

Supplementary methods

Definitions:

- body mass index (BMI; body weight [kg]/height [m]²)
- concurrent nephrotoxic drugs: ganciclovir, NSAIDs, and sulfamethoxazole/trimethoprim
- diabetes mellitus: use of glucose-lowering agents or fasting plasma glucose >126 mg/dl or plasma glucose >200 mg/dl or HbA1c >6.5%
- hypertension: current treatment with antihypertensive agents
- dyslipidemia: current treatment with lipid-lowering agents or either low density lipoprotein cholesterol >140 mg/dl, high density lipoprotein cholesterol <40 mg/dl, total cholesterol >240 mg/dl, or triglyceride >500 mg/dl
- hepatitis B infection: positive hepatitis B surface antigen
- hepatitis C infection: positive HCV antibody
- smoking: if one ever smoked or not

eGFR formula developed by the Japanese Society of Nephrology:

$$\text{eGFR} = 194 \times [\text{serum creatinine}]^{-1.094} \times [\text{age}]^{-0.287} \times [0.739 \text{ if female}] \text{ [24].}$$

Supplemental Digital Content 2. Figure S1 which describes patient enrollment. ppt

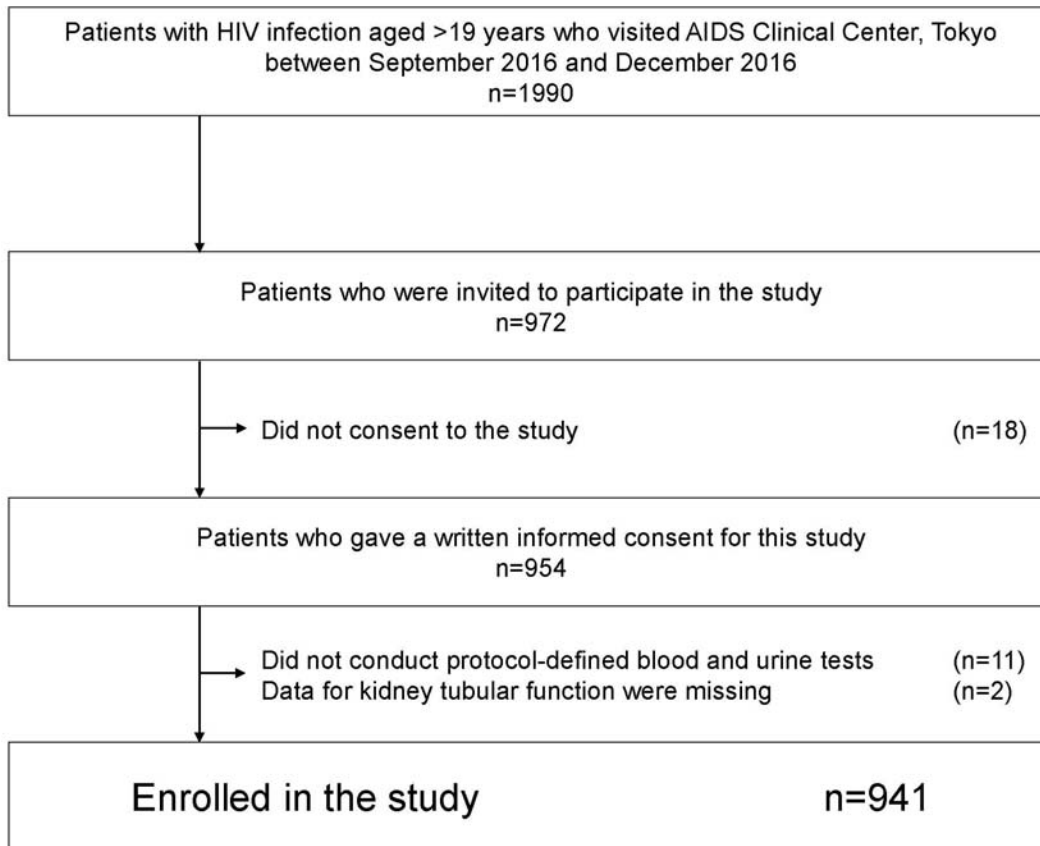


Table S1. The association between kidney tubular dysfunction and >5, >4, >3, >2 years of TDF use with current status of TDF use applying alternative definition of kidney tubular dysfunction (replacing NAG with tubular proteinuria).

