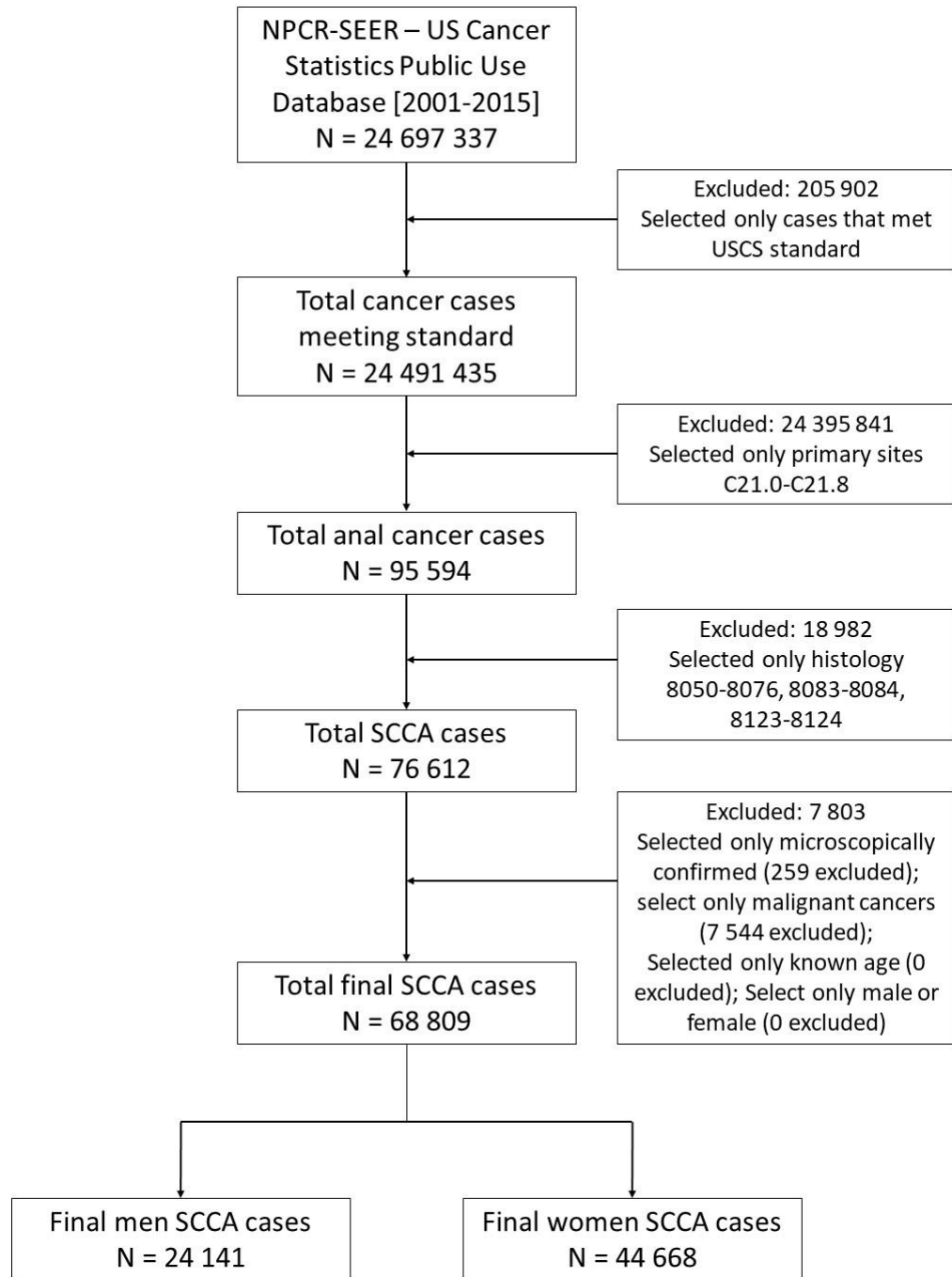
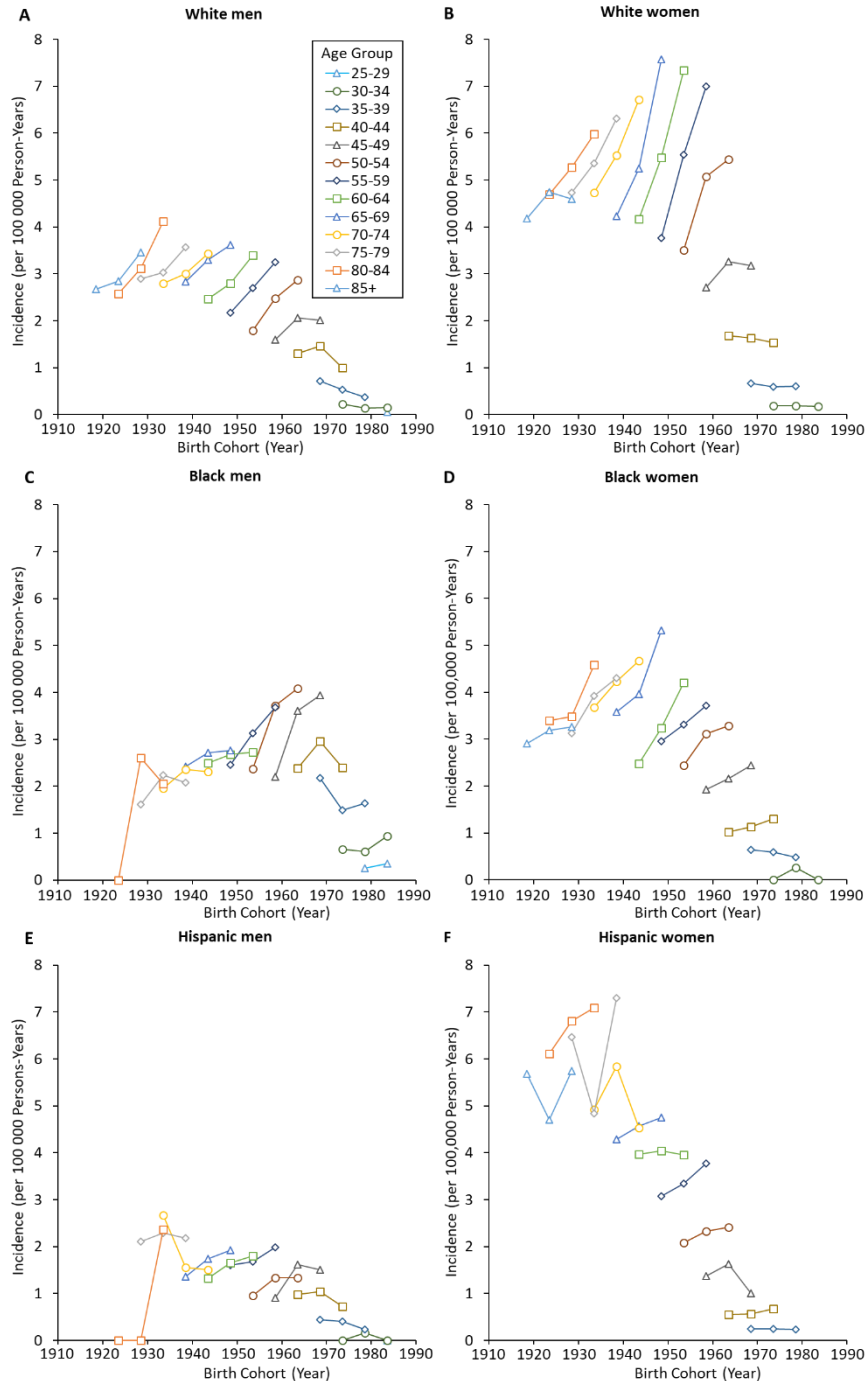


