SDC Table 1. Baseline clinical characteristics of HIV-infected persons, stratified by inclusion/exclusion status*

	Excluded from Study (n=8874)	Included in Study (n=10,841)
Age, years	46 (40, 52)	46 (40, 52)
Race, %		
White	39%	41%
Black	46%	49%
Other	15%	15%
Female, %	2.0%	2.3%
Comorbid Conditions, %		
Hypertension	33%	39%
Diabetes	6.0%	7.5%
Dyslipidemia	6.6%	15%
Smoking	11%	19%
Hepatitis C Virus	6.2%	16%
Measurements		
CD4+ Count, cells/mm^3	257 (42, 477)	220 (51, 410)
HIV Viral Load (1000 copies/mL)	19 (1, 110)	63 (16, 248)
Systolic blood pressure, mmHg	129 (116, 140)	127 (114, 139)
Diastolic blood pressure, mmHg	78 (70, 85)	77 (70, 84)
Body mass index, kg/m^2	25 (22, 28)	24 (22, 27)
Total cholesterol, mg/dL	167 (138, 195)	167 (140, 197)
Triglycerides, mg/dL	128 (96, 219)	138 (95, 211)
Low density lipoprotein, mg/dL	107 (81, 134)	98 (76, 124)
High density lipoprotein, mg/dL	36 (29, 46)	37 (29, 47)
Glucose, mg/dL	95 (86, 108)	94 (86, 106)
Albumin, g/dL	3.8 (3.3, 4.1)	3.9 (3.5, 4.2)
eGFR, $mL/min/1.73m^2$	91 (74, 111)	97 (82, 114)
eGFR <60$mL/min/1.73m^2$	1.2%	5.4%
Proteinuria	38%	33%

*Continuous variables reported as median (IQR). Proteinuria defined by urinalysis protein 30 mg/dL or greater.

SDC Table 2. Summary of events and person-years by exposure to tenofovir

Outcome	Events	Person-Years	Rate (per 1,000 Person-Years)
Proteinuria			
Tenofovir never users	2,646	32,421	81.6
Tenofovir ever users	754	5,711	132.0
Rapid Decline			
Tenofovir never users	2,349	43,693	53.8
Tenofovir ever users	729	7,896	92.3
Chronic Kidney Disease			
Tenofovir never users	352	46,724	7.5
Tenofovir ever users	181	9,692	18.7

SDC Table 3. Association of tenofovir exposure with risk* of alternative kidney disease outcomes

	Demographic-Adjusted Model†		Time-Dependent Cox Model‡		Marginal Structural Model§	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Doubling of Creatinine *(n=432 events)*						
Ever Tenofovir	1.40 (1.11-1.75)	**0.0039**	1.15 (0.88-1.50)	0.31	1.32 (0.99-1.76)	0.058
Cumulative Tenofovir (per year)	1.15 (0.99-1.33)	0.068	1.10 (0.92-1.32)	0.28	1.10 (0.93-1.30)	0.30
CKD and Proteinuria *(n=237 events)*						
Ever Tenofovir	2.04 (1.51-2.75)	**<0.0001**	1.69 (1.19-2.39)	**0.0032**	1.84 (1.30-2.60)	**0.0005**
Cumulative Tenofovir (per year)	1.46 (1.26-1.69)	**<0.0001**	1.35 (1.12-1.62)	**0.0014**	1.35 (1.15-1.58)	**0.0002**
eGFR-MDRD Decline of 3% or more *(n=3246 events)*						
Ever Tenofovir	1.52 (1.40-1.66)	**<0.0001**	1.37 (1.24-1.51)	**<0.0001**	1.52 (1.37-1.67)	**<0.0001**
Cumulative Tenofovir (per year)	1.19 (1.12-1.25)	**<0.0001**	1.11 (1.04-1.18)	**0.0014**	1.17 (1.10-1.24)	**<0.0001**
eGFR-MDRD Decline of 5% or more *(n=2347 events)*						
Ever Tenofovir	1.66 (1.51-1.82)	**<0.0001**	1.49 (1.33-1.66)	**<0.0001**	1.65 (1.47-1.85)	**<0.0001**
Cumulative Tenofovir (per year)	1.22 (1.14-1.29)	**<0.0001**	1.15 (1.07-1.24)	**<0.0001**	1.19 (1.12-1.27)	**<0.0001**

*Doubling of Creatinine analysis excludes patients who had CKD at baseline. CKD and Proteinuria analysis excludes patients with CKD or proteinuria at baseline.

