

Supplementary table 1: Participant characteristics of INSTI and non-INSTI users at the start of each drug class

	Total participants n(%)	INSTI users n(%)	PI users n(%)	NNRTI uses n(%)
Total	20865 (100)	10371 (50)	2498 (12)	3256 (16)
Sex				
Male	15529 (74)	7885 (78)	1656 (70)	2501 (77)
Female	5336 (26)	2486 (22)	842 (30)	755 (23)
Age (years)				
Median (IQR)	46 (38–53)	47 (38–54)	44 (36–52)	45 (38–53)
<40	6202 (30)	2916 (28)	904 (36)	991 (30)
≥40	14663 (70)	7455 (72)	1594 (64)	2265 (70)
HIV acquisition risk				
Heterosexual contact	7158 (34)	3358 (32)	960 (38)	1164 (36)
Men who have sex with men	9358 (45)	4881 (47)	887 (36)	1620 (50)
Injecting drug users	3108 (15)	1471 (14)	500 (20)	339 (10)
Other	507 (2)	289 (3)	61 (2)	51 (2)
Unknown or missing	734 (4)	372 (4)	90 (4)	82 (3)
Race				
White	15161 (73)	7307 (71)	1822 (73)	2490 (76)
Black	1510 (7)	701 (7)	240 (10)	206 (6)
Other	699 (3)	363 (4)	77 (3)	119 (4)
Unknown	3495 (17)	2000 (19)	359 (14)	441 (14)
Hepatitis C				

Negative	2588 (12)	1595 (15)	262 (10)	304 (9)
Positive	240 (1)	124 (1)	26 (1)	18 (1)
Unknown	18037 (86)	8652 (83)	2210 (88)	2934 (90)
Hepatitis B				
Negative	6405 (31)	3594 (35)	718 (29)	948 (29)
Positive	295 (1)	137 (1)	56 (2)	34 (1)
Unknown	14165 (68)	6640 (64)	1724 (69)	2274 (70)
CD4 cell count (cells/μL)				
Median (IQR)	568 (390–770)	576 (386–783)	510 (329–712)	587 (429–782)
\leq 200	1678 (8)	987 (10)	279 (11)	114 (4)
201-350	2608 (13)	1218 (11)	412 (16)	360 (11)
\geq 350	16579 (79)	8166 (79)	1807 (72)	2782 (85)
HIV viral load (copies/mL)				
median (IQR)	39 (19–91)	39 (19–372)	36 (19–3000)	33 (19–49)
<200	16197 (78)	7627 (74)	1681 (67)	2564 (79)
\geq 200	4668 (23)	2744 (26)	817 (33)	692 (21)
Prior AIDS				
No	19332 (93)	9854 (95)	2219 (89)	3065 (94)
Yes	1533 (7)	517 (5)	279 (11)	191 (6)
BMI (kg/m²)				
Median (IQR)	23 (21–25)	23 (21–25)	24 (21–26)	22 (12–26)
<21	5169 (25)	2668 (26)	662 (27)	716 (22)
21-23	5066 (24)	2467 (24)	595 (24)	856 (26)

23-26	6316 (30)	3161 (30)	760 (30)	996 (31)
27-30	3185 (15)	1523 (15)	364 (15)	507 (16)
>30	1129 (5)	552 (5)	117 (5)	181 (6)
ART naive				
No	17858 (86)	8485 (82)	2067 (83)	2666 (82)
Yes	3007 (14)	1886 (18)	431 (17)	590 (18)
Smoking				
Never	5758 (28)	2828 (27)	733 (29)	889 (27)
Current	1657 (8)	913 (9)	135 (5)	301 (9)
Past	2576 (12)	1359 (13)	268 (11)	437 (13)
Unknown	10874 (52)	5271 (51)	1362 (55)	1629 (50)
*Region				
Western Europe	9643 (46)	5613 (54)	922 (37)	1541 (47)
Southern Europe	2017 (10)	1004 (10)	266 (11)	344 (11)
Northern Europe and Australia	8959 (43)	3738 (36)	1310 (52)	1371 (42)
Eastern and east central Europe	246 (1)	16 (0)	0 (0)	0 (0)
**1-year DM risk per 100 PYS				
	(M=0·49, SD=1·54)	(M=0·43, SD 1·23)	(M=0·48, SD 1·25)	(M=0·47, SD 1·22)
median (IQR)		0·14 (0·09–0·22)	0·11 (0·07–0·22)	0·12 (0·07–0·22)

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

*Region - country inclusions

Western Europe (Austria, Belgium, France, Germany, Luxembourg, and Switzerland)

