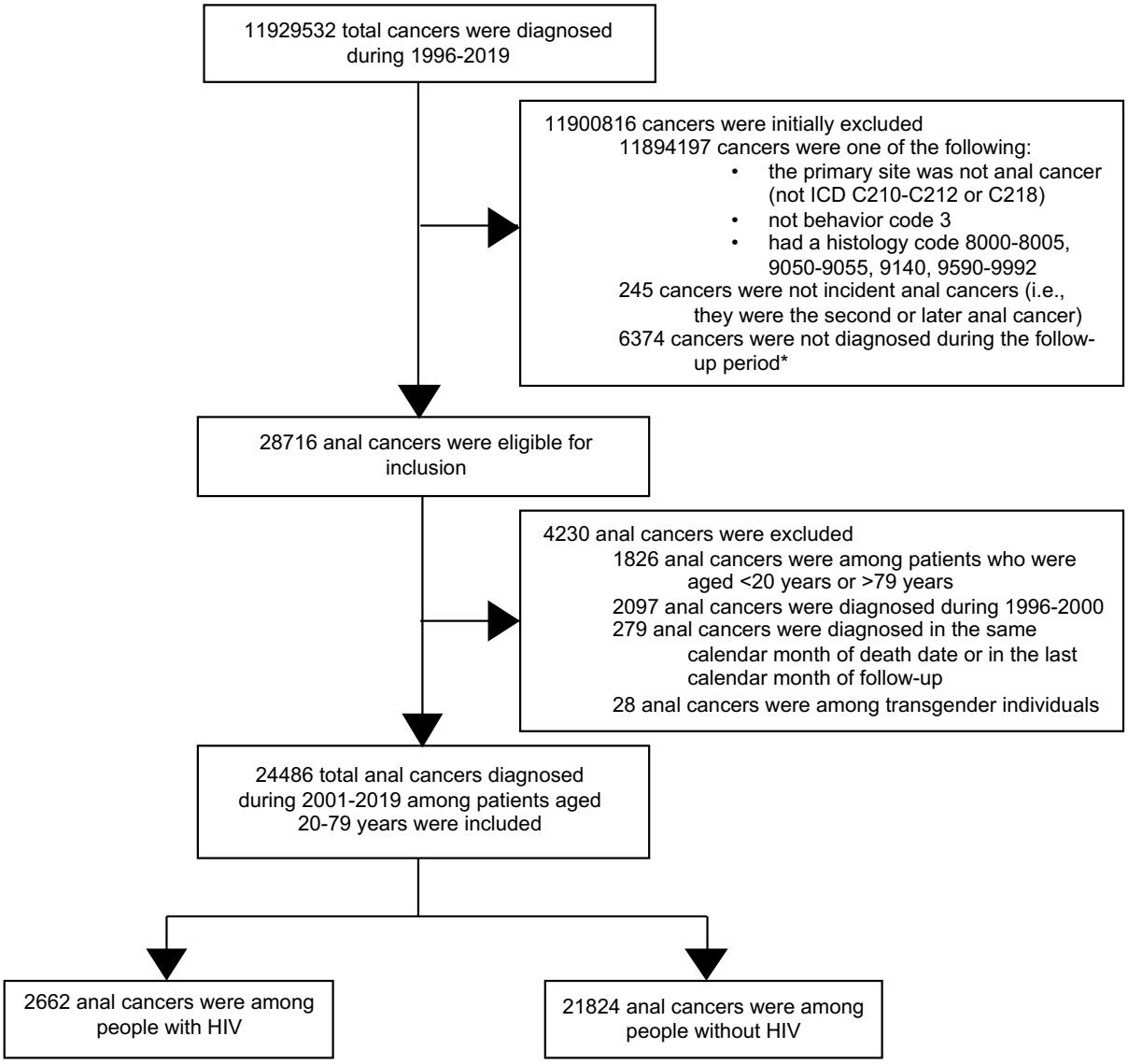
Supplementary Appendix

Contents **Page**



1. Supplementary Figure 1. Flow diagram of anal cancers included in the analysis.

* The follow-up period started in January of the study period for each registry site's start year and ended at the earlier of December of the study period end year or the month before the individual's 85th birthday.

2. Supplementary Table 1. Reclassification of anal-related cause of death among anal cancer patients in the HIV/AIDS Cancer Match Study, 2001-2019.

