

Table S1: Baseline Characteristics by Adjuvant Radiotherapy

Variable	Overall n = 8,375	Did Not Receive Adjuvant Radiotherapy n = 1,108	Received Adjuvant Radiotherapy n = 7,267	p-value
Age (mean, SD)	8,375	60.9 (10.4)	57.9 (9.1)	<0.001
Sex				0.258
Male	7,080	924 (83.4)	6,156 (84.7)	
Female	1,295	184 (16.6)	1,111 (15.3)	
Race				0.068
White	7,723	1,009 (91.1)	6,714 (92.4)	
Black	285	45 (4.1)	240 (3.3)	
Hispanic	178	24 (2.2)	154 (2.1)	
Asian/Pacific Islander	65	5 (0.5)	60 (0.8)	
Primary site				<0.001
Tonsil	6,079	714 (64.4)	5,365 (73.8)	
Base of tongue	1,932	318 (28.7)	1,614 (22.2)	
Other oropharynx	364	76 (6.9)	288 (4.0)	
Tumor Category				0.416
T1	4,319	584 (52.7)	3,735 (51.4)	
T2	4,056	524 (47.3)	3,532 (48.6)	
Nodal Category				<0.001
N0	809	215 (19.4)	594 (8.2)	
N1	6,755	797 (71.9)	5,958 (82.0)	
N2	421	36 (3.3)	385 (5.3)	
N3	340	48 (4.3)	292 (4.0)	
Tumor Margin Status				<0.001
Negative	3,983	651 (58.8)	3,332 (45.9)	
Positive	4,033	430 (38.8)	3,603 (49.6)	
Unknown	359	27 (2.4)	332 (4.6)	
Lymphovascular Invasion				<0.001
Negative	3,847	462 (41.7)	3,385 (46.6)	
Positive	2,809	489 (44.1)	2,320 (31.9)	
Unknown	1,719	157 (14.2)	1,562 (21.5)	
Extranodal Extension				<0.001
Negative	2,453	464 (41.9)	1,989 (27.4)	
Positive	3,238	386 (34.8)	2,852 (39.3)	
Unknown	2,684	258 (23.3)	2,426 (33.4)	
Level 4/5 Lymph Node				0.024
Negative	6,224	841 (75.9)	5,383 (74.1)	
Positive	1,710	197 (17.8)	1,513 (20.8)	
Unknown	441	70 (6.3)	371 (5.1)	
Charlson-Deyo Comorbidity Score				<0.001
0	6,836	852 (76.9)	5,984 (82.3)	
1	1,147	174 (15.7)	973 (13.4)	
2	251	47 (4.2)	204 (2.8)	
3	141	35 (3.2)	106 (1.5)	
Primary Payor				<0.001
Not Insured	186	33 (3.0)	153 (2.1)	
Private	5,330	581 (52.4)	4,749 (65.4)	
Medicaid / Medicare / Gov.	2,766	479 (43.2)	2,287 (31.5)	
Median Household Income				0.122
> \$63,000	2,888	366 (37.2)	2,522 (40.5)	
\$48,000 - 62,999	1,986	275 (28.0)	1,711 (27.5)	
\$38,000 - 47,999	1,493	208 (21.2)	1,285 (20.6)	
< \$38,000	849	134 (13.6)	715 (11.5)	