SUPPLEMENTARY MATERIALS

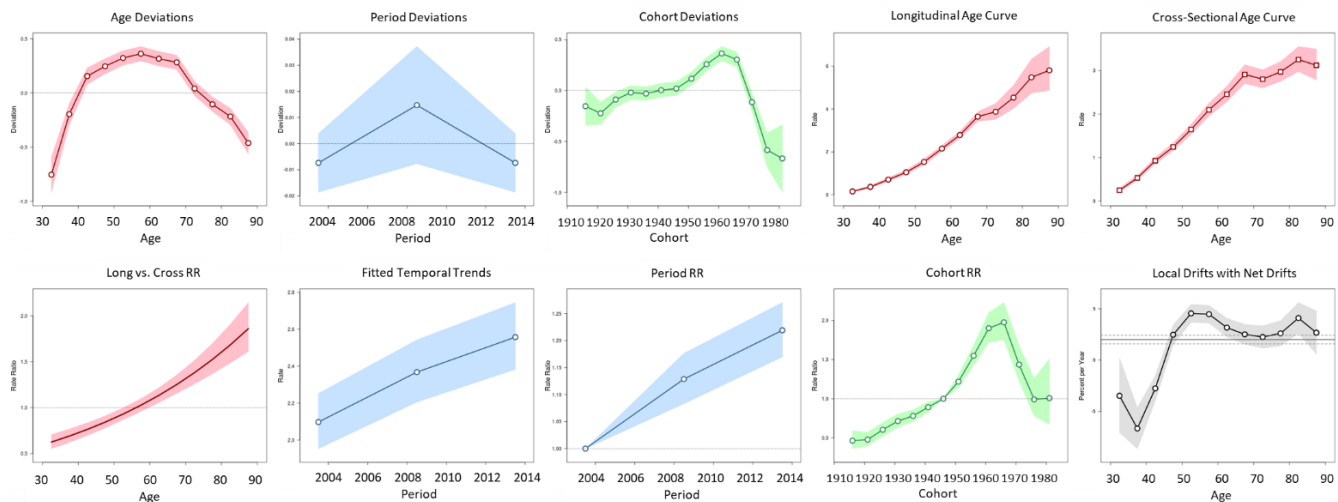


Supplementary Figure 1. Diagram depicting the sample flow of the study population

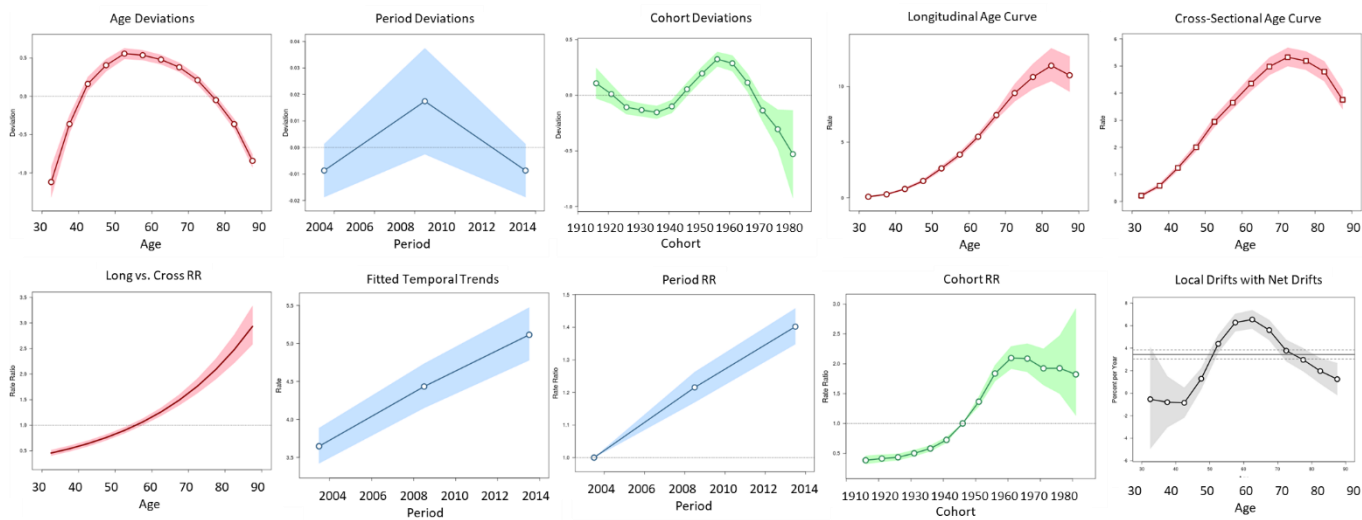


Supplementary Figure 2. Age-specific incidence rates* of squamous cell carcinoma of the anus by race and cohort year of birth: NPCR and SEER (2001-2015). Age-specific incidence rates of squamous cell carcinoma of the anus based on cohort year of birth in 15-year birth cohorts between 1916 and 1990. Each point represents a different birth cohort and the lines connect birth cohorts of similar age. Panels A, B, C, D, E, and F show incidence rates among Non-Hispanic White men, Non-Hispanic White women, Non-Hispanic Black men, Non-Hispanic Black women, Hispanic men, and Hispanic women, respectively.
 * Rates were calculated as number of cases per 100 000 person-years and age adjusted to the 2000 US standard population