Southern Europe (Argentina, Greece, Israel, Italy, Portugal, and Spain)

Northern Europe and Australia (Denmark, Finland, Iceland, Ireland, the Netherlands, Norway, Sweden, the UK, and Australia)

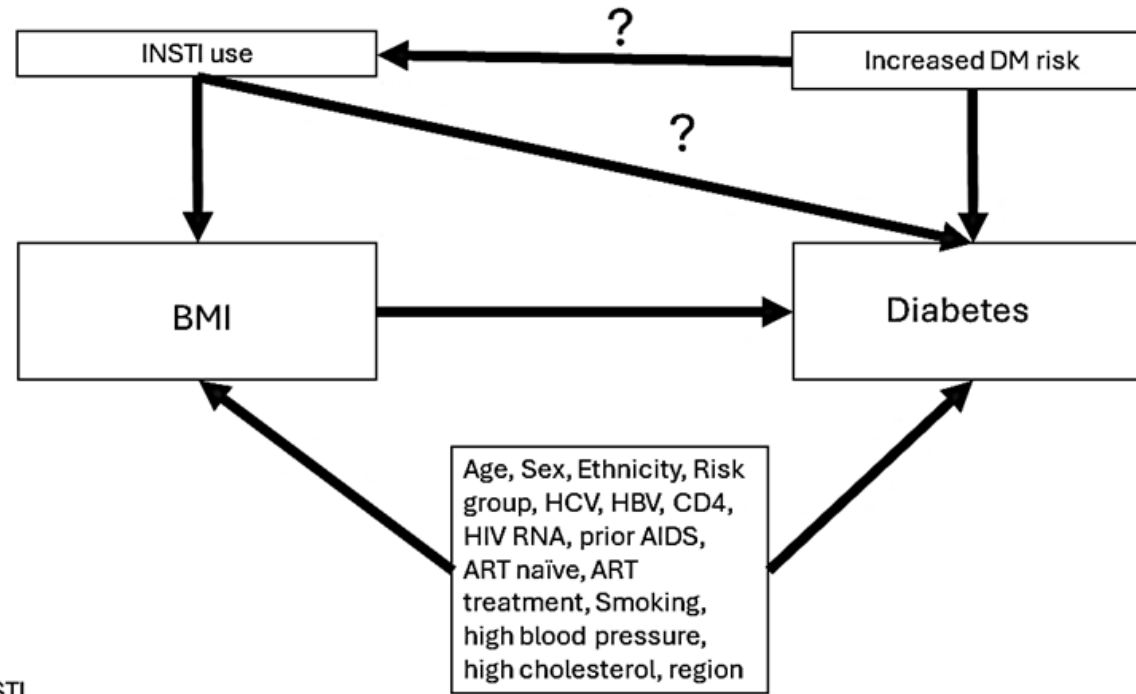
Eastern and east central Europe (Belarus, Estonia, Georgia, Latvia, Lithuania, Russia, and Ukraine)

**DM risk equation referenced from:

Petoumenos K, Worm SW, Fontas E, et al. Predicting the short-term risk of diabetes in HIV-positive patients: the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. *J Int AIDS Soc.* Oct 10 2012;15(2):17426. doi:10.7448/IAS.15.2.1742617426

Note: This table describes the participant characteristics of INSTI and non-INSTI users at the start of each drug class. Remaining participants that were not on an INSTI, PI, or NNRTI were those on NRTIs only. Further investigation of their ARVs identified unknown ARVs in their regimen. As such, they excluded from the INSTI, PI or NNRTI users in supplementary table 1.

Supplementary Figure 1: Directed acyclic graph



Exposure: INSTI
Outcome: Diabetes

Supplementary Table 2. Factors associated with DM – using 2 fasting blood glucose measurements >7.0 mmol/L to define DM

	Total patients	Follow up (years)	No. of Diabetes events	Crude rate/ 100PYS	Univariate			Multivariate		
					IRR	95% CI	P-value	IRR	95% CI	P-value
Total	21964 (100)	114707.08	103	0.09						
Sex										
Male	16371 (74)	84694.38	91	0.11	1			1		
Female	5593 (26)	30012.7	12	0.04	0.37	(0.20, 0.68)	0.001	0.46	(0.24, 0.91)	0.026
**Age (lnAge)										
Per unit increase	~	~	~	~	16.37	(4.74, 56.46)	<0.001	10.83	(3.71, 31.65)	<0.001
Risk group							0.03			0.013
Heterosexual contact	7635 (34)	41304.67	25	0.06	1			1		
Men who have sex with men	9751 (45)	50680.18	47	0.09	1.53	(0.94, 2.49)	0.085	1.26	(0.73, 2.19)	0.402
Injecting drug users	3245 (15)	16056.21	23	0.14	2.37	(1.34, 4.17)	0.003	2.56	(1.37, 4.79)	0.003
Other	543 (2)	2857.5	2	0.07	1.16	(0.27, 4.88)	0.843	1.31	(0.30, 5.82)	0.718
Unknown or missing	790 (4)	3808.53	6	0.16	2.6	(1.07, 6.34)	0.035	1.74	(0.67, 4.53)	0.26