Table S2: Cox Proportional Hazards Analysis of Patients with HPV-OPC

		Unadjusted Analysis			Adjusted Analyses															
		n=15,036			Any AF (n=12,780)			PSM (n=12,780)			ENE (n=12,780)			LVI (n=12,780)			LN4/5 (n=12,780)			
		HR	95% CI	p-value	aHRA _F	95% CI	p-value	aHR _{PSM}	95% CI	p-value	aHR _{ENE}	95% CI	p-value	aHR _{LVI}	95% CI	p-value	aHR _{LN4/5}	95% CI	p-value	
Age		1.057	1.052-1.062	<0.001	1.036	1.030-1.043	<0.001	1.037	1.031-1.043	<0.001	1.036	1.030-1.042	<0.001	1.037	1.031-1.043	<0.001	1.037	1.031-1.043	<0.001	
Sex		Male	1.000	--	--															
		Female	0.982	0.872-1.105	0.760															
Race		White	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		Black	1.712	1.412-2.075	<0.001	1.418	1.148-1.751	0.001	1.416	1.149-1.746	0.001	1.389	1.127-1.713	0.002	1.402	1.138-1.729	0.002	1.425	1.156-1.757	0.001
		Hispanic	0.696	0.488-0.992	0.045	0.709	0.484-1.038	0.077	0.683	0.466-1.000	0.050	0.684	0.467-1.002	0.051	0.667	0.456-0.977	0.038	0.689	0.470-1.009	0.055
		Asian/Pacific Islander	1.169	0.753-1.817	0.487	1.341	0.831-2.165	0.230	1.303	0.818-2.077	0.265	1.297	0.814-2.067	0.274	1.276	0.801-2.032	0.305	1.282	0.805-2.042	0.296
Primary site		Tonsil	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		Base of tongue	1.014	0.913-1.127	0.791	0.868	0.772-0.976	0.018	0.904	0.804-1.016	0.090	0.902	0.802-1.015	0.086	0.863	0.768-0.969	0.013	0.854	0.760-0.959	0.008
		Other oropharynx	1.706	1.432-2.032	<0.001	1.336	1.107-1.611	0.002	1.359	1.127-1.639	0.001	1.278	1.059-1.542	0.010	1.323	1.098-1.595	0.003	1.315	1.091-1.585	0.004
Tumor category		T1	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		T2	1.400	1.282-1.529	<0.001	1.287	1.169-1.417	<0.001	1.286	1.168-1.416	<0.001	1.313	1.193-1.445	<0.001	1.290	1.172-1.420	<0.001	1.313	1.193-1.445	<0.001
Nodal category		N0	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		N1	0.671	0.602-0.748	<0.001	0.783	0.691-0.888	<0.001	0.882	0.780-0.998	0.046	0.914	0.802-1.042	0.179	0.822	0.725-0.931	0.002	0.796	0.701-0.903	<0.001
		N2	1.208	0.989-1.475	0.064	1.468	1.170-1.843	0.001	1.606	1.284-2.007	<0.001	1.580	1.263-1.978	<0.001	1.561	1.248-1.953	<0.001	1.423	1.132-1.789	0.003
		N3	1.327	1.059-1.661	0.014	1.383	1.074-1.780	0.012	1.765	1.381-2.257	<0.001	1.677	1.299-2.165	<0.001	1.576	1.231-2.019	<0.001	1.432	1.113-1.843	0.005
		Unknown	1.178	0.725-1.912	0.509	1.036	0.582-1.843	0.905	1.069	0.614-1.861	0.815	0.972	0.558-1.693	0.921	1.169	0.671-2.034	0.582	1.095	0.627-1.911	0.751
Adverse features		No	1.000	--	--	1.000	--	--												
		Yes	1.438	1.312-1.576	<0.001	1.559	1.404-1.732	<0.001												