	Original			Reclassified					
	Overall	People with HIV		Overall		People with HIV			
		Yes	No			Yes		No	
Cause of Death	n	n	n	n	Δ [a]	n	Δ [a]	n	Δ [a]
Anal Cancer	2074	213	1861	2074	0	213	0	1861	0
Colon Cancer	648	34	614	611	-37	34	0	577	-37
Rectal Cancer	1606	174	1432	1540	-66	169	-5	1371	-61
Rectosigmoid Junction Cancer	275	18	257	273	-2	18	0	255	-2
All Anal-Related Cancers	4603	439	4164	4498	-105	434	-5	4064	-100

ICD = International Classification of Diseases.

[a] Δ denotes the absolute change from the original cause of death classification after reclassifying anal cancer patients with cause of death codes for colon, rectal, or rectosigmoid junction cancer and a corresponding incident cancer diagnosis of colon, rectal, or rectosigmoid junction cancer.

3. Supplementary Table 2. Leading causes of death and proportion of deaths attributed to anal cancer and anal-related cancers among anal cancer patients overall and by HIV status in the HIV/AIDS Cancer Match Study 2001-2019.

		People with HIV	
		Yes	No
Cause of Death	**ICD Codes**	**n (%)**	**n (%)**
Total population		2662	21824
All deaths (% of total population)		1161 (43·6%)	7722 (35·4%)
Total population among registries with COD data		2582	21051
All deaths among registries with COD data		1130 (43·8%)	7486 (35·6%)
Anal cancer	C210 C211 C212 C218	213 (8·2%)	1861 (8·8%)
Colon cancer	C187 C189	34 (1·3%)	577 (2·7%)
Rectal cancer	C20 C209	169 (6·5%)	1371 (6·5%)
Rectosigmoid junction cancer	C19 C199	18 (0·7%)	255 (1·2%)
All anal-related cancers	All codes above	434 (16·8%)	4064 (19·3%)
Leading cause of death [a] among registries with COD data			
1.		Anal-related cancer 434 (16·8%)	Anal-related cancer 4064 (19·3%)
2.		HIV 411 (15·9%)	Miscellaneous neoplasms 365 (1·7%)
3.		Ischemic heart disease 35 (1·4%)	Ischemic heart disease 334 (1·6%)
4.		Lung and bronchus cancer 21 (0·8%)	Lung and bronchus cancer 296 (1·4%)
5.		Miscellaneous Neoplasms 15 (0·6%)	COPD 176 (0·8%)

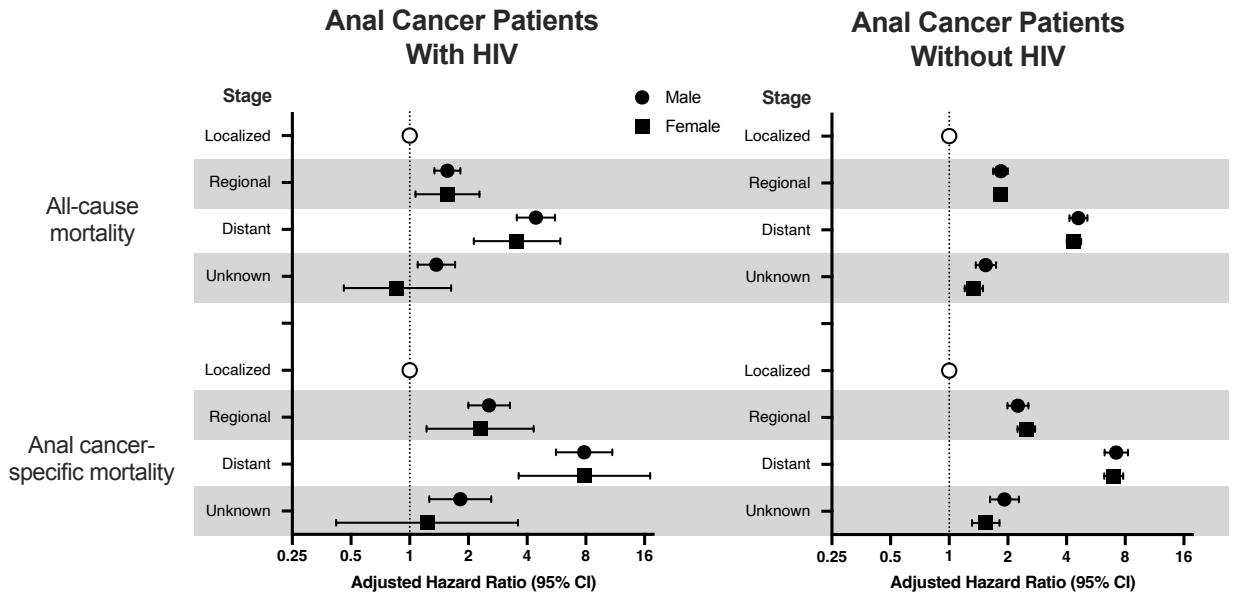
COD = cause of death; COPD = chronic obstructive pulmonary disease and allied conditions; ICD = International Classification of Diseases.