Ethnicity							<0.001
White	15884 (73)	83935.57	89	0.11	1		
Black	1661 (7)	9131.17	8	0.09	0.83	(0.40, 1.70)	0.605
Other	732 (3)	3767.15	1	0.03	0.25	(0.03, 1.80)	0.168
Unknown	3686 (17)	17873.19	5	0.03	0.26	(0.11, 0.65)	0.004
Hepatitis C							
Negative	3304 (15)	15032.11	3	0.02	1		
Positive	373 (2)	1680.5	2	0.12	5.96	(1.00, 35.69)	0.05
Not tested	18287 (83)	97994.48	98	0.1			
Hepatitis B							
Negative	6914 (32)	34267.92	25	0.07	1		
Positive	324 (2)	1645.38	2	0.12	1.67	(0.39, 7.03)	0.487
Not tested	14726 (67)	78793.78	76	0.1			
*CD4 count (cells/μL)							0.472
≤ 200	~	3818.12	3	0.08	0.91	(0.29, 2.87)	0.867
201-350	~	10498.68	13	0.12	1.43	(0.80, 2.56)	0.23
≥ 350	~	100390.28	87	0.09	1		

*HIV viral load (copies/mL)										
<200	~	108310.17	96	0.09	1					
≥200	~	6396.91	7	0.11	1.23	(0.57, 2.66)	0.59			
prior AIDS										
No	20347 (85)	105818.6	68	0.06	1			1		
Yes	1617 (15)	8888.48	35	0.39	6.13	(4.08, 9.21)	<0.001	5.29	(3.29, 8.49)	<0.001
**BMI (lnBMI)										
	~	~	~	~	20.57	(5.79, 73.06)	<0.001	35.96	(10.25, 126.17)	<0.001
ART naive										
No	18693	99424.64	98	0.1	1					
Yes	3271	15282.44	5	0.03	0.33	(0.14, 0.82)	0.016			
*ART treatment										
TDF	~	49771.49	33	0.07	1			1		
TAF	~	20481.84	12	0.06	0.88	(0.46, 1.71)	0.714	0.83	(0.42, 1.63)	0.585
no TDF/no TAF	~	44453.75	58	0.13	1.97	(1.28, 3.02)	0.002	1.74	(1.11, 2.73)	0.016

*INSTI use							
No	~	72350.93	66	0.09	1		
Yes	~	42356.15	37	0.09	0.96	(0.64, 1.43)	0.833
*Smoking							
Never	~	17819.31	0	0			
Current	~	38033.64	35	0.09			
Past	~	12242.66	0	0			
Unknown	~	46611.46	68	0.15			
**High blood pressure							
No	~	67630.15	54	0.08	1		
Yes	~	32065.05	31	0.1	1.21	(0.78, 1.88)	0.396
Unknown	~	15011.89	18	0.12			
*Cholesterol							
<200	~	65307.88	60	0.09	1		
≥200	~	37124.16	28	0.08	0.82	(0.52, 1.29)	0.389
Not tested	~	12275.05	15	0.12			

***Region						
Western Europe	10207 (46)	54352.91	0	0		
Southern Europe and Argentina	2098 (10)	9278.25	0	0		
Northern Europe and Australia	9408 (43)	50717.66	103	0.2		
Eastern and east central Europe	251 (1)	358.26	0	0		

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

*Time-updated variables. Total participant number varies due to multiple measures; therefore, this is not provided.

**Uses natural log. Total participant number varies due to multiple measures; therefore, this is not provided.

***Region - Region: Western Europe (Austria, Belgium, France, Germany, Luxembourg, and Switzerland); Southern Europe (Argentina, Greece, Israel, Italy, Portugal, and Spain); Northern Europe and Australia (Denmark, Finland, Iceland, Ireland, the Netherlands, Norway, Sweden, the UK, and Australia); Eastern and east central Europe (Belarus, Estonia, Georgia, Latvia, Lithuania, Russia, and Ukraine)

^a High blood pressure defined as systolic BP measurements ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or use of anti-hypertensives.