PSM		Negative	1.000	--	--				1.000	--	--									
		Positive	1.490	1.354-1.640	<0.001				1.572	1.412-1.750	<0.001									
		Unknown	1.291	1.116-1.494	0.001				1.270	1.081-1.491	0.004									
ENE		Negative	1.000	--	--						1.000	--	--							
		Positive	1.785	1.585-2.010	<0.001						1.744	1.524-1.995	<0.001							
		Unknown	1.882	1.696-2.089	<0.001						1.844	1.639-2.074	<0.001							
LVI		Negative	1.000	--	--									1.000	--	--				
		Positive	1.535	1.376-1.711	<0.001									1.450	1.285-1.637	<0.001				
		Unknown	1.109	0.997-1.234	0.058									1.169	1.042-1.311	0.008				
LN4/5		Negative	1.000	--	--												1.000	--	--	
		Positive	1.625	1.443-1.830	<0.001												1.626	1.422-1.861	<0.001	
		Unknown	1.170	0.972-1.408	0.097												1.215	0.993-1.488	0.059	
Adjuvant radiation		No	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		Yes	0.624	0.565-0.688	<0.001	0.689	0.613-0.774	<0.001	0.673	0.598-0.757	<0.001	0.641	0.569-0.721	<0.001	0.742	0.661-0.833	<0.001	0.747	0.666-0.838	<0.001
Charlson-Deyo Comorbidity score		0	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		1	1.864	1.668-2.084	<0.001	1.505	0.582-1.843	<0.001	1.505	1.334-1.698	<0.001	1.514	1.342-1.709	<0.001	1.514	1.342-1.709	<0.001	1.511	1.339-1.707	<0.001
		2	3.109	2.592-3.729	<0.001	1.953	1.598-2.387	<0.001	1.971	1.614-2.407	<0.001	1.973	1.616-2.409	<0.001	1.963	1.607-2.397	<0.001	1.978	1.620-2.415	<0.001
		3	4.866	3.930-6.024	<0.001	3.070	2.433-3.875	<0.001	3.054	2.425-3.848	<0.001	2.980	2.364-3.756	<0.001	3.005	2.384-3.788	<0.001	3.061	2.429-3.858	<0.001
Primary payor		Private	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		Medicare/Medicaid/Gov.	2.999	2.739-3.284	<0.001	1.721	1.531-1.934	<0.001	1.715	1.526-1.927	<0.001	1.715	1.526-1.926	<0.001	1.713	1.525-1.925	<0.001	1.709	1.521-1.921	<0.001
		Not insured	2.204	1.685-2.884	<0.001	2.099	1.575-2.797	<0.001	2.053	1.540-2.736	<0.001	2.053	1.497-2.657	<0.001	2.056	1.543-2.739	<0.001	2.107	1.582-2.807	<0.001
Median Household Income		> 63000	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
		48,000 - 62,999	1.396	1.236-1.578	<0.001	1.228	1.085-1.389	0.001	1.233	1.090-1.395	0.001	1.226	1.084-1.387	0.001	1.243	1.099-1.406	0.001	1.245	1.101-1.409	<0.001
		38,000 - 47,999	1.600	1.409-1.818	<0.001	1.321	1.160-1.504	<0.001	1.311	1.152-1.492	<0.001	1.291	1.133-1.470	<0.001	1.337	1.174-1.521	<0.001	1.333	1.171-1.517	<0.001
		<38,000	2.001	1.734-2.309	<0.001	1.550	1.336-1.799	<0.001	1.551	1.337-1.799	<0.001	1.529	1.317-1.774	<0.001	1.571	1.354-1.823	<0.001	1.542	1.329-1.789	<0.001