[a] Cause of death was determined using the groupings in the "Surveillance, Epidemiology, and End Results Cause of Death to Site Recode ICD-O-3 2023 Revision": https://seer.cancer.gov/codrecode/icdo3_d2023/.

4. Supplementary Table 3. Characteristics of anal cancer patients by sex and HIV status in the HIV/AIDS Cancer Match Study, 2001-2019.

	Male (N=9617)				Female (N=14869)		
	Overall	MSM with HIV	HIV Status		Overall	HIV Status	
Characteristic	N (%)	n (%)	Yes, n (%)	No, n (%)	N (%)	Yes, n (%)	No, n (%)
Year of Anal Cancer Diagnosis							
2001-2004	1648 (17·1%)	233 (14·9%)	333 (14·6%)	1315 (17·9%)	2462 (16·6%)	43 (11·4%)	2419 (16·7%)
2005-2009	3090 (32·1%)	482 (30·9%)	736 (32·2%)	2354 (32·1%)	4498 (30·3%)	101 (26·8%)	4397 (30·3%)
2010-2014	3362 (35·0%)	579 (37·1%)	811 (35·5%)	2551 (34·8%)	5483 (36·9%)	135 (35·8%)	5348 (36·9%)
2015-2019	1517 (15·8%)	268 (17·2%)	405 (17·7%)	1112 (15·2%)	2426 (16·3%)	98 (26·0%)	2328 (16·1%)
Chi-squared p-value			0·0003			<0·0001	
Age of Diagnosis years							
20-39	643 (6·7%)	243 (15·6%)	329 (14·4%)	314 (4·3%)	427 (2·9%)	50 (13·3%)	377 (2·6%)
40-59	4944 (51·4%)	1134 (72·6%)	1675 (73·3%)	3269 (44·6%)	7080 (47·6%)	279 (74·0%)	6801 (46·9%)
60-79	4030 (41·9%)	185 (11·8%)	281 (12·3%)	3749 (51·1%)	7362 (49·5%)	48 (12·7%)	7314 (50·5%)
Chi-squared p-value			<0·0001			<0·0001	
Median (IQR)	57·3 (48·8-66·3)	48·6 (42·8-55·0)	48·9 (43·2-55·3)	60·3 (51·9-68·5)	59·8 (52·4-68·1)	50·1 (44·0-55·3)	60·1 (52·7-68·3)
Race/Ethnicity							
NH White	6258 (65·1%)	724 (46·4%)	926 (40·5%)	5332 (72·7%)	10963 (73·7%)	58 (15·4%)	10905 (75·3%)
NH Black	1840 (19·1%)	499 (32·0%)	809 (35·4%)	1031 (14·1%)	1816 (12·2%)	189 (50·1%)	1627 (11·2%)
Hispanic	1181 (12·3%)	268 (17·2%)	445 (19·5%)	736 (10·0%)	1693 (11·4%)	115 (30·5%)	1578 (10·9%)
Other	107 (1·1%)	8 (0·5%)	DS	DS	164 (1·1%)	DS	DS
Unknown	231 (2·4%)	63 (4·0%)	DS	DS	233 (1·6%)	DS	DS
Chi-squared p-value			<0·0001			<0·0001	
Histology							
Squamous cell carcinoma	7756 (80·7%)	1501 (96·1%)	2194 (96·0%)	5562 (75·9%)	13219 (88·9%)	366 (97·1%)	12853 (88·7%)
Adenocarcinoma	1396 (14·5%)	21 (1·3%)	DS	DS	1016 (6·8%)	DS	DS
Other	465 (4·8%)	40 (2·6%)	DS	DS	634 (4·3%)	DS	DS
Chi-squared p-value			<0·0001			<0·0001	
Anal Cancer Stage							
Localized	4643 (48·3%)	837 (53·6%)	1229 (53·8%)	3414 (46·6%)	7049 (47·4%)	170 (45·1%)	6879 (47·5%)
Regional	2971 (30·9%)	458 (29·3%)	673 (29·5%)	2298 (31·3%)	4636 (31·2%)	132 (35·0%)	4504 (31·1%)
Distant	967 (10·1%)	102 (6·5%)	153 (6·7%)	814 (11·1%)	1747 (11·8%)	41 (10·9%)	1706 (11·8%)
Unknown	1036 (10·8%)	165 (10·6%)	230 (10·1%)	806 (11·0%)	1437 (9·7%)	34 (9·0%)	1403 (9·7%)
Chi-squared p-value			<0·0001			0·44	
Anal Cancer Treatment							
Any Anal Cancer Treatment							
Yes	8551 (88·9%)	1405 (90·0%)	2060 (90·2%)	6491 (88·5%)	13506 (90·8%)	349 (92·6%)	13157 (90·8%)
No/Unknown	1066 (11·1%)	157 (10·1%)	225 (9·9%)	841 (11·5%)	1363 (9·2%)	28 (7·4%)	1335 (9·2%)
Chi-squared p-value			0·031			0·24	
Surgery							
Yes	4523 (47·0%)	759 (48·6%)	1104 (48·3%)	3419 (46·6%)	5524 (37·2%)	169 (44·8%)	5355 (37·0%)
No/Unknown	5094 (53·0%)	803 (51·4%)	1181 (51·7%)	3913 (53·4%)	9345 (62·9%)	208 (55·2%)	9137 (63·1%)
Chi-squared p-value			0·16			0·0018	
Chemotherapy							
Yes	6144 (63·9%)	1010 (64·7%)	1444 (63·2%)	4700 (64·1%)	10912 (73·4%)	254 (67·4%)	10658 (73·5%)
No/Unknown	3473 (36·1%)	552 (35·3%)	841 (36·8%)	2632 (35·9%)	3957 (26·6%)	123 (32·6%)	3834 (26·5%)
Chi-squared p-value			0·43			0·0074	
Radiation							
Yes	6326 (65·8%)	1056 (67·6%)	1546 (67·7%)	4780 (65·2%)	11077 (74·5%)	275 (72·9%)	10802 (74·5%)
No/Unknown	3291 (34·2%)	506 (32·4%)	739 (32·3%)	2552 (34·8%)	3792 (25·5%)	102 (27·1%)	3690 (25·5%)
Chi-squared p-value			0·0301			0·48	