	OR	95% CI	P value		OR	95% CI	P value		OR	95% CI	P value		OR	95% CI	P value
Without TDF exposure	ref	ref	ref	Without TDF exposure	ref	ref	Ref	Without TDF exposure	ref	ref	ref	Without TDF exposure	ref	ref	ref
>5y of TDF use + current TDF use	11	4.43-28	<0.001	>4y + current TDF	10	4.08-25.2	<0.001	>3y + current TDF	9.5	3.85-23.5	<0.001	>2y + current TDF	10	4.06-24.5	<0.001
>5y of TDF use + past TDF use	2.7	0.72-9.86	0.14	>4y + no current TDF	3.4	1.06-11.1	0.039	>3y + no current TDF	4.5	1.59-12.8	0.005	>2y + no current TDF	4.4	1.62-12.2	0.004
<5y of TDF use + current TDF use	6.6	2.37-18.5	<0.001	<4y + current TDF	7.1	2.47-20.6	<0.001	<3y + current TDF	8.0	2.65-24.4	<0.001	<2y + current TDF	5.5	1.42-21	0.013
<5y of TDF use + past TDF use	4.8	1.73-13.4	0.003	<4y + no current TDF	4.5	1.54-12.9	0.006	<3y + no current TDF	3.3	0.97-11.1	0.057	<2y + no current TDF	2.9	0.69-12.4	0.14

TDF: tenofovir disoproxil fumarate, NAG: N-acetyl-β-D-glucosaminidase.

5 Each multivariate model was adjusted for age, sex, CD4 count, eGFR, body weight, history of AIDS, time from diagnosis of HIV-1 infection, diabetes mellitus, nephrotoxic drug use, and hypertension.

Table S2. The association between kidney tubular dysfunction and >5, >4, >3, >2 years of TDF use with current status of TDF use applying alternative definition of kidney tubular dysfunction (replacing non-diabetic glycosuria with tubular proteinuria).

10

	OR	95% CI	P value		OR	95% CI	P value		OR	95% CI	P value		OR	95% CI	P value
Without TDF exposure	ref	ref	ref	Without TDF exposure	ref	ref	Ref	Without TDF exposure	ref	ref	ref	Without TDF exposure	ref	ref	ref
>5y of TDF use + current TDF use	3.2	1.84-5.71	<0.001	>4y + current TDF	3.0	1.74-5.22	<0.001	>3y + current TDF	2.8	1.60-4.74	<0.001	>2y + current TDF	2.9	1.68-4.87	<0.001
>5y of TDF use + past TDF use	1.8	0.82-3.98	0.14	>4y + no current TDF	1.8	0.84-3.67	0.13	>3y + no current TDF	2.2	1.12-4.14	0.022	>2y + no current TDF	2.2	1.18-4.05	0.013
<5y of TDF use + current TDF use	2.2	1.15-4.37	0.017	<4y + current TDF	2.4	1.17-4.89	0.016	<3y + current TDF	3.1	1.44-6.56	0.004	<2y + current TDF	2.7	1.08-6.72	0.033
<5y of TDF use + past TDF use	2.1	1.11-4.04	0.023	<4y + no current TDF	2.2	1.14-4.34	0.020	<3y + no current TDF	1.8	0.85-3.92	0.13	<2y + no current TDF	1.5	0.60-3.98	0.37

TDF: tenofovir disoproxil fumarate.

Each multivariate model was adjusted for age, sex, CD4 count, eGFR, body weight, history of AIDS, time from diagnosis of HIV-1 infection, diabetes mellitus, nephrotoxic drug use, and hypertension.

20