Table S3: Cox Proportional Hazards Analysis in Patients with AF-positive HPV-OPC

		Unadjusted Analysis			Adjusted Analyses														
		n=8,375			Any AF n=7,103			PSM n=7,103			ENE n=7,103			LVI n=7,103			LN4/5 n=7,103		
		HR	95% CI	p-value	aHR _{AF}	95% CI	p-value	aHR _{PSM}	95% CI	p-value	aHR _{ENE}	95% CI	p-value	aHR _{LVI}	95% CI	p-value	aHR _{LN4/5}	95% CI	p-value
Age		1.050	1.044-1.056	<0.001	1.030	1.023-1.038	<0.001	1.030	1.023-1.038	<0.001	1.030	1.022-1.037	<0.001	1.030	1.023-1.038	<0.001	1.031	1.023-1.038	<0.001
Sex	Male	1.000	--	--															
	Female	1.028	0.885-1.195	0.714															
Race	White	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	Black	1.578	1.222-2.037	<0.001	1.356	1.027-1.792	0.032	1.354	1.025-1.789	0.033	1.376	1.042-1.818	0.025	1.344	1.017-1.776	0.037	1.367	1.035-1.806	0.028
	Hispanic	0.734	0.461-1.169	0.192	0.776	0.480-1.255	0.302	0.778	0.481-1.259	0.307	0.790	0.488-1.278	0.336	0.763	0.472-1.234	0.270	0.796	0.492-1.288	0.353
	Asian/Pacific Islander	1.115	0.616-2.018	0.720	1.417	0.759-2.647	0.274	1.410	0.755-2.634	0.281	1.410	0.755-2.634	0.282	1.406	0.753-2.626	0.285	1.416	0.758-2.644	0.275
Primary Site	Tonsil	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	Base of tongue	0.913	0.796-1.046	0.189	0.799	0.687-0.929	0.004	0.832	0.715-0.969	0.018	0.839	0.720-0.978	0.025	0.797	0.686-0.927	0.003	0.790	0.679-0.918	0.002
	Other oropharynx	1.552	1.227-1.965	<0.001	1.252	0.976-1.607	0.077	1.275	0.993-1.637	0.057	1.260	0.981-1.618	0.070	1.238	0.964-1.589	0.094	1.226	0.956-1.574	0.109
T Stage	T1	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	T2	1.448	1.296-1.619	<0.001	1.349	1.195-1.523	<0.001	1.339	1.186-1.512	<0.001	1.334	1.182-1.505	<0.001	1.332	1.180-1.505	<0.001	1.350	1.196-1.524	<0.001
N Stage	N0	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	N1	0.646	0.548-0.762	<0.001	0.800	0.672-0.953	0.013	0.868	0.725-1.039	0.122	0.883	0.731-1.067	0.198	0.795	0.667-0.948	0.010	0.731	0.611-0.875	0.001
	N2	1.233	0.965-1.575	0.094	1.665	1.277-2.172	<0.001	1.719	1.315-2.248	<0.001	1.709	1.305-2.237	<0.001	1.641	1.258-2.141	<0.001	1.423	1.081-1.872	0.012
	N3	1.082	0.820-1.428	0.579	1.272	0.943-1.714	0.115	1.410	1.039-1.912	0.027	1.373	1.004-1.877	0.047	1.262	0.936-1.702	0.128	1.097	0.808-1.489	0.553
	Unknown	0.773	0.363-1.647	0.505	0.594	0.220-1.605	0.304	0.569	0.211-1.538	0.267	0.528	0.195-1.427	0.208	0.617	0.228-1.669	0.342	0.563	0.208-1.526	0.259
PSM	Negative	1.000	--	--				1.000	--	--									
	Positive	1.284	1.145-1.439	<0.001				1.323	1.162-1.507	<0.001									
	Unknown	1.361	1.054-1.759	0.018				1.486	1.127-1.960	0.005									
ENE	Negative	1.000	--	--							1.000	--	--						
	Positive	1.477	1.273-1.713	<0.001							1.409	1.198-1.656	<0.001						
	Unknown	1.723	1.484-2.001	<0.001							1.680	1.423-1.983	<0.001						
LVI	Negative	1.000	--	--										1.000	--	--			
	Positive	1.328	1.173-1.503	<0.001										1.176	1.027-1.348	0.019			
	Unknown	1.101	0.950-1.277	0.202										1.157	0.988-1.355	0.070			
LN4/5	Negative	1.000	--	--													1.000	--	--
	Positive	1.438	1.266-1.632	<0.001													1.420	1.231-1.639	<0.001
	Unknown	1.296	1.029-1.632	0.027													1.235	0.953-1.599	0.111
Adjuvant Radiation	No	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	Yes	0.484	0.422-0.554	<0.001	0.595	0.513-0.691	<0.001	0.564	0.485-0.657	<0.001	0.556	0.478-0.647	<0.001	0.602	0.518-0.700	<0.001	0.598	0.515-0.694	<0.001
Charlson-Deyo Comorbidity Score	0	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	1	1.774	1.541-2.042	<0.001	1.422	1.220-1.657	<0.001	1.425	1.223-1.661	<0.001	1.425	1.223-1.660	<0.001	1.422	1.221-1.657	<0.001	1.424	1.222-1.660	<0.001
	2	2.793	2.212-3.525	<0.001	1.775	1.368-2.302	<0.001	1.767	1.362-2.294	<0.001	1.786	1.377-2.317	<0.001	1.762	1.358-2.286	<0.001	1.781	1.373-2.311	<0.001
	3	4.301	3.296-5.612	<0.001	2.838	2.123-3.794	<0.001	2.847	2.130-3.807	<0.001	2.868	2.145-3.837	<0.001	2.803	2.096-3.748	<0.001	2.839	2.122-3.796	<0.001
Primary Payor	Private	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	Medicare/Medicaid/Gov.	2.821	2.518-3.160	<0.001	1.803	1.560-2.084	<0.001	1.802	1.559-2.082	<0.001	1.803	1.560-2.083	<0.001	1.800	1.557-2.081	<0.001	1.787	1.546-2.067	<0.001
	Not insured	2.419	1.748-3.348	<0.001	2.283	1.619-3.218	<0.001	2.240	1.588-3.160	<0.001	2.217	1.572-3.128	<0.001	2.258	1.601-3.184	<0.001	2.312	1.640-3.260	<0.001
Median Household Income	> 63000	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--	1.000	--	--
	48,000 - 62,999	1.509	1.297-1.755	<0.001	1.343	1.153-1.565	<0.001	1.335	1.146-1.556	<0.001	1.328	1.140-1.547	<0.001	1.348	1.157-1.570	<0.001	1.348	1.157-1.570	<0.001
	38,000 - 47,999	1.566	1.332-1.841	<0.001	1.305	1.107-1.539	0.002	1.290	1.094-1.521	0.002	1.286	1.091-1.517	0.003	1.308	1.109-1.542	0.001	1.303	1.106-1.537	0.002
	<38,000	1.913	1.592-2.297	<0.001	1.479	1.224-1.788	<0.001	1.471	1.217-1.778	<0.001	1.452	1.202-1.756	<0.001	1.488	1.232-1.799	<0.001	1.453	1.202-1.756	<0.001

