

Trends in Cancer Incidence in Different ART-Eras amongst People with HIV Supplementary Material

Table S1. Cancers reported during follow-up, split into AIDS-defining and non-AIDS-defining cancers.

AIDS-defining cancers (n=950)		Non-AIDS-defining cancers (n=2814)	
Cancer	Frequency	Cancer	Frequency
Non-Hodgkin's Lymphoma	447	Lung cancer	390
Kaposi's Sarcoma	423	Anal cancer	284
Cervical cancer	80	Prostate cancer	248
		Unknown non-AIDS defining cancer	244
		Liver cancer (HCC)	192
		Hodgkin's Lymphoma	168
		Unspecified head and neck cancer	135
		Malignant melanoma	135
		Breast cancer	133
		Bladder cancer	99
		Colon cancer	98
		Pancreatic cancer	97
		Other cancers*	89
		Kidney cancer	57
		Rectum cancer	53
		Oesophageal cancer	52
		Gynaecological cancer	51
		Stomach cancer	42
		Testicular seminoma	31
		Penile cancer	29
		Gall bladder cancer	28
		Acute myeloid leukaemia	21
		Oral cavity cancer	17
		Brain cancer	14
		Laryngeal cancer	14
		Unspecified oropharyngeal cancer	13
		Multiple myeloma	12
		Unspecified leukaemia	10
		Thyroid cancer	9
		Lip cancer	8
		Connective tissue cancer	8
		Acute lymphoid leukaemia	6
		Chronic myeloid leukaemia	6
		Hypopharyngeal cancer	4

	Sino/nasal cavity cancer	4
	Chronic lymphoid leukaemia	3
	Saliva gland cancer	3
	Bone cancer	3
	Uterine cancer	1
	Rhinopharyngeal cancer	1

*other rare cancer, no further details.

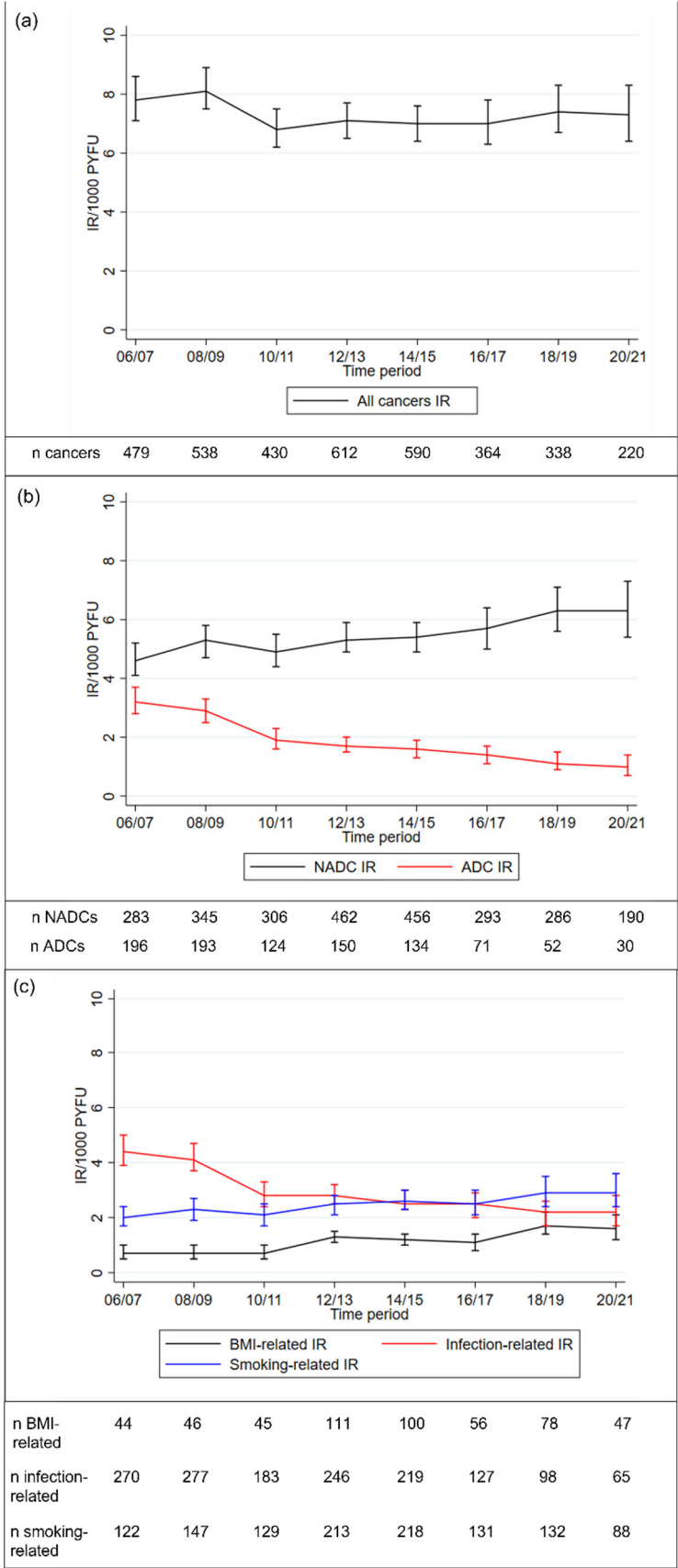
Table S2. Cancers reported during follow-up, split by infection-related, smoking-related, and BMI-related cancers.