A. Non-Hispanic White Men



B. Non-Hispanic White Women

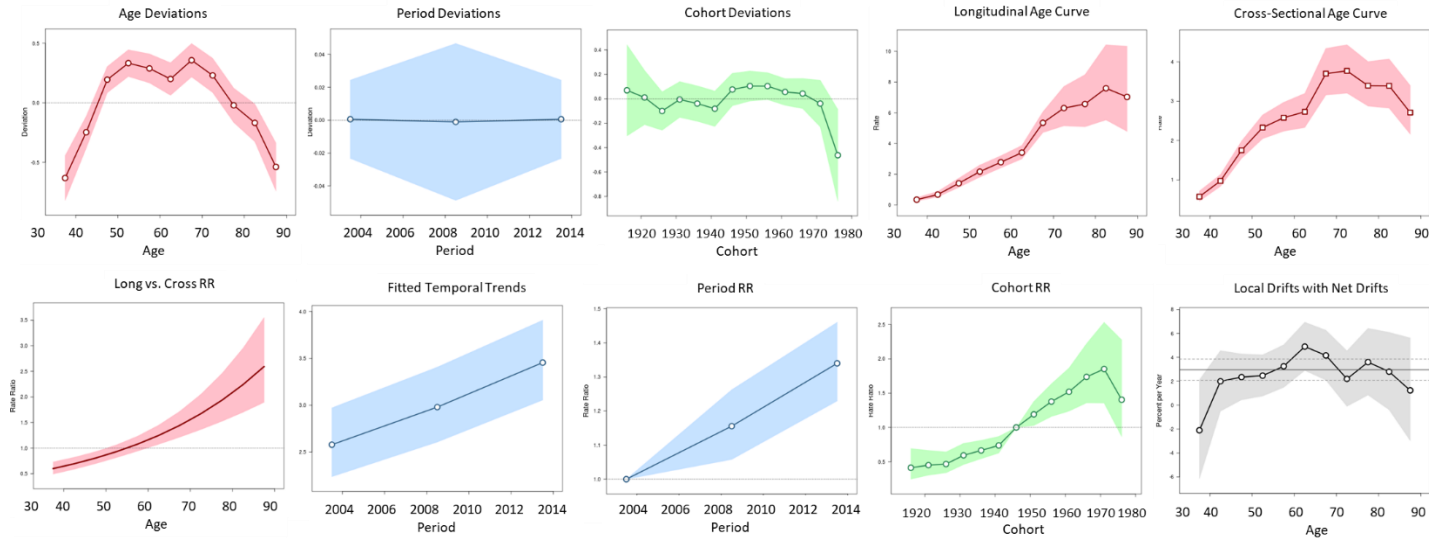


Supplementary Figure 3. Age-specific incidence rates of squamous cell carcinoma of the anus by race and cohort year of birth: NPCR and SEER (2001-2015).

C. Non-Hispanic Black Men

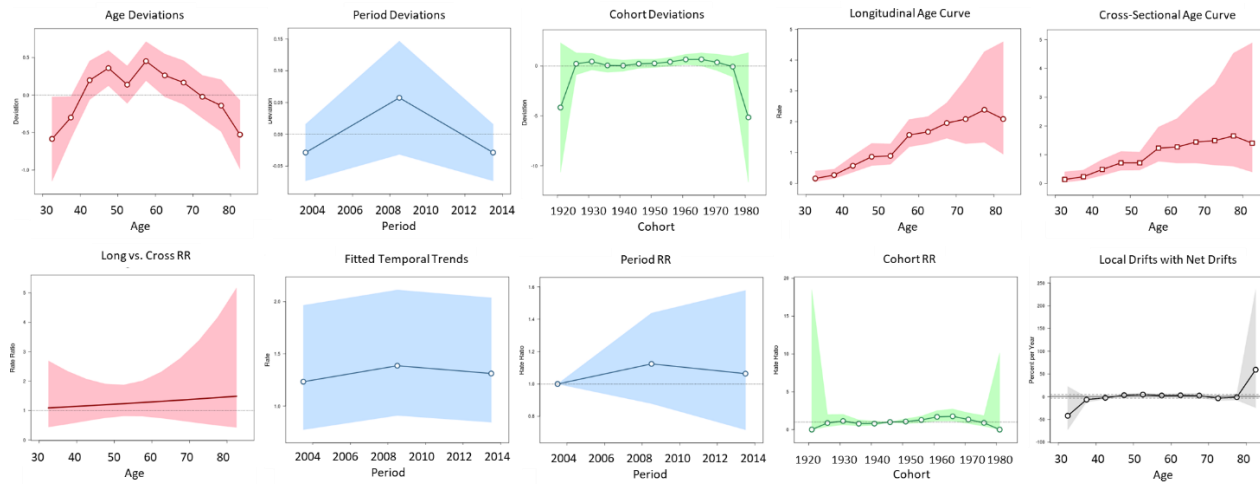


D. Non-Hispanic Black Women

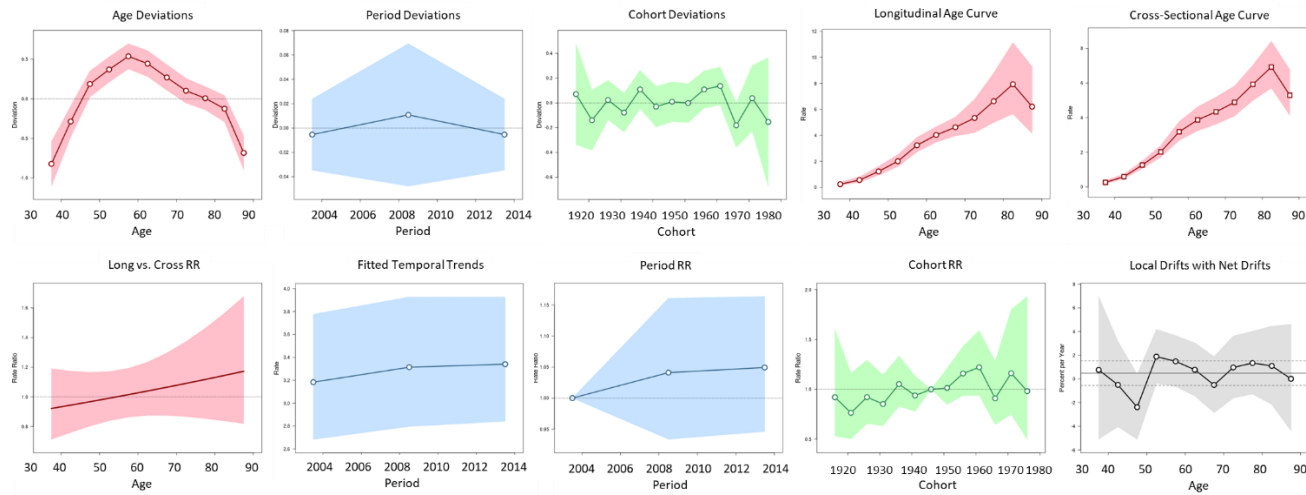


Supplementary Figure 3 (continued). Age-specific incidence rates of squamous cell carcinoma of the anus by race and cohort year of birth: NPCR and SEER (2001-2015).

