable

\*Comparison of AIDS-defining illnesses across the ART (low) & ADI (+) and ART (high) & ADI (+) groups.

Supplementary Table 4: Cumulative incidences of hypertension, diabetes, dyslipidemia, and cardiovascular diseases

Study outcomes	Overall	Study group			
	study cohort	ART (low) & ADI (-)	ART (low) & ADI (+)	ART (high) & ADI (-)	ART (high) & ADI (+)
<b>Hypertension</b>	7.68%	6.62%	11.35%	11.79%	11.38%
<b>Diabetes</b>	2.44%	2.31%	2.50%	3.27%	2.15%
<b>Dyslipidemia</b>	11.79%	7.29%	16.92%	33.03%	28.62%
<b>Cardiovascular diseases</b>	1.02%	0.86%	3.27%	1.28%	0.31%

Abbreviations: ART, antiretroviral therapy; ADI, AIDS-defining illness



Supplementary Table 5: Hazard ratios (95% confidence interval) of developing hypertension, diabetes, dyslipidemia, and cardiovascular diseases after the first year of HIV diagnosis between study groups

Study group	Reference group	Study outcomes			
		Hypertension	Diabetes	Dyslipidemia	CVDs
<b>ART (low) &amp; ADI (-)</b>	ART (low) & ADI (+)	<b>0.71 (0.54-0.94)</b>	1.05 (0.59-1.86)	<b>0.46 (0.37-0.58)</b>	<b>0.39 (0.22-0.69)</b>
<b>ART (high) &amp; ADI (-)</b>	ART (low) & ADI (+)	1.11 (0.81-1.51)	1.31 (0.71-2.44)	<b>1.99 (1.58-2.52)</b>	0.51 (0.24-1.05)
<b>ART (high) &amp; ADI (+)</b>	ART (low) & ADI (+)	0.94 (0.62-1.42)	0.82 (0.33-2.07)	<b>1.72 (1.29-2.31)</b>	N/A *
<b>ART (high) &amp; ADI (-)</b>	ART (low) & ADI (-)	1.66 (1.39-1.98)	1.32 (0.96-1.83)	<b>4.70 (4.16-5.30)</b>	1.36 (0.79-2.32)
<b>ART (high) &amp; ADI (+)</b>	ART (low) & ADI (-)	1.39 (0.99-1.96)	0.81 (0.38-1.74)	<b>3.70 (2.96-4.63)</b>	N/A *
<b>ART (high) &amp; ADI (-)</b>	ART (high) & ADI (+)	1.18 (0.82-1.70)	1.74 (0.78-3.88)	1.21 (0.96-1.52)	N/A *

Abbreviations: ART, antiretroviral therapy; ADI, AIDS-defining illness; N/A, not applicable

\*Hazard ratios were not applicable due to limited event numbers.

Supplementary Table 6: Percentage of study patients exposed to specific type of ART at the first year of HIV diagnosis (n=10,693)

Study group	ART (low) and ADI (-) (n=8,440)	ART (low) and ADI (+) (n=520)	ART (high) and ADI (-) (n=1,408)	ART (high) and ADI (+) (n=325)
Exposure to NRTI	99.5%	99.5%	99.7%	99.4%
Exposure to NNRTI	57.5%	63.1%	57.1%	59.1%
Exposure to PI	54.0%	57.4%	53.8%	56.9%

Abbreviations: ART, antiretroviral therapy; ADI, AIDS-defining illness; NRTI, nucleoside reverse transcriptase inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor.

Notes:

1. The majority of the patients were treated with combination of ART (e.g., NRTI combined with NNRTI or PI), and thus the sum of percentages for the types of drug exposure within the study group will be greater than 100%.
2. The utilization of integrase inhibitors and chemokine-receptor-5 receptor antagonists (<5%) is not analyzed because these drugs were not available and not regarded as first-line therapy during the study period.