DS = data suppressed (cell count <6 or to prevent the computation of other small cells); IQR = interquartile range; MSM = men who have sex with men.



5. Supplementary Figure 2. Association between anal cancer stage and all-cause and anal cancer-specific mortality by HIV status and sex among anal cancer patients in the HIV/AIDS Cancer Match Study, 2001-2019.

6. Supplementary Table 4. Association between anal cancer stage and all-cause and anal cancer-specific mortality by HIV status and sex among anal cancer patients in the HIV/AIDS Cancer Match Study, 2001-2019.

	People with HIV		People without HIV	
	Male	Female	Male	Female
	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)
All-cause mortality [a]				
Anal cancer stage				
Localized	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Regional	1.56 (1.34-1.82)	1.56 (1.07-2.28)	1.84 (1.68-2.00)	1.84 (1.71-1.98)
Distant	4.44 (3.54-5.56)	3.55 (2.13-5.92)	4.60 (4.14-5.12)	4.36 (4.01-4.75)
Unknown	1.37 (1.10-1.71)	0.86 (0.46-1.63)	1.54 (1.37-1.74)	1.34 (1.20-1.49)
Anal cancer-specific mortality [b]				
Anal cancer stage				
Localized	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Regional	2.55 (2.00-3.27)	2.30 (1.22-4.32)	2.25 (1.99-2.55)	2.49 (2.24-2.76)
Distant	7.85 (5.63-10.93)	7.87 (3.62-17.11)	7.20 (6.27-8.27)	6.99 (6.25-7.82)
Unknown	1.82 (1.26-2.62)	1.23 (0.42-3.59)	1.92 (1.62-2.28)	1.54 (1.31-1.81)

aHR = adjusted hazard ratio; CI = confidence interval.

[a] The Cox proportional hazard model for all-cause mortality was adjusted for year of anal cancer diagnosis, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, surgery, chemotherapy, and radiation; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group.

[b] The Cox proportional hazard model for anal cancer-specific mortality was adjusted for year of anal cancer diagnosis, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, and any treatment; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group; Analyses for anal cancer-specific mortality excluded Connecticut due to missing cause of death information

7. Supplementary Table 5. Association between year of anal cancer diagnosis and risk of all-cause mortality and anal cancer-specific mortality among anal cancer patients in the HIV/AIDS Cancer Match Study, 2001-2019.