D. Hispanic Men



D. Hispanic Women



Supplementary Figure 3 (continued). Age-specific incidence rates of squamous cell carcinoma of the anus by race and cohort year of birth: NPCR and SEER (2001-2015)

Supplementary Table 1. Rate Ratios for Squamous Cell Carcinoma of the Anus, Comparing Age at Cancer Diagnosis According to Race/Ethnicity among Men

Age	2001-2005	2006-2010	2011-2015	Age	2001-2005	2006-2010	2011-2015
	Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)		Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)
Non-Hispanic White							
30-34	Ref	Ref	Ref				
35-39	3.09 (2.38-4.06)	3.66 (2.60-5.26)	2.39 (1.68-3.43)	35-39 vs 30-34	3.09 (2.38-4.06)	3.66 (2.60-5.26)	2.39 (1.68-3.43)
40-44	5.62 (4.40-7.27)	10.01 (7.30-14.06)	6.42 (4.73-8.88)	40-44 vs 35-39	1.82 (1.56-2.12)	2.73 (2.29-3.27)	2.69 (2.15-3.38)
45-49	6.92 (5.43-8.93)	14.15 (10.37-19.78)	12.93 (9.64-17.70)	45-49 vs 40-44	1.23 (1.09-1.39)	1.41 (1.26-1.58)	2.01 (1.76-2.31)
50-54	7.74 (6.08-9.98)	16.93 (12.43-23.64)	18.44 (13.81-25.16)	50-54 vs 45-49	1.12 (1.01-1.25)	1.20 (1.09-1.32)	1.43 (1.30-1.57)
55-59	9.40 (7.38-12.13)	18.45 (13.54-25.77)	20.86 (15.63-28.45)	55-59 vs 50-54	1.22 (1.09-1.36)	1.09 (0.99-1.19)	1.13 (1.04-1.23)
60-64	10.65 (8.35-13.76)	19.13 (14.03-26.76)	21.80 (16.33-29.75)	60-64 vs 55-59	1.13 (1.01-1.27)	1.04 (0.94-1.14)	1.05 (0.96-1.13)
65-69	12.27 (9.60-15.88)	22.56 (16.52-31.58)	23.17 (17.34-31.65)	65-69 vs 60-64	1.15 (1.02-1.30)	1.18 (1.06-1.31)	1.06 (0.97-1.16)
70-74	12.11 (9.45-15.70)	20.58 (15.00-28.93)	22.07 (16.45-30.24)	70-74 vs 65-69	0.99 (0.87-1.12)	0.91 (0.81-1.03)	0.95 (0.86-1.05)
75-79	12.52 (9.74-16.29)	20.77 (15.09-29.27)	22.92 (17.02-31.52)	75-79 vs 70-74	1.03 (0.90-1.19)	1.01 (0.88-1.15)	1.04 (0.92-1.17)
80-84	11.17 (8.56-14.73)	21.35 (15.42-30.25)	26.45 (19.57-36.47)	80-84 vs 75-79	0.89 (0.75-1.05)	1.03 (0.88-1.20)	1.15 (1.01-1.32)
85 +	11.59 (8.73-15.50)	19.46 (13.90-27.82)	22.21 (16.32-30.80)	85+ vs 80-84	1.04 (0.84-1.28)	0.91 (0.76-1.09)	0.84 (0.72-0.98)
Non-Hispanic Black							

30-34	Ref	Ref	Ref				
35-39	3.33 (2.31-4.88)	2.47 (1.65-3.76)	1.74 (1.25-2.44)	35-39 vs 30-34	3.33 (2.31-4.88)	2.47 (1.65-3.76)	1.74 (1.25-2.44)
40-44	3.65 (2.55-5.33)	4.93 (3.42-7.29)	2.55 (1.88-3.50)	40-44 vs 35-39	1.10 (0.86-1.39)	2.00 (1.54-2.60)	1.46 (1.12-1.91)
45-49	3.36 (2.33-4.95)	5.99 (4.19-8.81)	4.21 (3.17-5.67)	45-49 vs 40-44	0.92 (0.72-1.17)	1.22 (1.00-1.48)	1.65 (1.34-2.04)
50-54	3.63 (2.50-5.37)	6.17 (4.30-9.10)	4.36 (3.29-5.87)	50-54 vs 45-49	1.08 (0.83-1.40)	1.03 (0.85-1.25)	1.04 (0.87-1.24)
55-59	3.76 (2.54-5.64)	5.20 (3.57-7.75)	3.93 (2.94-5.32)	55-59 vs 50-54	1.03 (0.77-1.38)	0.84 (0.68-1.04)	0.90 (0.75-1.09)
60-64	3.82 (2.52-5.85)	4.45 (2.98-6.80)	2.91 (2.12-4.03)	60-64 vs 55-59	1.02 (0.72-1.43)	0.86 (0.65-1.13)	0.74 (0.58-0.93)
65-69	3.72 (2.39-5.82)	4.50 (2.93-7.02)	2.94 (2.09-4.17)	65-69 vs 60-64	0.97 (0.65-1.44)	1.01 (0.71-1.42)	1.01 (0.75-1.36)
70-74	2.99 (1.78-4.97)	3.92 (2.42-6.37)	2.47 (1.64-3.69)	70-74 vs 65-69	0.81 (0.49-1.30)	0.87 (0.57-1.32)	0.84 (0.57-1.22)
75-79	2.47 (1.31-4.46)	3.71 (2.13-6..37)	2.22 (1.36-3.55)	75-79 vs 70-74	0.82 (0.42-1.55)	0.95 (0.55-1.60)	0.90 (0.54-1.48)
80-84	N/A	4.33 (2.31-7.86)	2.19 (1.18-3.84)	80-84 vs 75-79	N/A	1.17 (0.60-2.23)	0.98 (0.50-1.89)
85 +	N/A	N/A	N/A	85+ vs 80-84	N/A	N/A	N/A
Hispanic							
30-34	N/A	Ref	N/A				
35-39	Ref	2.59 (1.41-4.97)	Ref	35-39 vs 30-34	N/A	2.59 (1.41-4.97)	N/A
40-44	2.21 (1.46-3.41)	6.70 (3.90-12.23)	3.14 (1.95-5.23)	40-44 vs 35-39	2.21 (1.46-3.41)	2.59 (1.75-3.89)	3.14 (1.95-5.23)
45-49	2.05 (1.31-3.25)	10.40 (6.13-18.80)	6.53 (4.19-10.56)	45-49 vs 40-44	0.93 (0.63-1.36)	1.55 (1.16-2.08)	2.08 (1.54-2.83)