Table S4 - Baseline Characteristics of the Propensity Score Matched Cohort

		Overall HPV-OPC n= 1,678	No Adjuvant Radiotherapy n=460	Adjuvant Radiotherapy n=1,218	p-value
Age mean (SD)		61.6 (9.5)	62.5 (10.0)	61.2 (9.3)	0.011
Race	White	1,540 (91.8)	420 (91.3)	1,120 (92.0)	0.962
	Black	88 (5.2)	25 (5.4)	63 (5.2)	
	Hispanic	41 (2.4)	12 (2.6)	29 (2.4)	
	Asian/Pacific Islander	9 (0.5)	3 (0.7)	6 (0.5)	
Primary site	Tonsil	1031 (61.4)	268 (58.3)	763 (62.6)	0.254
	Base of tongue	557 (33.2)	166 (36.1)	391 (32.1)	
	Other oropharynx	90 (5.4)	26 (5.7)	64 (5.3)	
T Stage	T1	879 (52.4)	235 (51.1)	644 (52.9)	0.513
	T2	799 (47.6)	225 (48.9)	574 (47.1)	
N Stage	N0	178 (10.6)	87 (18.9)	91 (7.5)	<0.001
	N1	1,401 (83.5)	349 (75.9)	1,052 (86.4)	
	N2	40 (2.4)	8 (1.7)	32 (2.6)	
	N3	59 (3.5)	16 (3.5)	43 (3.5)	
Primary Payor	Private insurance	813 (48.5)	210 (45.7)	603 (49.5)	0.362
	Medicare/Medicaid/Gov.	812 (48.4)	234 (50.9)	578 (47.5)	
	Not insured	53 (3.2)	16 (3.5)	37 (3.0)	
Median Household Income	> \$63,000	564 (33.6)	143 (31.1)	421 (34.6)	0.559
	\$48,000 - \$62,999	477 (28.4)	138 (30.0)	339 (27.8)	
	\$38,000 - \$47,999	378 (22.5)	104 (22.6)	274 (22.5)	
	< \$38,000	259 (15.4)	75 (16.3)	184 (15.1)	
Charlson Deyo Score	0	1,286 (76.6)	346 (75.2)	940 (77.2)	0.835
	1	291 (17.3)	86 (18.7)	205 (16.8)	
	2	48 (2.9)	13 (2.8)	35 (2.9)	
	3	53 (3.2)	15 (3.3)	38 (3.1)	
Tumor Margin Status	Negative	1,255 (74.8)	349 (75.9)	906 (74.4)	0.532
	Positive	423 (25.2)	111 (24.1)	312 (25.6)	
Lymphovascular Invasion	Negative	798 (47.6)	212 (46.1)	586 (48.1)	0.459
	Positive	880 (52.4)	248 (53.9)	632 (51.9)	
Extranodal Extension	Negative	993 (59.2)	287 (62.4)	706 (58.0)	0.100
	Positive	685 (40.8)	173 (37.6)	512 (42.0)	
Level 4/5 Lymph Node	Negative	1,300 (77.5)	365 (79.4)	935 (76.8)	0.259
	Positive	378 (22.5)	95 (20.7)	283 (23.2)	