Not tested values were included in the analysis as a separate category but were excluded from test for heterogeneity.

Supplementary Table 3. Factors associated with Diabetes using Poisson regression - using 2 fasting blood glucose >7.0 , HbA1C >6.5, use of diabetic medication or clinical reporting of DM as definition of DM

	Total patients	Follow up (years)	No. of Diabetes events	Crude rate/ 100PYS	Univariate			Multivariate		
					IRR	95% CI	P-value	IRR	95% CI	P-value
Total	20995 (100)	108510.44	667	0.61						
Sex										
Male	15614 (74)	79879.35	522	0.65	1			1		
Female	5381 (26)	28631.1	145	0.51	0.77	(0.64, 0.93)	0.007	0.65	(0.52, 0.80)	<0.001
**Age (lnAge)										
Per unit increase	~	~	~	~	11.28	(7.92, 16.05)	<0.001	9.67	(6.54, 14.29)	<0.001
Risk group							0.006			0.013
Heterosexual contact	7202 (34)	38533.58	275	0.71	1			1		
Men who have sex with men	9396 (45)	48356.28	255	0.53	0.74	(0.62, 0.88)	0.001	0.82	(0.67, 1.01)	0.06
Injecting drug users	3139 (15)	15394.04	91	0.59	0.83	(0.65, 1.05)	0.119	1.25	(0.96, 1.62)	0.096
Other	514 (2)	2687.93	17	0.63	0.89	(0.54, 1.45)	0.629	1.14	(0.69, 1.87)	0.617
Unknown or missing	744 (4)	3538.62	29	0.82	1.15	(0.78, 1.68)	0.479	1.13	(0.76, 1.67)	0.543

Ethnicity							<0.001			<0.001
White	15227 (73)	79730.8	449	0.56	1			1		
Black	1531 (7)	8262.94	90	1.09	1.93	(1.54, 2.43)	<0.001	2.03	(1.57, 2.63)	<0.001
Other	702 (3)	3568.08	25	0.7	1.24	(0.83, 1.86)	0.288	2.13	(1.40, 3.24)	<0.001
Unknown	3535 (17)	16948.63	103	0.61	1.08	(0.87, 1.34)	0.486	1.14	(0.91, 1.42)	0.25
Hepatitis C										
Negative	3220 (15)	14559.48	68	0.47	1					
Positive	365 (2)	1642.11	5	0.3	0.65	(0.26, 1.62)	0.356			
Not tested	17410 (83)	92308.85	594	0.64						
Hepatitis B										
Negative	6666 (32)	207	0.63	0.55	1					
Positive	312 (2)	15	0.96	0.58	1.52	(0.90, 2.57)	0.115			
Not tested	14017 (67)	445	0.6	0.55						
*CD4 count (cells/μL)										0.150
\leq 200	~	3612.4	31	0.86	1.42	(0.99, 2.04)	0.055			
201-350	~	9970.32	64	0.64	1.07	(0.82, 1.38)	0.631			
\geq 350	~	94927.73	572	0.6	1					

*HIV viral load (copies/mL)										
<200	~	102282.1	639	0.62	1					
≥200	~	6228.35	28	0.45	0.72	(0.49, 1.05)	0.088			
prior AIDS										
No	19466 (93)	100107.07	617	0.62	1					
Yes	1529 (7)	8403.38	50	0.59	0.97	(0.72, 1.29)	0.811			
**BMI (lnBMI)	~	~	~	~	31.37	(19.70, 49.94)	<0.001	25.89	(15.95, 42.01)	<0.001
ART naive										
No	17800 (85)	93678.12	613	0.65	1					
Yes	3195 (15)	14832.33	54	0.36	0.56	(0.42, 0.73)	<0.001			
*ART treatment							0.001			0.238
TDF	~	47698.08	246	0.52	1			1		
TAF	~	19126.72	135	0.71	1.37	(1.11, 1.69)	0.003	1.02	(0.81, 1.28)	0.861
no TDF/no TAF	~	41685.65	286	0.69	1.33	(1.12, 1.58)	0.001	1.15	(0.96, 1.38)	0.118

