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**Figure S1.** CONSORT diagram illustrating the patient selection for this study.

**Table S1.** Distribution of HPV indication in the patients with information on HPV status (*n*=5,927).

|  |  |
| --- | --- |
| **HPV status definition** | ***n* (%)** |
| Negative for any type  | 2,404 (40.6) |
| Positive for low-risk types\* | 201 (3.4) |
| Positive for high-risk types other than 16 or 18\*\* | 153 (2.6) |
| Positive for high-risk type 16 without type 18 or type 18 unknown | 961 (16.2) |
| Positive for high-risk type 18 without type 16 or type 16 unknown | 7 (0.1) |
| Positive for high-risk types 16 and 18 | 184 (3.1) |
| Positive for high-risk types, not specified | 356 (6.0) |
| Positive, risk and type not specified | 1,661 (28.0) |

\*Low-risk HPV types tested were HPV 6, 11, 32, 34, 40, 42, 44, 54, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87 and 89

\*\* Other high-risk HPV types tested were HPV 26, 31, 33, 35, 36, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82 and 85

**Table S2.** Univariable Cox proportional hazards regression for overall survival in the unmatched cohort.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Hazard ratio (95% CIs)** | **P-value** |
| HPV status (positive = 1, negative = 0)  | 0.78 (0.69 , 0.88) | **<0.001** |
| Age (≥65y = 1, <65y = 0) | 2.19 (2.10 , 2.28) | **<0.001** |
| Sex (female = 1, male = 0) | 0.77 (0.74 , 0.80) | **<0.001** |
| Race White  Black  Asian Other | 1.0 (ref)1.13 (1.07 , 1.21)1.09 (0.88 , 1.36)0.84 (0.67 , 1.06) | **<0.001** |
| Ethnicity Non-Hispanic  Hispanic  Unknown | 1.0 (ref)0.78 (0.70 , 0.87)0.92 (0.83 , 1.02) | **<0.001** |
| Charlson-Deyo co-morbidity score 0  1  ≥2 | 1.0 (ref)1.65 (1.56 , 1.75)1.96 (1.84 , 2.10) | **<0.001** |
| T Stage T1 T2 T3 T4 | 1.0 (ref)1.63 (1.52 , 1.76)2.61 (2.42 , 2.82)3.08 (2.80 , 3.39) | **<0.001** |
| N Stage N0 N1 N2 N3 | 1.0 (ref)1.48 (1.37 , 1.60)1.73 (1.61 , 1.85)2.27 (2.10 , 2.44) | **<0.001** |
| Primary tumor site, n (%) Unspecified anus  Anal canal Cloacogenic zone Overlap rectum/anus/anal canal | 1.0 (ref)0.87 (0.83 , 0.91)1.08 (0.86 , 1.35)1.25 (1.17 ,1.33) | **<0.001** |
| Tumor size, n (%) <2cm  2-3.9cm 4-5.9cm ≥6cm | 1.0 (ref)1.52 (1.40 , 1.64)2.07 (1.91 , 2.24)2.96 (2.72 , 3.22) | **<0.001** |
| Systemic therapy None  Single agent  Multi agent Unknown type and number | 1.0 (ref)1.39 (1.29 , 1.49)0.87 (0.83 , 0.91)1.00 (0.91 , 1.11) | **<0.001** |
| Surgery of primary site (yes = 1, no = 0) | 0.69 (0.66 , 0.72) | **<0.001** |
| Type of facility Community cancer program  Comprehensive community cancer program Academic/Research program Integrated network cancer program | 1.0 (ref)0.92 (0.86 , 0.99)0.82 (0.76 , 0.88)0.86 (0.79 , 0.95) | **<0.001** |
| Median income quartiles Lowest 2nd 3rd Highest | 1.0 (ref)0.96 (0.90 , 1.02)0.85 (0.80 , 0.90)0.73 (0.69 , 0.78) | **<0.001** |

**Table S3.** Multivariable Cox proportional hazards regression for all patients in the matched cohort.

|  |  |
| --- | --- |
|  | **All patients (*n* = 4,206)** |
| **Variable** | **Hazard ratio (95% CIs)** | **P-value** |
| HPV status (positive = 1, negative = 0)  | 0.87 (0.76 , 1.01) | 0.059 |
| Age (≥65y = 1, <65y = 0) | 2.09 (1.81 , 2.41) | **<0.001** |
| Sex (female = 1, male = 0) | 0.65 (0.56 , 0.75) | **<0.001** |
| Race White  Black  Asian Other | 1.0 (ref)1.15 (0.92 , 1.44)0.76 (0.24 , 2.36)1.07 (0.55 , 2.07) | 0.62 |
| Ethnicity Non-Hispanic  Hispanic  Unknown | 1.0 (ref)0.64 (0.44 , 0.94)0.84 (0.53 , 1.33) | 0.059 |
| Charlson-Deyo co-morbidity score 0  1  ≥2 | 1.0 (ref)1.69 (1.40 , 2.03)2.47 (1.99 , 3.07) | **<0.001** |
| Systemic therapy None  Single agent Multi agent Unknown type and number | 1.0 (ref)1.30 (1.00 , 1.68)0.77 (0.63 , 0.95)0.78 (0.50 , 1.19) | **<0.001** |
| Surgery of primary site (yes = 1, no = 0) | 0.49 (0.41 , 0.59) | **<0.001** |
| Type of facility Community cancer program  Comprehensive community cancer program Academic/Research program Integrated network cancer program | 1.0 (ref)0.82 (0.64 , 1.04)0.86 (0.67 , 1.10)0.85 (0.62 , 1.15) | 0.44 |
| Median income quartiles Lowest 2nd 3rd Highest | 1.0 (ref)1.01 (0.81 , 1.26)1.03 (0.83 , 1.27)0.84 (0.68 , 1.05) | 0.15 |



**Figure S2.** Time trends of HPV testing and HPV positivity. Only 23 patients had HPV status reported in 2008 and as such these data are not included because the proportions may be misleading.