Figure S1. Patient Inclusion and Analytic Approach

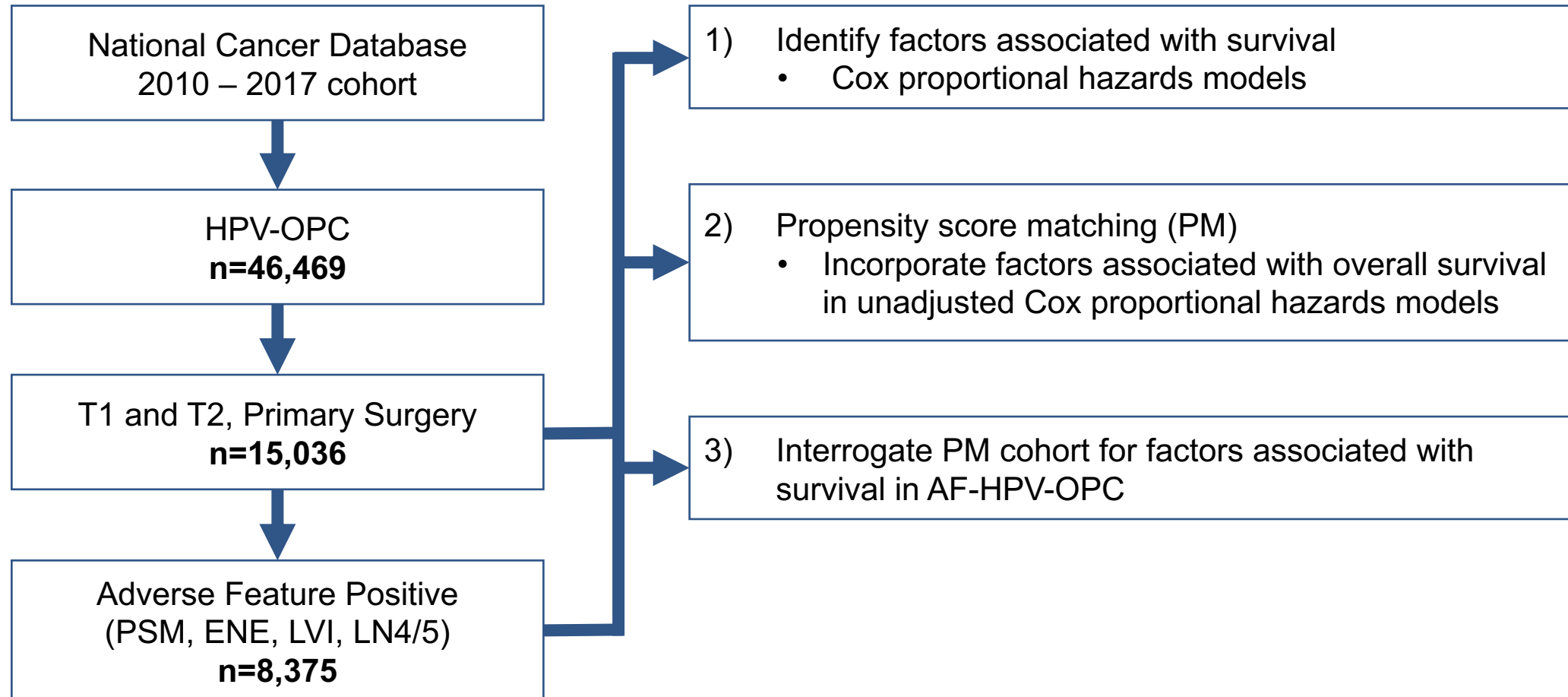


Figure S2. Propensity Score Matching Plot