†Demographic adjusted Cox model includes drug exposure, age, sex, race, and time.

‡Time-dependent multivariable adjusted model includes exposure to tenofovir and all other antiretroviral drugs, age, sex, race, baseline comorbid conditions (diabetes, hypertension, dyslipidemia, prevalent cardiovascular disease, smoking, drug abuse, hepatitis B and C virus infection), baseline measurements (CKD or proteinuria, BMI category), and current measurements (CD4 count, viral load, CKD or proteinuria, lipids, diabetes, and hypertension).

§Marginal structural model includes all baseline variables in multivariable model.

SDC Table 4. Association of current and past tenofovir use with risk of kidney disease outcomes.

Outcome	Current vs. Never		Past (≤6 months) vs. Never		Past (>6 months) vs. Never	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Proteinuria	1.80 (1.60-2.02)	<.0001	1.63 (1.37-1.93)	<.0001	1.42 (1.19-1.70)	0.0001
Rapid decline	1.45 (1.29-1.64)	<.0001	1.43 (1.20-1.69)	<.0001	1.15 (0.97-1.36)	0.10
CKD	1.70 (1.33-2.18)	<.0001	1.87 (1.33-2.63)	0.0003	1.81 (1.31-2.52)	0.0004

All estimates based on multivariable adjusted time-dependent Cox models described in Table 2.

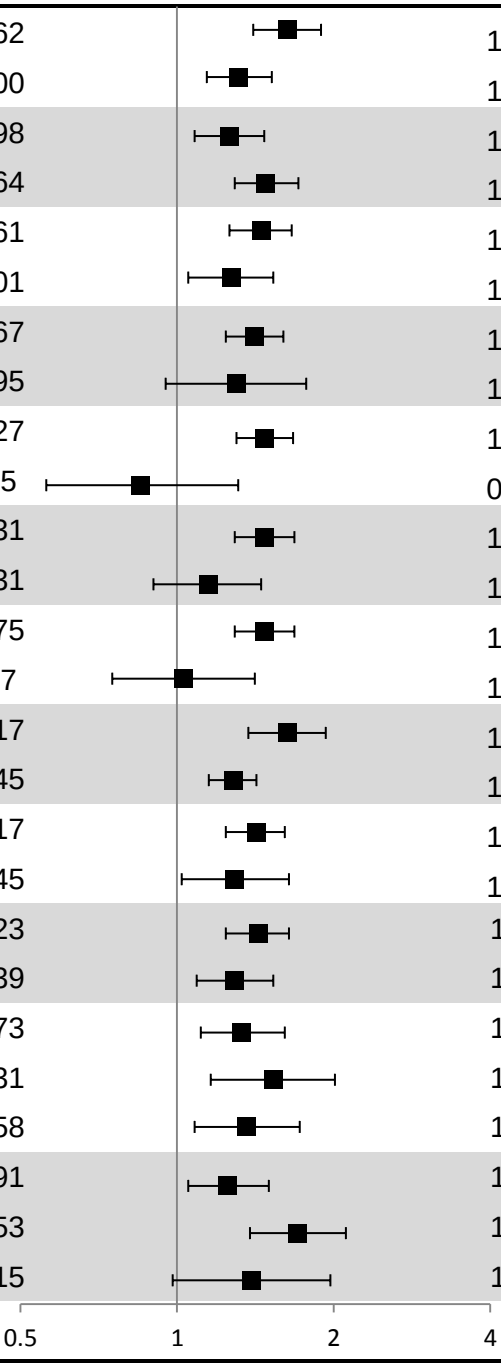
SDC Table 5. Association of era* of antiretroviral use and cumulative tenofovir with risk of kidney disease outcomes