	All-Cause Mortality [a] p-trend [c]	Anal Cancer-Specific Mortality [b] p-trend [c]
Overall	<0·0001	0·0008
People With HIV	<0·0001	0·13
People Without HIV	<0·0001	0·0019

[a] The Cox proportional hazard model for all-cause mortality was adjusted for sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, surgery, chemotherapy, and radiation; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group.

[b] The Cox proportional hazard model for anal cancer-specific mortality was adjusted for sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, and any treatment; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group; Analyses for anal cancer-specific mortality excluded Connecticut due to missing cause of death information.

[c] p-trends were calculated using Cox proportional hazard models, treating year of anal cancer diagnosis as a continuous variable.

8. Supplementary Table 6. Sensitivity analysis comparing the adjusted hazard ratios for all-cause mortality and anal cancer-specific mortality using different year inclusion criteria among anal cancer patients in the HIV/AIDS Cancer Match Study.

	2001-2019 aHR (95% CI)	2001-2018 aHR (95% CI)	2001-2017 aHR (95% CI)	2001-2016 aHR (95% CI)
All-Cause Mortality [a]				
Overall				
No HIV	Ref	Ref	Ref	Ref
PWH	1·53 (1·42-1·64)	1·52 (1·42-1·64)	1·52 (1·41-1·64)	1·52 (1·41-1·63)
Male				
No HIV	Ref	Ref	Ref	Ref
PWH	1·35 (1·24-1·47)	1·35 (1·24-1·46)	1·35 (1·24-1·47)	1·34 (1·23-1·46)
Female				
No HIV	Ref	Ref	Ref	Ref
PWH	2·47 (2·10-2·90)	2·47 (2·10-2·91)	2·49 (2·11-2·93)	2·48 (2·10-2·93)
Anal Cancer-Specific Mortality [b]				
Overall				
No HIV	Ref	Ref	Ref	Ref
PWH	1·06 (0·94-1·18)	1·05 (0·94-1·18)	1·05 (0·94-1·18)	1·05 (0·94-1·18)
Male				
No HIV	Ref	Ref	Ref	Ref
PWH	0·97 (0·85-1·10)	0·96 (0·85-1·10)	0·97 (0·85-1·10)	0·96 (0·85-1·10)
Female				
No HIV	Ref	Ref	Ref	Ref
PWH	1·52 (1·18-1·97)	1·51 (1·17-1·96)	1·52 (1·17-1·98)	1·54 (1·18-2·00)

aHR = adjusted hazard ratio; CI = confidence interval; PWH= people with HIV.

[a] The Cox proportional hazard model for all-cause mortality was adjusted for year of anal cancer diagnosis, sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, surgery, chemotherapy, and radiation (in the sex-stratified models, all covariates were adjusted for except for sex).

[b] The Cox proportional hazard model for anal cancer-specific mortality was adjusted for year of anal cancer diagnosis, sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, and any treatment (in the sex-stratified models, all covariates were adjusted for except for sex); Analyses for anal cancer-specific mortality excluded Connecticut due to missing cause of death information.

9. Supplementary Table 7. Sensitivity analysis comparing trends in all-cause mortality and anal cancer-specific mortality across year of anal cancer diagnosis using different year inclusion criteria among anal cancer patients in the HIV/AIDS Cancer Match Study.

	2001-2019 p-trend	2001-2018 p-trend	2001-2017 p-trend	2001-2016 p-trend
All-Cause Mortality [a]				
Overall	<0·0001	<0·0001	<0·0001	<0·0001
People with HIV	<0·0001	<0·0001	<0·0001	<0·0001
People without HIV	<0·0001	<0·0001	<0·0001	<0·0001
Anal Cancer-Specific Mortality [b]				
Overall	0·0008	0·0008	0·0014	0·014
People with HIV	0·13	0·074	0·086	0·23
People without HIV	0·0019	0·0024	0·0042	0·024

[a] The Cox proportional hazard model for all-cause mortality was adjusted for sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, surgery, chemotherapy, and radiation; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group.

[b] The Cox proportional hazard model for anal cancer-specific mortality was adjusted for sex, age at anal cancer diagnosis, race/ethnicity, histology, anal cancer stage, registry region, and any treatment; Models among people with HIV additionally adjusted for AIDS and HIV transmission risk group; Analyses for anal cancer-specific mortality excluded Connecticut due to missing cause of death information.