*INSTI use										
No	~	69028.16	345	0.5	1			1		
Yes	~	39482.28	322	0.82	1.63	(1.40, 1.90)	<0.001	1.48	(1.25, 1.74)	<0.001
							0.194			
*Smoking										
Never	~	16617.27	102	0.61	1					
Current	~	36513.6	203	0.56	0.91	(0.71, 1.15)	0.415			
Past	~	11243.58	82	0.73	1.19	(0.89, 1.59)	0.245			
Unknown	~	44135.99	280	0.63	1.03	(0.82, 1.30)	0.776			
*^aHigh blood pressure										
No	~	64649.71	300	0.46	1			1		
Yes	~	29461.77	273	0.93	2.00	(1.69, 2.35)	<0.001	1.31	(1.11, 1.55)	0.002
Unknown	~	14398.97	94	0.65						
*Cholesterol										
<200	~	61181.5	365	0.6	1					
≥200	~	35489.35	233	0.66	1.10	(0.93, 1.30)	0.254			
Not tested	~	11839.6	69	0.58						

***Region							0.002			0.012
Western Europe	9739 (46)	51043.58	368	0.72	1			1		
Southern Europe and Argentina	2033 (10)	8905.96	35	0.39	0.55	(0.39, 0.77)	0.001	0.62	(0.43, 0.88)	0.008
Northern Europe and Australia	8977 (43)	48210.16	264	0.55	0.76	(0.65, 0.89)	0.001	0.81	(0.68, 0.95)	0.012
Eastern and east central Europe	246 (1)	350.75	0	0						

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

*Time-updated variables. Total participant number varies due to multiple measures; therefore, this is not provided.

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^a High blood pressure defined as systolic BP measurements ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or use of anti-hypertensives.

Not tested values were included in the analysis as a separate category but were excluded from test for heterogeneity.

Supplementary table 4. Factors associated with DM - using 2 random blood glucose >11.1 , HbA1C >6.5, use of diabetic medication or clinical reporting of DM as the definition of DM

	Total patients	Follow up (years)	No. of Diabetes events	Crude rate/ 100PYS	Univariate			Multivariate		
					IRR	95% CI	P-value	IRR	95% CI	p-value
Total	21044 (100)	108770.96	671	0.62						
Sex										
Male	15655 (74)	80101.18	525	0.66	1			1		
Female	5389 (26)	28669.77	146	0.51	0.78	(0.65, 0.93)	0.007	0.64	(0.52, 0.80)	<0.001
**Age (lnAge)										
Per unit increase	~	~	~	~	11.37	(7.99, 16.17)	<0.001	9.72	(6.57, 14.37)	<0.001
Risk group							0.002			0.013
Heterosexual contact	7216 (34)	38610.66	282	0.73	1			1		
Men who have sex with men	9419 (45)	48490.23	254	0.52	0.72	(0.61, 0.85)	<0.001	0.79	(0.65, 0.97)	0.025
injecting drug users	3151 (15)	15445.34	89	0.58	0.79	(0.62, 1.00)	0.051	1.19	(0.92, 1.54)	0.191
Other	514 (2)	2688.51	18	0.67	0.92	(0.57, 1.48)	0.721	1.17	(0.72, 1.91)	0.519
Unknown or missing	744 (4)	3536.22	28	0.79	1.08	(0.74, 1.60)	0.684	1.06	(0.71, 1.58)	0.783
Ethnicity							<0.001			<0.001

White	15274 (73)	79986.56	451	0.56	1			1		
Black	1531 (7)	8268.8	91	1.1	1.95	(1.56, 2.44)	<0.001	2.00	(1.55, 2.60)	<0.001
Other	703 (3)	3574.83	24	0.67	1.19	(0.79, 1.80)	0.405	2.03	(1.33, 3.11)	0.001
Unknown	3536 (17)	16940.77	105	0.62	1.1	(0.89, 1.36)	0.382	1.16	(0.93, 1.44)	0.185
Hepatitis C										
Negative	3221 (15)	14563.94	68	0.47	1					
Positive	365 (2)	1637.72	5	0.31	0.65	(0.26, 1.62)	0.359			
Not tested	17458 (83)	92569.29	598	0.65						
Hepatitis B										
Negative	6666 (32)	32684.06	207	0.63	1					
Positive	314 (2)	1568.82	13	0.83	1.31	(0.75, 2.29)	0.347			
Not tested	14064 (67)	74518.08	451	0.61						
*CD4 count (cells/μL)										
≤ 200	~	3614.82	32	0.89	1.47	(1.03, 2.09)	0.035			
201-350	~	9984.28	64	0.64	1.06	(0.82, 1.37)	0.653			
≥ 350	~	95171.85	575	0.6	1					