50-54	2.17 (1.34-3.51)	8.59 (4.95-15.80)	5.76 (3.65-9.44)	50-54 vs 45-49	1.06 (0.68-1.64)	0.83 (0.61-1.12)	0.88 (0.67-1.16)
55-59	3.65 (2.32-5.80)	10.84 (6.22-20.02)	8.56 (5.46-13.95)	55-59 vs 50-54	1.68 (1.08-2.64)	1.26 (0.89-1.78)	1.49 (1.11-1.98)
60-64	3.01 (1.76-5.10)	10.67 (5.94-20.17)	7.80 (4.84-12.97)	60-64 vs 55-59	0.82 (0.49-1.35)	0.99 (0.66-1.45)	0.91 (0.66-1.24)
65-69	3.10 (1.72-5.45)	11.22 (6.03-21.78)	8.30 (5.03-14.08)	65-69 vs 60-64	1.03 (0.55-1.89)	1.05 (0.66-1.67)	1.06 (0.73-1.55)
70-74	6.07 (3.63-10.09)	10.04 (5.04-20.46)	6.51 (3.62-11.78)	70-74 vs 65-69	1.96 (1.09-3.59)	0.89 (0.50-1.58)	0.78 (0.47-1.27)
75-79	4.77 (2.51-8.72)	14.78 (7.48-29.93)	9.46 (5.25-17.12)	75-79 vs 70-74	0.79 (0.41-1.47)	1.47 (0.89-2.77)	1.45 (0.82-2.57)
80-84	N/A	N/A	10.22 (5.29-19.46)	80-84 vs 75-79	N/A	N/A	1.08 (0.57-2.02)
85 +	N/A	N/A	N/A	85+ vs 80-84	N/A	N/A	N/A

N/A Statistic not displayed due to fewer than 16 cases.

Supplementary Table 2. Rate Ratios for Squamous Cell Carcinoma of the Anus, Comparing Age at Cancer Diagnosis According to Race/Ethnicity among Women.

Age	2001-2005	2006-2010	2011-2015	Age	2001-2005	2006-2010	2011-2015
	Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)		Rate Ratio (95% CI)	Rate Ratio (95% CI)	Rate Ratio (95% CI)
Non-Hispanic White							
30-34	Ref	Ref	Ref				
35-39	3.53 (2.65-4.77)	3.09 (2.27-4.27)	3.38 (2.48-4.68)	35-39 vs 30-34	3.53 (2.65-4.77)	3.09 (2.27-4.27)	3.38 (2.48-4.68)
40-44	8.84 (6.78-11.72)	8.56 (6.47-11.53)	8.63 (6.51-11.66)	40-44 vs 35-39	2.51 (2.16-2.92)	2.77 (2.34-3.28)	2.55 (2.14-3.06)
45-49	14.25 (10.99-18.81)	17.10 (13.02-22.89)	17.80 (13.54-23.85)	45-49 vs 40-44	1.61 (1.46-1.78)	2.00 (1.81-2.21)	2.06 (1.85-2.30)
50-54	18.43 (14.22-24.29)	26.54 (20.25-35.45)	30.53 (23.31-40.77)	50-54 vs 45-49	1.29 (1.19-1.40)	1.55 (1.45-1.67)	1.71 (1.59-1.85)
55-59	19.80 (15.27-26.11)	28.98 (22.12-38.72)	39.24 (29.98-52.37)	55-59 vs 50-54	1.07 (0.99-1.16)	1.09 (1.03-1.16)	1.29 (1.21-1.36)
60-64	21.97 (16.93-29.00)	28.63 (21.83-38.28)	41.22 (31.49-55.02)	60-64 vs 55-59	1.11 (1.02-1.21)	0.99 (0.92-1.05)	1.05 (0.99-1.11)
65-69	22.27 (17.13-27.43)	27.47 (20.91-36.78)	42.46 (32.42-56.70)	65-69 vs 60-64	1.01 (0.92-1.11)	0.96 (0.89-1.03)	1.03 (0.97-1.09)
70-74	24.90 (19.17-32.90)	28.89 (21.97-38.72)	37.68 (28.72-50.40)	70-74 vs 65-69	1.12 (1.02-1.23)	1.05 (0.97-1.14)	0.89 (0.83-0.95)
75-79	24.91 (19.16-32.94)	28.00 (21.27-37.57)	35.44 (26.96-47.50)	75-79 vs 70-74	1.00 (0.91-1.10)	0.97 (0.89-1.06)	0.94 (0.87-1.02)
80-84	24.71 (18.96-32.75)	27.60 (20.93-37.08)	33.56 (25.46-45.07)	80-84 vs 75-79	0.99 (0.90-1.10)	0.99 (0.89-1.09)	0.95 (0.86-1.04)
85 +	21.99 (16.83-29.19)	24.80 (18.79-33.34)	25.81 (19.57-34.69)	85+ vs 80-84	0.89 (0.79-0.99)	0.90 (0.81-0.99)	0.77 (0.70-0.85)
Non-Hispanic Black							