Infection-related cancers (n=1677)		Smoking-related cancers ¹ (n=1372)		BMI-related cancers ² (n=719)	
Cancer	Frequency	Cancer	Frequency	Cancer	Frequency
Non-Hodgkin's Lymphoma	447	Lung cancer	390	Liver cancer (HCC)	192
Kaposi's Sarcoma	423	Liver cancer (HCC)	192	Breast cancer	117
Anal cancer	284	Unspecified head and neck cancer	135	Colon cancer	98
Liver cancer (HCC)	192	Bladder cancer	99	Pancreatic cancer	97
Hodgkin's Lymphoma	168	Colon cancer	98	Kidney cancer	57
Cervical cancer	80	Pancreatic cancer	97	Rectum cancer	53
Stomach cancer	42	Cervical cancer	80	Oesophageal cancer	52
Penile cancer	29	Kidney cancer	57	Gall bladder cancer	28
Unspecified oropharyngeal cancer	13	Rectum cancer	53	Thyroid cancer	9
		Oesophageal cancer	52		
		Stomach cancer	42		
		Acute myeloid leukaemia	21		
		Oral cavity cancer	17		
		Laryngeal cancer	14		
		Unspecified oropharyngeal cancer	13		
		Hypopharyngeal cancer	4		
		Sino/nasal cavity cancer	4		
		Saliva gland cancer	3		
		Rhinopharyngeal cancer	1		

¹Smoking-related cancers were included, irrespective of an individual's smoking status at the time of diagnosis.

²BMI-related cancers were included, irrespective of an individual's BMI at the time of diagnosis.

Figure S1. Age-standardised incidence rates and 95% confidence intervals over time, with liver cancer removed, for (a) all cancers; (b) ADCs and NADCs; (c) infection-related, smoking-related, and BMI-related cancers.



Abbreviations: ADC—AIDS-defining cancer; NADC—non-AIDS-defining cancer; IR—incidence rate.

Figure S2. Median CD4 count at time of cancer diagnosis for: a) all cancer; b) non-AIDS defining cancers; c) AIDS defining cancers.