No	~	69256.28	345	0.50	1			1		
Yes	~	39514.68	326	0.83	1.66	(1.42, 1.93)	<0.001	1.53	(1.30, 1.80)	<0.001
*Smoking							0.15			
Never	~	16624.05	108	0.65	1					
Current	~	36629.69	203	0.55	0.85	(0.68, 1.08)	0.182			
Past	~	11242.58	85	0.76	1.16	(0.88, 1.55)	0.296			
Unknown	~	44274.63	275	0.62	0.96	(0.77, 1.19)	0.693			
*^aHigh blood pressure										
No	~	64747.84	291	0.45	1			1		
Yes	~	29566.95	282	0.95	2.12	(1.80, 2.50)	<0.001	1.39	(1.18, 1.65)	<0.001
Unknown	~	14456.16	98	0.68						
*Cholesterol										
<200	~	61308.08	368	0.6	1					
≥200	~	35589.17	233	0.65	1.09	(0.93, 1.29)	0.300			
Not tested	~	11873.7	70	0.59						
Region							0.0001			0.006

Western Europe	9729 (46)	50983.55	373	0.73	1			1		
Southern Europe	2031 (10)	8899.24	36	0.4	0.55	(0.39, 0.78)	0.001	0.63	(0.44, 0.90)	0.011
Northern Europe and Australia	9038 (43)	48537.42	262	0.54	0.74	(0.63, 0.86)	<0.001	0.78	(0.66, 0.92)	0.004
Eastern and east central Europe	246 (1)	350.75	0	0						

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

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^a High blood pressure defined as systolic BP measurements ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or use of anti-hypertensives.

Not tested values were included in the analysis as a separate category but were excluded from test for heterogeneity.

Supplementary Table 5. Factors associated with DM- including all variables that are significant in univariate analysis

	Total patients	Follow up (years)	No. of Diabetes events	Crude rate/ 100PYS	Univariate			Multivariate		
					IRR	95% CI	p-value	IRR	95% CI	p-value
Total	20865 (100)	107640.53	785	0.73						
Sex										
Male	15529 (74)	79276.67	617	0.78	1			1		
Female	5336 (26)	28363.86	168	0.59	0.76	(0.64, 0.90)	0.002	0.69	(0.57, 0.85)	<0.001
**Age (lnAge)										
Per unit increase	~	~	~	~	8.42	(6.12, 11.61)	<0.001	7.77	(5.51, 10.95)	<0.001
Risk group							0.028			0.004
Heterosexual contact	7158 (34)	38219.52	307	0.8	1			1		
Men who have sex with men	9358 (45)	48080.8	306	0.64	0.79	(0.68, 0.93)	0.004	0.87	(0.72, 1.05)	0.142
injecting drug users	3108 (15)	15204.66	118	0.78	0.97	(0.78, 1.19)	0.751	1.31	(1.04, 1.65)	0.023
Other	507 (2)	2645.09	23	0.87	1.08	(0.71, 1.65)	0.714	1.33	(0.87, 2.04)	0.191
Unknown or missing	734 (4)	3490.46	31	0.89	1.11	(0.76, 1.60)	0.594	1.05	(0.72, 1.53)	0.795
Ethnicity							<0.001			<0.001
White	15161 (73)	79196.05	546	0.69	1			1		

Black	1510 (7)	8153.4	93	1.14	1.65	(1.33, 2.06)	<0.001	1.75	(1.36, 2.24)	<0.001
Other	699 (3)	3551.78	27	0.76	1.1	(0.75, 1.62)	0.62	1.75	(1.18, 2.60)	0.005
Unknown	3495 (17)	16739.29	119	0.71	1.03	(0.85, 1.26)	0.762	1.09	(0.89, 1.33)	0.406
Hepatitis C										
Negative	3206 (15)	14476.27	87	0.6	1					
Positive	364 (2)	1632.19	6	0.37	0.61	(0.27, 1.40)	0.244			
Not tested	17295 (83)	91532.07	692	0.76						
Hepatitis B										
Negative	6618 (32)	32368.38	249	0.77	1			1		
Positive	313 (2)	1547.98	18	1.16	1.51	(0.94, 2.44)	0.091	1.49	(0.92, 2.41)	0.107
Not tested	13934 (67)	73724.18	518	0.7						
*CD4 count (cells/μL)							<0.001			<0.001
\leq 200	~	3541.44	52	1.47	2.08	(1.57, 2.76)	<0.001	2.17	(1.63, 2.88)	<0.001
201-350	~	9868.63	69	0.7	0.99	(0.77, 1.27)	0.951	0.95	(0.74, 1.22)	0.676
\geq 350	~	94230.46	664	0.7	1			1		
*HIV viral load (copies/mL)										