35-39	Ref	Ref	Ref				
40-44	1.59 (1.08-2.35)	1.94 (1.31-2.91)	2.69 (1.78-4.17)	40-44 vs 35-39	1.59 (1.08-2.35)	1.94 (1.31-2.91)	2.69 (1.78-4.17)
45-49	3.00 (2.12-4.31)	3.69 (2.59-5.37)	5.05 (3.45-7.62)	45-49 vs 40-44	1.89 (1.41-2.55)	1.90 (1.45-2.53)	1.88 (1.44-2.45)
50-54	3.81 (2.70-5.46)	5.31 (3.77-7.65)	6.80 (4.69-10.17)	50-54 vs 45-49	1.27 (0.99-1.63)	1.44 (1.16-1.78)	1.35 (1.10-1.65)
55-59	4.60 (3.25-6.63)	5.65 (3.99-8.17)	7.69 (5.30-11.49)	55-59 vs 50-54	1.21 (0.94-1.55)	1.06 (0.87-1.31)	1.13 (0.94-1.36)
60-64	3.86 (2.65-5.70)	5.53 (3.85-8.09)	8.70 (5.98-13.03)	60-64 vs 55-59	0.84 (0.63-1.12)	0.98 (0.78-1.23)	1.13 (0.94-1.36)
65-69	5.57 (3.87-8.14)	6.75 (4.68-9.92)	11.02 (7.56-16.54)	65-69 vs 60-64	1.44 (1.06-1.97)	1.22 (0.94-1.58)	1.27 (1.04-1.54)
70-74	5.73 (3.93-8.45)	7.21 (4.95-10.69)	9.69 (6.53-14.76)	70-74 vs 65-69	1.03 (0.75-1.40)	1.07 (0.81-1.41)	0.88 (0.70-1.10)
75-79	4.87 (3.23-7.40)	6.69 (4.48-10.11)	8.90 (5.89-13.81)	75-79 vs 70-74	0.85 (0.59-1.21)	0.93 (0.67-1.27)	0.92 (0.69-1.22)
80-84	5.30 (3.38-8.27)	5.95 (3.81-9.32)	9.51 (6.13-15.00)	80-84 vs 75-79	1.09 (0.71-1.66)	0.89 (0.60-1.31)	1.07 (0.76-1.49)
85 +	4.52 (2.78-7.28)	5.44 (3.42-8.65)	6.76 (4.24-10.91)	85+ vs 80-84	0.85 (0.52-1.39)	0.91 (0.58-1.43)	0.71 (0.48-1.05)
Hispanic							
35-39	Ref	Ref	Ref				
40-44	2.21 (1.24-4.06)	2.30 (1.35-4.01)	2.89 (1.77-4.89)	40-44 vs 35-39	2.21 (1.24-4.06)	2.30 (1.35-4.01)	2.89 (1.77-4.89)
45-49	5.47 (3.27-9.59)	6.64 (4.18-11.01)	4.34 (2.70-7.22)	45-49 vs 40-44	2.48 (1.65-3.78)	2.89 (2.03-4.18)	1.50 (1.07-2.12)
50-54	8.28 (5.00-14.40)	9.46 (5.99-15.62)	10.33 (6.66-16.75)	50-54 vs 45-49	1.51 (1.10-2.09)	1.43 (1.10-1.85)	2.38 (1.82-3.14)
55-59	12.24 (7.43-21.19)	13.60 (8.65-22.37)	16.18 (10.50-26.09)	55-59 vs 50-54	1.48 (1.10-1.99)	1.44 (1.13-1.83)	1.57 (1.27-1.93)

60-64	15.75 (9.54-27.33)	16.44 (01.41-27.13)	16.99 (10.95-27.52)	60-64 vs 55-59	1.29 (0.96-1.73)	1.21 (0.95-1.54)	1.05 (0.85-1.29)
65-69	17.06 (10.25-29.78)	18.59 (11.67-30.89)	20.37 (13.08-33.10)	65-69 vs 60-64	1.08 (0.79-1.47)	1.13 (0.87-1.47)	1.20 (0.96-1.50)
70-74	19.56 (11.70-34.27)	23.77 (14.92-39.51)	19.46 (12.30-32.04)	70-74 vs 65-69	1.15 (0.83-1.59)	1.28 (0.97-1.69)	0.96 (0.74-1.23)
75-79	25.68 (15.35-45.04)	19.70 (12.03-33.46)	31.33 (19.96-51.24)	75-79 vs 70-74	1.31 (0.94-1.84)	0.83 (0.60-1.13)	1.61 (1.23-2.11)
80-84	24.28 (13.89-44.04)	27.71 (16.88-47.17)	30.44 (19.03-50.55)	80-84 vs 75-79	0.95 (0.64-1.39)	1.41 (0.99-2.00)	0.97 (0.73-1.29)
85 +	22.56 (12.46-41.99)	19.15 (11.01-34.08)	24.63 (15.12-41.49)	85+ vs 80-84	0.93 (0.57-1.49)	0.69 (0.45-1.05)	0.81 (0.58-1.13)

N/A Statistic not displayed due to fewer than 16 cases.

Supplementary Table 3. Trends in Anal Squamous Cell Carcinoma Incidence Rates* During 2001-2015

Characteristic	Trend†							
	1			2			Overall (2001-2015)	
	Year	APC (95% CI)	<i>P</i> Value‡	Year	APC (95% CI)	<i>P</i> Value‡	AAPC (95% CI)	<i>P</i> Value‡
Overall	2001-2009	3.85 (2.95 to 4.76)	<0.001	2009-2015	1.22 (0.08 to 2.37)	0.04	2.71 (2.09 to 3.34)	<0.001
Races								
NHW	2001-2009	4.17 (3.17 to 5.17)	<0.001	2009-2015	1.81 (0.54 to 3.10)	0.01	3.15 (2.45 to 3.85)	<0.001
NHB	2001-2015	2.66 (1.77 to 3.57)	<0.001				2.66 (1.77 to 3.57)	<0.001
Hispanic	2001-2015	0.42 (-0.49 to 1.33)	0.34				0.42 (-0.49 to 1.33)	0.34
Other§	2001-2015	-0.12 (-2.11 to 1.92)	0.90				-0.12 (-2.11 to 1.92)	0.90
Age at diagnosis, y								
<40	2001-2015	-2.17 (-3.61 to -0.72)	0.007				-2.17 (-3.61 to -0.72)	0.007
40-49	2001-2009	3.70 (2.25 to 5.17)	<0.001	2009-2015	-4.45 (-6.54 to -2.31)	0.001	0.13 (-0.97 to 1.23)	0.82
50-59	2001-2009	6.85 (5.22 to 8.51)	<0.001	2009-2015	1.40 (-0.45 to 3.28)	0.12	4.48 (3.40 to 5.57)	<0.001
60-69	2001-2015	4.44 (3.92 to 4.96)	<0.001				4.44 (3.92 to 4.96)	<0.001
≥70	2001-2015	2.34 (1.94 to 2.74)	<0.001				2.34 (1.94 to 2.74)	<0.001
SEER Summary Stage 2000								
Localized	2001-2015	1.88 (1.41 to 2.36)	<0.001				1.88 (1.41 to 2.36)	<0.001
Regional	2001-2007	7.98 (4.86 to 11.21)	<0.001	2007-2015	1.94 (0.47 to 3.43)	0.02	4.49 (3.11 to 5.88)	<0.001
Distant	2001-2005	14.73 (6.93 to 23.09)	0.001	2005-2015	4.83 (3.56 to 6.11)	<0.001	7.57 (5.51 to 9.66)	<0.001
Unknown	2001-2013	-0.45 (-1.20 to 0.32)	0.22	2013-2015	-9.09 (-20.27 to 3.67)	0.14	-1.73 (-3.43 to 0.00)	0.05