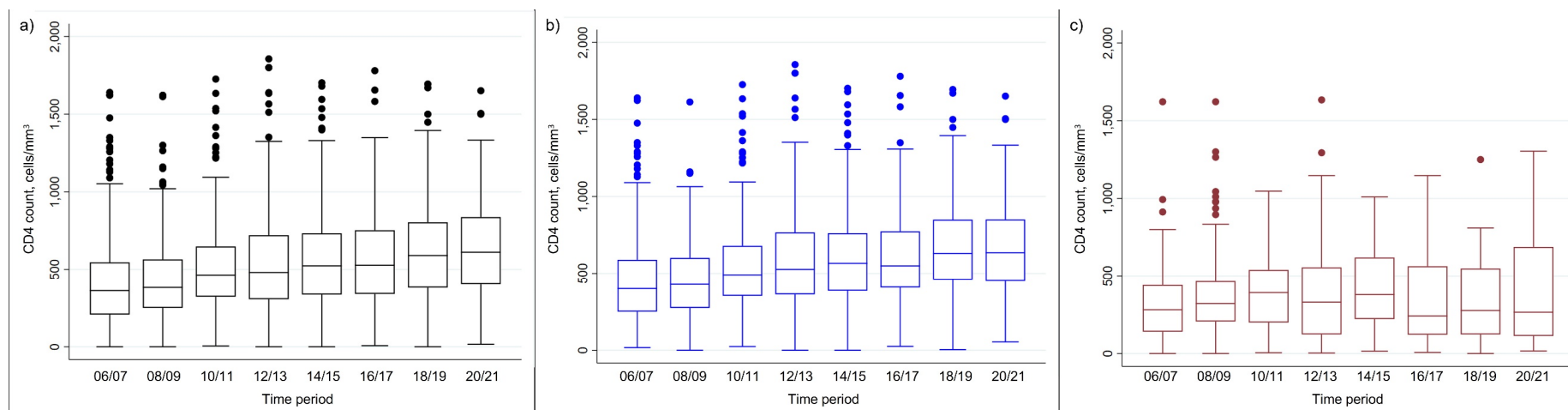


Table S3. Results from a range of sensitivity analyses for all cancer, AIDS-defining cancer, non-AIDS-defining cancer.

			All cancer			AIDS-defining cancer			Non-AIDS-defining cancer		
Regression model	n participants (PYFU) included	Time period	IRR	(95% CI)	P	IRR	(95% CI)	P	IRR	(95% CI)	P
Adjusted for demographics, HIV-related factors, and ART ¹	64,937 (490,376)	06/07	1		0.41	1		<0.0001	1		<0.0001
		08/09	1.05	(0.92, 1.18)		0.92	(0.75, 1.13)		1.12	(0.96, 1.30)	
		10/11	0.89	(0.79, 1.02)		0.72	(0.56, 0.91)		1.05	(0.90, 1.23)	
		12/13	0.95	(0.85, 1.08)		0.58	(0.46, 0.72)		1.24	(1.07, 1.44)	
		14/15	0.95	(0.84, 1.07)		0.51	(0.40, 0.64)		1.28	(1.10, 1.48)	
		16/17	0.98	(0.85, 1.14)		0.41	(0.30, 0.54)		1.43	(1.20, 1.70)	
		18/19	1.00	(0.85, 1.16)		0.33	(0.24, 0.46)		1.52	(1.28, 1.82)	
		20/21	1.00	(0.84, 1.18)		0.29	(0.19, 0.45)		1.55	(1.28, 1.89)	
Including time updated exposure to ART ²	64,937 (490,376)	06/07	1		0.18	1		0.40	1		0.0001
		08/09	1.08	(0.95, 1.22)		0.99	(0.81, 1.22)		1.12	(0.96, 1.31)	
		10/11	1.01	(0.88, 1.15)		1.01	(0.79, 1.30)		1.06	(0.91, 1.24)	
		12/13	1.08	(0.95, 1.22)		0.83	(0.66, 1.06)		1.25	(1.08, 1.44)	
		14/15	1.10	(0.97, 1.25)		0.83	(0.65, 1.07)		1.27	(1.09, 1.48)	
		16/17	1.17	(1.00, 1.36)		0.75	(0.55, 1.02)		1.42	(1.19, 1.70)	
		18/19	1.23	(1.05, 1.45)		0.75	(0.52, 1.08)		1.52	(1.26, 1.84)	
		20/21	1.26	(1.04, 1.52)		0.73	(0.46, 1.16)		1.55	(1.26, 1.92)	
Adjusted for demographics, HIV-related factors, and ART,	64,937 (490,376)	06/07	1		0.30	1		<0.0001	1		<0.0001
		08/09	1.04	(0.92, 1.18)		0.83	(0.68, 1.02)		1.13	(0.97, 1.32)	
		10/11	0.89	(0.78, 1.01)		0.53	(0.41, 0.67)		1.09	(0.93, 1.28)	
		12/13	0.96	(0.85, 1.09)		0.49	(0.39, 0.61)		1.24	(1.08, 1.44)	
		14/15	0.96	(0.85, 1.08)		0.43	(0.34, 0.54)		1.28	(1.10, 1.48)	