<200	~	101484.98	738	0.73	1					
≥200	~	6155.55	47	0.76	1.05	(0.78, 1.41)	0.746			
prior AIDS										
No	19332 (93)	99263.38	725	0.73	1					
Yes	1533 (7)	8377.14	60	0.72	0.98	(0.75, 1.28)	0.884			
**BMI (lnBMI)										
	~	~	~	~	20.04	(13.98, 28.73)	<0.001	17.28	(11.80, 25.29)	<0.001
ART naive										
No	17681 (85)	41204.04	279	0.68	1					
Yes	3184 (15)	66436.48	506	0.76	1.12	(0.97, 1.30)	0.115			
*ART treatment										
TDF	~	47399.17	298	0.63	1			1		
TAF	~	18901.94	151	0.8	1.27	(1.04, 1.55)	0.016	0.99	(0.80, 1.21)	0.895
no TDF/no TAF	~	41339.42	336	0.81	1.29	(1.11, 1.51)	0.001	1.14	(0.97, 1.35)	0.109
*INSTI use										
No	~	68656.31	414	0.6	1			1		

Yes	~	38984.22	371	0.95	1.58	(1.37, 1.82)	<0.001	1.42	(1.22, 1.65)	<0.001
*Smoking										0.387
Never	~	16497	117	0.71	1					
Current	~	36197.27	258	0.71	1.00	(0.81, 1.25)	0.964			
Past	~	11126.93	96	0.86	1.22	(0.93, 1.59)	0.155			
Unknown	~	43819.32	314	0.72	1.01	(0.82, 1.25)	0.924			
*^aHigh blood pressure										
No	~	64147.41	335	0.52	1			1		
Yes	~	29158.71	311	1.07	2.04	(1.75, 2.38)	<0.001	1.39	(1.19, 1.63)	<0.001
Unknown	~	14334.41	139	0.97						
*Cholesterol										
<200	~	60562.55	429	0.71	1					
≥200	~	35282.05	248	0.7	0.99	(0.85, 1.16)	0.923			
Not tested	~	11795.94	108	0.92						
***Region							0.008			0.063
Western Europe	9643 (46)	50469.47	412	0.82	1			1		

Southern Europe and Argentina	2017 (10)	8817.81	46	0.52	0.64	(0.47, 0.87)	0.004	0.68	(0.49, 0.92)	0.014
Northern Europe and Australia	8959 (43)	48002.5	327	0.68	0.83	(0.72, 0.96)	0.015	0.88	(0.75, 1.02)	0.099
Eastern and east central Europe	246 (1)	350.75	0	0						

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

*Time-updated variables. Total participant number varies due to multiple measures; therefore, this is not provided.

**Uses natural log. Total participant number varies due to multiple measures; therefore, this is not provided.

***Region - Region: Western Europe (Austria, Belgium, France, Germany, Luxembourg, and Switzerland); Southern Europe (Argentina, Greece, Israel, Italy, Portugal, and Spain); Northern Europe and Australia (Denmark, Finland, Iceland, Ireland, the Netherlands, Norway, Sweden, the UK, and Australia); Eastern and east central Europe (Belarus, Estonia, Georgia, Latvia, Lithuania, Russia, and Ukraine)

^aHigh blood pressure defined as systolic BP measurements ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or use of anti-hypertensives.

Not tested values were included in the analysis as a separate category but were excluded from test for heterogeneity.

Supplementary table 6: Factors associated with Diabetes using Poisson regression - using natural log of BMI, Age, CD4, blood pressure, and cholesterol

	Total patients	Follow up (years)	No. of Diabetes events	Crude rate/ 100PYS	Univariate			Multivariate		
					IRR	95% CI	P-value	IRR	95% CI	P-value
Total	20865 (100)	107640.53	785	0.73						
Sex										
Male	15529 (74)	79276.67	617	0.78	1			1		
Female	5336 (26)	28363.86	168	0.59	0.76	(0.64, 0.90)	0.002	0.67	(0.53, 0.85)	0.001
**Age (lnAge)										
Per unit increase	~	~	~	~	8.42	(6.12, 11.61)	<0.001	6.95	(4.65, 10.38)	<0.001
Risk group							0.028			0.023
Heterosexual contact	7158 (34)	38219.52	307	0.8	1			1		
Men who have sex with men	9358 (45)	48080.8	306	0.64	0.79	(0.68, 0.93)	0.004	0.92	(0.74, 1.14)	0.441
Injecting drug users	3108 (15)	15204.66	118	0.78	0.97	(0.78, 1.19)	0.751	1.37	(1.04, 1.80)	0.024
Other	507 (2)	2645.09	23	0.87	1.08	(0.71, 1.65)	0.714	1.37	(0.84, 2.23)	0.207
Unknown or missing	734 (4)	3490.46	31	0.89	1.11	(0.76, 1.60)	0.594	0.9	(0.56, 1.45)	0.672
Ethnicity							<0.001			<0.001
White	15161 (73)	79196.05	546	0.69	1			1		
Black	1510 (7)	8153.4	93	1.14	1.65	(1.33, 2.06)	<0.001	1.91	(1.44, 2.54)	<0.001
Other	699 (3)	3551.78	27	0.76	1.1	(0.75, 1.62)	0.62	2.29	(1.48, 3.53)	<0.001
Unknown	3495 (17)	16739.29	119	0.71	1.03	(0.85, 1.26)	0.762	1.23	(0.97, 1.55)	0.089