Abbreviations: APC, annual percentage change; AAPC, average annual percentage change;

* Rates were calculated as number of cases per 100 000 person-years and age adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint).

‡ Statistical significance was determined when the APCs and AAPCs are significantly different from zero at the $\alpha=0.05$ level

§ Others include Asian/Pacific Islander, American Indian/Alaskan Native, and other.

Supplementary Table 4. Trends in Anal Squamous Cell Carcinoma Incidence Rates* During 2001-2015 among Men

Characteristic	Trend†										
	1			2			3			Overall (2001-2015)	
	Year	APC (95% CI)	P Value‡	Year	APC (95% CI)	P Value‡	Year	APC (95% CI)	P Value‡	AAPC (95% CI)	P Value‡
Men (Overall)	2001-2009	3.65 (2.14 to 5.19)	<0.001	2009-2015	0.27 (-1.67 to 2.25)	0.76				2.19 (1.13 to 3.26)	<0.001
Race/Ethnicity											
NHW	2001-2015	2.33 (1.65 to 3.01)	<0.001							2.33 (1.65 to 3.01)	<0.001
NHB	2001-2015	2.82 (1.32 to 4.35)	0.001							2.82 (1.32 to 4.35)	0.001
Hispanic	2001-2015	0.64 (-0.82 to 2.12)	0.36							0.64 (-0.82 to 2.12)	0.36
Other§	2002-2015	-1.50 (-3.78 to 0.83)	0.18							-1.50 (-3.78 to 0.83)	0.18
Age at diagnosis, y											
<40	2001-2015	-2.86 (-4.44 to -1.25)	0.002							-2.86 (-4.44 to -1.25)	0.002
40-49	2001-2009	5.47 (3.47 to 7.51)	<0.001	2009-2015	-8.77 (-3.19 to -4.66)	<0.001				0.38 (-1.09 to 1.88)	0.61
50-59	2001-2015	4.20 (3.16 to 5.24)	<0.001							4.20 (3.16 to 5.24)	<0.001
60-69	2001-2015									2.68 (1.70 to 3.67)	<0.001
≥70	2001-2004	11.68 (1.01 to 23.47)	0.04	2004-2008	-1.80 (-10.16 to 7.33)	0.64	2008-2015	3.85 (1.65 to 6.09)	0.004	3.81 (0.84 to 6.86)	0.01
SEER Summary Stage 2000											
Localized	2001-2015	1.30 (0.63 to 1.98)	0.001							1.30 (0.63 to 1.98)	0.001
Regional	2001-2005	12.09 (2.32 to 22.79)	0.02	2005-2015	1.84 (0.09 to 3.63)	0.04				4.67 (2.05 to 7.36)	<0.001

Distant	2001-2004	22.13 (4.60 to 42.60)	0.02	2004-2015	5.23 (3.78 to 6.69)	<0.001				8.64 (5.35 to 12.03)	<0.001
Unknown	2001-2015	-1.20 (-2.18 to -0.21)	0.02							-1.20 (-2.18 to -0.21)	0.02

Abbreviations: APC, annual percentage change; AAPC, average annual percentage change;

* Rates were calculated as number of cases per 100 000 person-years and age adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint).

‡ Statistical significance was determined when the APCs and AAPCs are significantly different from zero at the $\alpha=0.05$ level

§ Others include Asian/Pacific Islander, American Indian/Alaskan Native, and other.

|| The overall time period is 2002-2015 for other men.

Supplementary Table 5. Trends in Anal Squamous Cell Carcinoma Incidence Rates* During 2001-2015 among Women

Characteristic	Trend†							
	1			2			Overall (2001-2015)	
	Year	APC (95% CI)	P Value‡	Year	APC (95% CI)	P Value‡	AAPC (95% CI)	P Value‡
Women (Overall)	2001-2009	4.08 (3.30 to 4.88)	<0.001	2009-2015	1.83 (0.84 to 2.83)	0.002	3.11 (2.57 to 3.66)	<0.001
Races								
NHW	2001-2009	4.65 (3.73 to 5.57)	<0.001	2009-2015	2.44 (1.29 to 3.61)	0.001	3.70 (3.06 to 4.34)	<0.001
NHB	2001-2015	2.57 (1.67 to 3.49)	<0.001				2.57 (1.67 to 3.49)	<0.001
Hispanic	2001-2015	0.42 (-0.42 to 1.27)	0.30				0.42 (-0.42 to 1.27)	0.30
Other§	2002-2015	-0.23 (-2.49 to 2.09)	0.84				-0.23 (-2.49 to 2.09)	0.84
Age at diagnosis, y								
<40	2001-2015	-1.30 (-3.16 to 0.59)	0.16				-1.30 (-3.16 to 0.59)	0.16
40-49	2001-2009	2.29 (0.37 to 4.25)	0.02	2009-2015	-3.08 (-5.96 to -0.12)	0.04	-0.05 (-1.52 to 1.45)	0.95
50-59	2001-2007	8.85 (6.23 to 11.53)	<0.001	2007-2015	2.17 (0.99 to 3.38)	0.002	4.98 (3.84 to 6.13)	<0.001
60-69	2001-2015	5.34 (4.78 to 5.90)	<0.001				5.34 (4.78 to 5.90)	<0.001
≥70	2001-2015	2.45 (1.96 to 2.92)	<0.001				2.45 (1.96 to 2.92)	<0.001
SEER Summary Stage 2000								
Localized	2001-2015	2.29 (1.81 to 2.78)	<0.001				2.29 (1.81 to 2.78)	<0.001
Regional	2001-2008	7.40 (5.34 to 9.51)	<0.001	2008-2015	2.00 (0.49 to 3.53)	0.01	4.67 (3.55 to 5.80)	<0.001
Distant	2001-2005	14.32 (4.34 to 25.27)	0.009	2005-2015	4.89 (3.23 to 6.57)	<0.001	7.50 (4.84 to 10.23)	<0.001
Unknown	2001-2009	0.86 (-1.10 to 2.86)	0.36	2009-2015	-3.46 (-6.31 to -0.52)		-1.02 (-2.49 to 0.48)	0.18

Abbreviations: APC, annual percentage change; AAPC, average annual percentage change;

* Rates were calculated as number of cases per 100 000 person-years and age adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint).