with all variables fixed at baseline ³		16/17	1.01	(0.87, 1.16)		0.37	(0.28, 0.50)		1.38	(1.17, 1.62)	
		18/19	1.03	(0.89, 1.19)		0.30	(0.21, 0.41)		1.49	(1.26, 1.76)	
		20/21	1.02	(0.87, 1.20)		0.26	(0.17, 0.39)		1.51	(1.26, 1.82)	
Excluding individuals with a cancer prior to baseline ¹	61,053 (461,530)	06/07	1		0.60	1		<0.0001	1		<0.0001
		08/09	1.04	(0.92, 1.19)		0.90	(0.73, 1.11)		1.13	(0.96, 1.33)	
		10/11	0.92	(0.80, 1.06)		0.74	(0.58, 0.95)		1.09	(0.92, 1.29)	
		12/13	0.96	(0.84, 1.09)		0.55	(0.44, 0.70)		1.28	(1.10, 1.50)	
		14/15	0.94	(0.82, 1.07)		0.51	(0.40, 0.64)		1.29	(1.10, 1.50)	
		16/17	1.01	(0.87, 1.18)		0.41	(0.30, 0.55)		1.52	(1.26, 1.82)	
		18/19	0.98	(0.83, 1.15)		0.33	(0.23, 0.46)		1.54	(1.27, 1.86)	
		20/21	0.98	(0.81, 1.17)		0.30	(0.20, 0.46)		1.55	(1.26, 1.90)	
Including centrally validated events only ¹	64,881 (426,803)	06/07	1		0.24	1		<0.0001	1		<0.0001
		08/09	1.06	(0.93, 1.19)		0.93	(0.76, 1.15)		1.12	(0.96, 1.31)	
		10/11	0.92	(0.81, 1.05)		0.75	(0.58, 0.96)		1.07	(0.91, 1.25)	
		12/13	1.06	(0.93, 1.20)		0.67	(0.51, 0.87)		1.33	(1.14, 1.55)	
		14/15	1.02	(0.90, 1.17)		0.44	(0.32, 0.59)		1.41	(1.21, 1.65)	
		16/17	0.93	(0.79, 1.09)		0.41	(0.30, 0.57)		1.34	(1.12, 1.62)	
		18/19	0.92	(0.79, 1.08)		0.41	(0.30, 0.56)		1.35	(1.12, 1.63)	
		20/21	0.88	(0.74, 1.05)		0.32	(0.21, 0.48)		1.34	(1.09, 1.64)	

¹Poisson regression model adjusted for age, gender, ethnicity, CD4 count, CD4 nadir, prior cancer, ART-experience and viral suppression status, all fixed at baseline, and smoking status, body mass index, hepatitis C, hepatitis B, hypertension, diabetes, AIDS event, cardiovascular disease, end stage liver disease, end stage renal disease, all time updated.

²Poisson regression model adjusted for age, gender, ethnicity, CD4 count, CD4 nadir, prior cancer, all fixed at baseline, and smoking status, body mass index, hepatitis C, hepatitis B, hypertension, diabetes, AIDS event, cardiovascular disease, end stage liver disease, end stage renal disease, exposure to integrase inhibitors, protease inhibitors, nucleoside reverse transcriptase inhibitors, and non-nucleoside reverse transcriptase inhibitors all time updated.

³Poisson regression model adjusted for the same variables as 1, with all variables fixed at baseline.

Table S4. Results from a range of sensitivity analyses for infection-related cancer, smoking-related cancer, and BMI-related cancer.

			Infection-related cancer			Smoking-related cancer			BMI-related cancer		
Regression model	n participants (PYFU) included	Time period	IRR	(95% CI)	P	IRR	(95% CI)	P	IRR	(95% CI)	P
Adjusted for demographics, HIV-related factors, and ART ¹	64,937 (490,376)	06/07	1		<0.0001	1		0.0005	1		0.0001
		08/09	0.96	(0.82, 1.14)		1.15	(0.92, 1.44)		1.00	(0.72, 1.39)	
		10/11	0.75	(0.63, 0.91)		1.09	(0.87, 1.38)		1.05	(0.75, 1.47)	
		12/13	0.71	(0.59, 0.84)		1.37	(1.11, 1.69)		1.64	(1.23, 2.20)	
		14/15	0.65	(0.54, 0.77)		1.46	(1.18, 1.80)		1.53	(1.14, 2.07)	
		16/17	0.59	(0.48, 0.74)		1.52	(1.18, 1.95)		1.42	(0.99, 2.02)	
		18/19	0.49	(0.38, 0.62)		1.61	(1.24, 2.08)		1.86	(1.32, 2.63)	
		20/21	0.52	(0.40, 0.69)		1.71	(1.29, 2.26)		1.80	(1.23, 2.64)	
Including time updated exposure to ART ²	64,937 (490,376)	06/07	1		0.51	1		0.0020	1		0.0018
		08/09	1.01	(0.86, 1.19)		1.14	(0.91, 1.42)		0.98	(0.70, 1.37)	
		10/11	0.92	(0.76, 1.11)		1.10	(0.87, 1.38)		1.00	(0.72, 1.40)	
		12/13	0.89	(0.75, 1.07)		1.36	(1.10, 1.69)		1.57	(1.18, 2.11)	
		14/15	0.87	(0.72, 1.04)		1.44	(1.16, 1.79)		1.45	(1.07, 1.97)	
		16/17	0.85	(0.68, 1.07)		1.51	(1.17, 1.96)		1.33	(0.92, 1.92)	
		18/19	0.76	(0.58, 1.00)		1.62	(1.23, 2.12)		1.72	(1.20, 2.48)	
		20/21	0.86	(0.64, 1.16)		1.72	(1.28, 2.31)		1.63	(1.10, 2.44)	
Adjusted for demographics, HIV-related factors, and ART, with all	64,937 (490,376)	06/07	1		<0.0001	1		0.0002	1		<0.0001
		08/09	0.92	(0.78, 1.09)		1.17	(0.93, 1.46)		1.01	(0.73, 1.41)	
		10/11	0.66	(0.55, 0.79)		1.14	(0.91, 1.44)		1.10	(0.79, 1.53)	
		12/13	0.68	(0.57, 0.81)		1.40	(1.14, 1.72)		1.68	(1.26, 2.24)	
		14/15	0.63	(0.52, 0.74)		1.49	(1.21, 1.83)		1.58	(1.18, 2.11)	

