

## Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

**eTable 1. Optimal Hyperparameters, DeepSurv and N-MTLR Models**

<b>Parameter</b>	<b>DeepSurv Model</b>	<b>N-MTLR Model</b>
<b>Neural Network Structure (Layer: activation; nodes)</b>	1: LeCun Tanh; 64 2: Sinc; 128 3: Log Sigmoid; 32 4: Inverse Square Root; 128 5: Swish; 16	1: Sinc; 32 2: Sigmoid; 32 3: Log Log; 8 4: Arc Tan; 8
<b>Learning Rate</b>	0.00001	0.0001
<b>Number of Epochs</b>	6000	4000
<b>Dropout</b>	0.1	0.1
<b>L2 Regularization</b>	0.0001	0.001
<b>Batch Normalization</b>	False	False
<b>L2 Smoothing Regularization</b>		0.001
<b>Bins</b>		100

**eTable 2. Optimal Hyperparameters, Random Survival Forest**

<b>Parameter</b>	<b>Random Survival Forest Model</b>
<b>Trees</b>	80
<b>Max Features</b>	0.1
<b>Max Depth</b>	40
<b>Min Node Size</b>	80
<b>Sample Size Percent</b>	60%
<b>Importance Mode</b>	Permutation

**eTable 3. Missing Values for Features in the Final Data Set, Prior to Imputation**

	<b>Number Missing (% Total)</b>
<b>Gender</b>	0 (0)
<b>Age</b>	0 (0)
<b>Year of Diagnosis</b>	0 (0)
<b>Ethnicity</b>	279 (0.8)
<b>Academic Center</b>	1,199 (3.6)
<b>Charlson/Deyo Score</b>	0 (0)
<b>Status At Last Contact</b>	0 (0)
<b>Primary Site</b>	0 (0)
<b>Tumor stage</b>	0 (0)
<b>Nodal Stage</b>	0 (0)
<b>Measured Tumor Size</b>	5,027 (15.0)
<b>Tumor Thickness (n, % of oral cavity cancers)<sup>a</sup></b>	9,670 (61.1)
<b>Differentiation</b>	2,518 (7.5)
<b>LVI</b>	15,969 (47.6)
<b>Lymph Nodes Positive</b>	4,465 (13.3)
<b>Lymph Node Levels Involved</b>	
I, II, III	2,211 (6.6)
IV, V, Retropharyngeal	2,269 (6.8)
Parapharyngeal	2,227 (6.6)
<b>HPV Positivity<sup>b</sup></b>	
Oropharynx	5,972 (53.5)

Non-oropharynx	18,182 (81.3)
<b>Multiagent Chemotherapy</b>	1,581 (0)
<b>Time from Surgery to Completion of RT</b>	1,508 (4.7)
<b>RT Dose</b>	0 (0)
<b>Adequate Lymph Node Dissection (18+ Nodes Examined)</b>	79 (0.2)

<sup>a</sup>For tumor thickness, percent missing is calculated as a percentage of oral cavity cancers

<sup>b</sup>For HPV positivity, percent missing values are calculated as a percentage of total oropharynx cancers, and as a percentage of total non-oropharynx cancers.

**eTable 4. Permutation Feature Importance**

**Given as % decrease in concordance index with permutation.** A high reduction in concordance index with variable permutation indicates that feature is important in prediction of prognosis.

<b>Feature</b>	<b>DeepSurv</b>	<b>N-MTLR</b>	<b>RSF</b>	<b>Average</b>
<b>Life Expectancy</b>	4.0922	4.4706	4.5369	4.3666
<b>Year of Diagnosis 2013 - 2016</b>	2.4761	1.5635	2.8574	2.299
<b>Tumor Stage T4</b>	2.3638	2.0986	0.6507	1.7044
<b>HPV+ (Oropharynx)</b>	1.157	1.0594	1.4945	1.237
<b>Tonsillar Subsite</b>	0.8495	1.2884	0.921	1.0196
<b>5-9 Lymph Nodes Positive</b>	1.4671	0.5078	0.5448	0.8399
<b>Tumor Size</b>	0.4326	0.1226	1.644	0.7331
<b>2-4 Lymph Nodes Positive</b>	0.656	0.729	0.2707	0.5519
<b>10+ Lymph Nodes Positive</b>	0.8419	0.6268	0.126	0.5316
<b>Tongue Subsite</b>	0.6829	0.7121	0.0724	0.4892
<b>Tumor Stage T3</b>	0.7585	0.6258	0.0643	0.4828
<b>Charlson/Dayo Score 0-1</b>	0.6489	0.4133	0.1649	0.409
<b>HPV+ (Non-oropharynx)</b>	0.4005	-0.048	0.6712	0.3414
<b>Level II Lymph Nodes Involved</b>	0.1787	0.3874	0.3788	0.315
<b>Larynx primary</b>	0.1357	0.5185	0.1998	0.2847
<b>Floor of Mouth Subsite</b>	0.2739	0.4239	0.1008	0.2662
<b>Nodal Stage N2</b>	0.2095	0.4524	0.00498	0.2223
<b>Adequate Lymph Node Dissection (18+ Nodes Examined)</b>	0.3122	0.227	0.12	0.2197