‡ Statistical significance was determined when the APCs and AAPCs are significantly different from zero at the $\alpha=0.05$ level

§ Others include Asian/Pacific Islander, American Indian/Alaskan Native, and other.

Supplementary Table 6. Trends in Observed Anal Cancer Mortality Rate* During 2001-2016 in the United States

Characteristic	Trend†							
	1			2			Overall (2001-2016)	
	Year	APC (95% CI)	P Value‡	Year	APC (95% CI)	P Value‡	AAPC (95% CI)	P Value‡
Overall	2001-2016	3.07 (2.59 to 3.55)	<0.001				3.07 (2.59 to 3.55)	<0.001
Sex								
Men	2001-2016	3.44 (2.63 to 4.27)	<0.001				3.44 (2.63 to 4.27)	<0.001
Women	2001-2016	2.94 (2.28 to 3.60)	<0.001				2.94 (2.28 to 3.60)	<0.001
Race/Ethnicity								
NHW	2001-2016	3.32 (2.79 to 3.85)	<0.001				3.32 (2.79 to 3.85)	<0.001
NHB	2001-2016	3.17 (2.10 to 4.25)	<0.001				3.17 (2.10 to 4.25)	<0.001
Hispanic	2001-2016	2.45 (0.58 to 4.35)	0.01				2.45 (0.58 to 4.35)	0.01
Others§	2001-2016	-0.15 (-5.17 to 5.14)	0.95				-0.15 (-5.17 to 5.14)	0.95
Age at death, y								
<40	2001-2016	-0.79 (-3.49 to 1.98)	0.55				-0.79 (-3.49 to 1.98)	0.55
40-49	2001-2009	5.39 (1.61 to 9.31)	0.009	2009-2015	-2.40 (-6.49 to 1.87)	0.24	1.68 (-0.81 to 4.24)	0.19
50-59	2001-2016	3.64 (2.60 to 4.70)	<0.001				3.64 (2.60 to 4.70)	<0.001
60-69	2001-2016	4.89 (3.99 to 5.79)	<0.001				4.89 (3.99 to 5.79)	<0.001
≥70	2001-2016	2.66 (2.13 to 3.19)	<0.001				2.66 (2.13 to 3.19)	<0.001

Abbreviations: APC, annual percentage change; AAPC, average annual percentage change;

* Rates were calculated as number of deaths per 100 000 person-years and age adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint).

‡ Statistical significance was determined when the APCs and AAPCs are significantly different from zero at the $\alpha=0.05$ level

§ Others include Asian/Pacific Islander, American Indian/Alaskan Native, and other.

Supplementary Table 7. Trends in Anal Cancer and Squamous Cell Carcinoma Incidence-based Mortality Rate* During 2001-2016 in the US

Characteristic	Trends†							
	1			2			Overall (2001-2016)	
	Year	APC (95% CI)	P Value‡	Year	APC (95% CI)	P Value‡	AAPC (95% CI)	P Value‡
Anal Cancer	2001-2016	1.78 (0.47 to 3.10)	0.01				1.78 (0.47 to 3.10)	0.01
SCCA	2001-2016	1.91 (0.47 to 3.38)	0.01				1.91 (0.47 to 3.38)	0.01
SCCA by patient characteristics								
Men	2001-2016	2.71 (0.30 to 5.18)	0.03				2.71 (0.30-5.18)	0.03
Women	2001-2016	1.28 (-0.57 to 3.17)	0.16				1.28 (-0.57 to 3.17)	0.16
Race/ethnicity								
NH White	2001-2016	2.07 (0.39 to 3.78)	0.02				2.07 (0.39 to 3.78)	0.02
NH Black	2001-2016	2.15 (-1.44 to 5.88)	0.22				2.15 (-1.44 to 5.88)	0.22
Hispanic	2001-2016	3.20 (-2.30 to 9.02)	0.24				3.20 (-2.30 to 9.02)	0.24
Others§	2001-2016	-0.59 (-6.70 to 5.93)	0.85				-0.59 (-6.70 to 5.93)	0.85
Stage at diagnosis								
Localized	2001-2016	2.64 (-1.04 to 6.46)	0.15				2.64 (-1.04 to 6.46)	0.15
Regional	2001-2007	13.35 (0.68 to 27.60)	0.04	2007-2016	-2.90 (-8.14 to 2.64)	0.27	3.30 (-1.89 to 8.77)	0.22
Distant	2001-2016	1.62 (-1.23 to 4.54)	0.25				1.62 (-1.23 to 4.54)	0.25
Unknown	2001-2016	-0.49 (-4.84 to 4.06)	0.82				-0.49 (-4.84 to 4.06)	0.82
Age at diagnosis								
<40	2001-2016	-2.45 (-8.51 to 4.01)	0.42				-2.45 (-8.51 to 4.01)	0.42
40-49	2001-2016	1.17 (-2.55 to 5.03)	0.52				1.17 (-2.55 to 5.03)	0.52
50-59	2001-2016	2.89 (-0.55 to 6.46)	0.09				2.89 (-0.55 to 6.46)	0.09
60-69	2001-2016	4.95 (2.24 to 7.73)	0.001				4.95 (2.24 to 7.73)	0.001
>70	2001-2016	0.90 (-1.56 to 3.43)	0.45				0.90 (-1.56 to 3.43)	0.45

* Rates were calculated as number of deaths per 100 000 person-years and age adjusted to the 2000 US standard population.

† The calendar period of each segment was defined based on the identification of calendar years when a statistically significant change in the APC occurred (ie, the joinpoint).

‡ Statistical significance was determined when the APCs and AAPCs are significantly different from zero at the $\alpha=0.05$ level

§ Others include Asian/Pacific Islander, American Indian/Alaskan Native, and other.