variables fixed at baseline ³		16/17	0.61	(0.49, 0.75)	1.49	(1.17, 1.88)	1.39	(0.99, 1.94)
		18/19	0.50	(0.39, 0.63)	1.58	(1.24, 2.01)	1.86	(1.35, 2.57)
		20/21	0.52	(0.40, 0.68)	1.61	(1.23, 2.11)	1.77	(1.24, 2.54)
Excluding individuals with a cancer prior to baseline ¹	61,053 (461,530)	06/07	1	<0.0001	1	0.0025	1	0.0007
		08/09	0.96	(0.81, 1.14)	1.13	(0.90, 1.44)	0.95	(0.68, 1.35)
		10/11	0.77	(0.63, 0.93)	1.15	(0.90, 1.46)	1.06	(0.76, 1.50)
		12/13	0.69	(0.58, 0.83)	1.41	(1.13, 1.75)	1.66	(1.23, 2.23)
		14/15	0.64	(0.53, 0.77)	1.47	(1.18, 1.84)	1.50	(1.10, 2.04)
		16/17	0.61	(0.49, 0.77)	1.56	(1.20, 2.03)	1.49	(1.04, 2.14)
		18/19	0.47	(0.36, 0.60)	1.55	(1.18, 2.04)	1.72	(1.20, 2.47)
		20/21	0.50	(0.37, 0.67)	1.64	(1.22, 2.21)	1.60	(1.06, 2.39)
Including centrally validated events only ¹	64,881 (426,803)	06/07	1	<0.0001	1	<0.0001	1	<0.0001
		08/09	0.98	(0.82, 1.17)	1.16	(0.93, 1.45)	1.01	(0.72, 1.41)
		10/11	0.77	(0.63, 0.94)	1.14	(0.90, 1.43)	1.08	(0.78, 1.51)
		12/13	0.82	(0.67, 1.01)	1.63	(1.31, 2.02)	1.96	(1.46, 2.64)
		14/15	0.70	(0.56, 0.86)	1.70	(1.37, 2.11)	1.79	(1.32, 2.43)
		16/17	0.65	(0.51, 0.82)	1.33	(1.01, 1.74)	1.11	(0.75, 1.64)
		18/19	0.56	(0.43, 0.71)	1.29	(0.98, 1.69)	1.42	(0.98, 2.06)
		20/21	0.57	(0.43, 0.75)	1.32	(0.98, 1.77)	1.34	(0.89, 2.01)

¹Poisson regression model adjusted for age, gender, ethnicity, CD4 count, CD4 nadir, prior cancer, ART-experience and viral suppression status, all fixed at baseline, and smoking status, body mass index, hepatitis C, hepatitis B, hypertension, diabetes, AIDS event, cardiovascular disease, end stage liver disease, end stage renal disease, all time updated.

²Poisson regression model adjusted for age, gender, ethnicity, CD4 count, CD4 nadir, prior cancer, all fixed at baseline, and smoking status, body mass index, hepatitis C, hepatitis B, hypertension, diabetes, AIDS event, cardiovascular disease, end stage liver disease, end stage renal disease, exposure to integrase inhibitors, protease inhibitors, nucleoside reverse transcriptase inhibitors, and non-nucleoside reverse transcriptase inhibitors all time updated.

³Poisson regression model adjusted for the same variables as 1, with all variables fixed at baseline.