Hepatitis C							
Negative	3206 (15)	14476.27	87	0.6	1		
Positive	364 (2)	1632.19	6	0.37	0.61	(0.27, 1.40)	0.244
Not tested	17295 (83)	91532.07	692	0.76			
Hepatitis B							
Negative	6618 (32)	32368.38	249	0.77	1		
Positive	313 (2)	1547.98	18	1.16	1.51	(0.94, 2.44)	0.091
Not tested	13934 (67)	73724.18	518	0.7			
*CD4 cell counts (lnCD4)							
Per unit increase	~	~	~	~	0.84	(0.75, 0.95)	0.007
*HIV viral load (copies/mL)							
<200	~	101484.98	738	0.73	1		
≥200	~	6155.55	47	0.76	1.05	(0.78, 1.41)	0.746
prior AIDS							
No	19332 (93)	99263.38	725	0.73	1		
Yes	1533 (7)	8377.14	60	0.72	0.98	(0.75, 1.28)	0.884
**BMI (lnBMI)							
	~	~	~	~	20.04	(13.98, 28.73)	<0.001
ART naive							
No	17681 (85)	92879.16	713	0.77	1		
Yes	3184 (15)	14761.37	72	0.49	0.64	(0.50, 0.81)	<0.001
							25.34 (15.23, 42.17) <0.001

*ART treatment							0.003			<i>0.157</i>
TDF	~	47399.17	298	0.63	1			<i>1</i>		
TAF	~	18901.94	151	0.8	1.27	(1.04, 1.55)	0.016	<i>1.05</i>	<i>(0.83, 1.32)</i>	<i>0.700</i>
no TDF/no TAF	~	41339.42	336	0.81	1.29	(1.11, 1.51)	0.001	<i>1.20</i>	<i>(0.99, 1.45)</i>	<i>0.067</i>
*INSTI use										
No	~	68656.31	414	0.6	1			<i>1</i>		
Yes	~	38984.22	371	0.95	1.58	(1.37, 1.82)	<0.001	<i>1.32</i>	<i>(1.12, 1.55)</i>	0.001
*Smoking							0.387			
Never	~	16497	117	0.71	1					
Current	~	36197.27	258	0.71	1.00	(0.81, 1.25)	0.964			
Past	~	11126.93	96	0.86	1.22	(0.93, 1.59)	0.155			
Unknown	~	43819.32	314	0.72	1.01	(0.82, 1.25)	0.924			
**Blood Pressure (lnBP)										
Per unit increase	~	~	~	~	18.87	(10.60,33.58)	<0.001	<i>4.11</i>	<i>(2.18, 7.77)</i>	<0.001
**Total Cholesterol (lnCholesterol)										
Per unit increase	~	~	~	~	0.62	(0.45, 0.86)	0.005	<i>0.52</i>	<i>(0.37, 0.75)</i>	<0.001
***Region							0.008			
Western Europe	9643 (46)	50469.47	412	0.82	1					
Southern Europe	2017 (10)	8817.81	46	0.52	0.64	(0.47, 0.87)	0.004			
Northern Europe and Australia	8959 (43)	48002.5	327	0.68	0.83	(0.72, 0.96)	0.015			
Eastern and east central Europe	246 (1)	350.75	0	0						

N, number; IRR, incident rate ratio; HIV, human immunodeficiency virus ; AIDS, Acquired immunodeficiency syndrome; BMI, Body mass index ; ART, Antiretroviral therapy; TDF, Tenofovir disoproxil fumarate; TAF, Tenofovir alafenamide; INSTI, integrase strand transfer inhibitor

*Time-updated variables. Total participant number varies due to multiple measures; therefore, this is not provided.

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Not tested values were included in the analysis as a separate category but were excluded from test for heterogeneity.