Outcome	Tenofovir x Era Interaction	Era	Tenofovir Effect (per year of use)	P Value	Overall Tenofovir Effect (From Table 2)
Proteinuria					
Era x Tenofovir	p = 0.014	Early	2.15 (1.26, 3.68)	0.0051	1.34 (1.25-1.45)
		Mid	1.48 (1.28, 1.71)	<.0001	
		Late	1.23 (1.16, 1.31)	<.0001	
Rapid Decline					
Era x Tenofovir	p = 0.0018	Early	1.69 (0.96, 3.00)	0.071	1.11 (1.03-1.18)
		Mid	1.34 (1.18, 1.53)	<.0001	
		Late	1.04 (0.98, 1.12)	0.20	
Chronic Kidney Disease					
Era x Tenofovir	p = 0.12	Early	3.34 (1.23-9.04)	0.018	1.33 (1.18-1.51)
		Mid	1.60 (1.25-2.05)	0.0002	
		Late	1.35 (1.21-1.50)	<.0001	

*Early = <2003, mid = 2003-04, late = 2005-07. All estimates based on multivariable adjusted time-dependent Cox models described in Table 2.

SDC Figure 1. Association between cumulative tenofovir exposure and risk of CKD in subgroups defined by baseline characteristics (*excluding those with CKD at baseline*)*

Characteristic	Events (n)	Participants (n)	Hazard Ratio (95% CI)	Interaction P Value
Age <46 years	163	5262	1.63 (1.40, 1.89)	**0.043**
Age ≥46 years	370	4900	1.31 (1.14, 1.52)	
Black	245	4998	1.26 (1.08, 1.47)	0.13
Non-black	288	5164	1.48 (1.29, 1.71)	
No Proteinuria	365	8261	1.45 (1.26, 1.66)	0.27
Proteinuria	168	1901	1.27 (1.05, 1.53)	
No Smoking	464	8267	1.41 (1.24, 1.60)	0.64
Smoking	69	1895	1.30 (0.95, 1.77)	
No CVD	460	9427	1.47 (1.30, 1.67)	**0.016**
CVD	73	735	0.85 (0.56, 1.31)	
No Dyslipidemia	428	8731	1.47 (1.29, 1.68)	0.071
Dyslipidemia	105	1431	1.15 (0.90, 1.45)	
No Diabetes	449	9475	1.47 (1.29, 1.68)	**0.041**
Diabetes	84	687	1.03 (0.75, 1.41)	
No Hypertension	178	6417	1.63 (1.37, 1.93)	**0.018**
Hypertension	355	3745	1.28 (1.15, 1.42)	
No Drug Abuse	391	6417	1.42 (1.24, 1.61)	0.50
Drug Abuse	142	3745	1.29 (1.02, 1.64)	
Viral Load <100,000copies/mL	347	6823	1.43 (1.24-1.64)	0.37
Viral Load >100,000copies/mL	186	3339	1.29 (1.09-1.53)	
CD4 Count 0-199 cells/mm^3	267	4473	1.33 (1.11-1.61)	0.28
CD4 Count 200-350 cells/mm^3	115	2131	1.53 (1.16-2.01)	
CD4 Count >350 cells/mm^3	151	3558	1.36 (1.08-1.72)	
BMI <25 kg/m^2	285	5391	1.25 (1.05-1.50)	0.64
BMI 25-30 kg/m^2	174	3153	1.70 (1.38-2.11)	
BMI >30 kg/m^2	66	1215	1.39 (0.98-1.97)	



*CV risk category based on Framingham risk score (<10% = low, 10-20% = moderate, >20% = high). All estimates based on multivariable adjusted Cox models described in Table 2. P value for test of interaction between cumulative tenofovir use and characteristic reported. Abbreviations: CI (confidence interval), eGFR (estimated glomerular filtration rate), CVD (cardiovascular disease), BMI (body mass index).