<b>Time from Surgery to Completion of Adjuvant Treatment &gt; 100 Days</b>	0.4894	-0.00636	0.1667	0.2166
<b>Level I Lymph Nodes Involved</b>	0.2214	0.2486	0.1676	0.2125
<b>Base of Tongue Subsite</b>	0.1352	0.3989	0.0103	0.1815
<b>Received Chemo</b>	0.2981	0.2099	-0.00742	0.1669
<b>Buccal Mucosa Subsite</b>	0.2326	0.1229	-0.00064	0.1183
<b>Nodal Stage N1</b>	0.071	0.1966	0.039	0.1022
<b>Male Gender</b>	0.2082	0.0606	0.029	0.0993
<b>Alveolar Ridge Subsite</b>	0.0516	0.2616	-0.039	0.0915
<b>Nodal Stage N3</b>	0.0645	0.2072	0.00155	0.0911
<b>Retromolar Trigone Subsite</b>	0.0963	0.1469	0.0208	0.088
<b>Well Differentiated</b>	-0.00415	0.2316	0.0115	0.0797
<b>Radiation Dose</b>	-0.015	-0.032	0.2644	0.0723
<b>Lymphovascular Invasion</b>	-0.0024	0.1139	0.0554	0.0556
<b>Treatment at Academic Center</b>	0.0538	0.0991	0.0106	0.0545
<b>1 Lymph Node Positive</b>	0.1959	-0.061	-0.00494	0.0434
<b>Moderately Differentiated</b>	0.0406	-0.021	0.0912	0.0368
<b>Black Race</b>	0.00727	0.0638	0.0278	0.0329
<b>Multiagent Chemotherapy</b>	0.0628	0.0387	-0.00352	0.0327
<b>Retropharyngeal Lymph Nodes Involved</b>	0.0337	0.0527	-0.00041	0.0287
<b>Hypopharynx primary</b>	-0.08	0.1568	-0.00887	0.0228
<b>Parapharyngeal Lymph Nodes Involved</b>	0.0587	-0.019	0	0.0133
<b>Tumor Thickness (Depth)</b>	0.0645	0.0146	-0.04	0.0129

<b>Level IV Lymph Nodes Involved</b>	0.0858	-0.122	0.0695	0.0112
<b>Year of Diagnosis 2009 - 2012</b>	-0.0127	-0.00885	0.0287	0.00237
<b>Poorly Differentiated</b>	-0.054	0.0304	0.0249	0.000514
<b>Level III Lymph Nodes Involved</b>	0.0672	-0.23	0.1524	-0.00361
<b>Level V Lymph Nodes Involved</b>	-0.077	0.0299	0.0322	-0.0049



**eTable 5. Hazard Ratios for Subgroups**

Hazard ratios are calculated for survival of patients receiving treatment recommended by a model compared to those who did not.

<b>HR (95% CI)</b>	<b>HPV+ Oropharynx</b>	<b>HPV-</b>	<b>Age &gt; 70</b>	<b>Age ≤ 70</b>
<b>DeepSurv</b>	0.95 (0.53 – 1.69)	0.79 (0.63– 1.00)	0.74 (0.62 – 0.89)	0.87 (0.79– 0.95)
<b>N-MLTR</b>	0.67 (0.66 – 1.04)	0.83 (0.66 – 1.04)	0.86 (0.71 – 1.03)	0.89 (0.81 – 0.98)
<b>RSF</b>	0.46 (0.25 – 0.84)	0.80 (0.64 – 1.01)	0.89 (0.74 – 1.06)	0.93 (0.84 – 1.02)

**eFigure. Survival Outcomes for Treatment According to Machine Learning Model Recommendations, Test Cohort**

**Top – DeepSurv Model, Middle – N-MLTR Model, Bottom – RSF Model.**

