



Prediction models of death for patients with head and neck squamous cell carcinoma

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Introduction

Head and neck squamous cell carcinoma (HNSCC) is among the most prevalent neoplasms in the world¹. Likewise in other malignancies, the TNM System is the main tool for the prediction of 5-year overall survival and is based on anatomical, histological, and clinical information, as well as data on Human Papillomavirus (HPV) infection²⁻⁴. However, the efficacy of this system is criticized by joining patients into heterogeneous categories, as well as for not being able to predict individualized probabilities of death⁵.

Objective

To create a 5-year mortality prediction model to be applied at the first presentation, that performs better than TNM, as well as to evaluate the incremental contribution of HPV status to this model.

Methods

A retrospective study of data prospectively collected between July 2000 and August 2011 by the GENCAPO study group. Data were mined using Classification and Regression Trees, Random Forests, and Boosted and Regression Trees. Logistic Regression (LR) and Artificial Neural Network (ANN) models were created for all tumor sites and for each site separately. Methods of internal validation, discrimination - by the area under the ROC curve (AUC) - and calibration - Goodness of Fit test - were performed. Paraffin-embedded tumor samples from 692 patients were tested for HPV DNA by polymerase chain reactions (PCR). The contribution of HPV on model performance was analyzed by the coefficient of determination and the AUC.

Results

1811 patients were analyzed, and HPV was positive in 8,7% of all tumors and in 11,8% of oropharyngeal tumors. After data mining the predictive variables, 28 were selected. The LR model for all sites selected tumor volume, sex, age, and lymph node enlargement as significant variables, with an AUC=0.77, while the ANN model obtained an AUC=0.76. The LR models for oral cavity and oropharynx tumors selected the same variables as the model for all sites, the LR model for larynx excluded sex as a significant variable (Table 1). The AUC for tumors of the oral cavity were 0.78 (LR) and 0.75 (ANN); for oropharynx were 0.72 (LR) and 0.65 (ANN); and for larynx were 0.71 (LR) and 0.75 (ANN) (Table 2). All models, except for the hypopharynx, presented good calibration. The survival curves according to the quartiles of predicted risk of death (Q1≤25%, 25%<Q2≤50%, 50%<Q3≤75%, Q4>75%) and according to the TNM stage were compared. The quartile curves presented a better visual separation than the TNM stage curves (Tables 3-6). There was no prediction increment by adding HPV status to any of the models.

Conclusion

It was possible to develop models with good performance to predict 5- year survival, with easy to retrieve information, that were superior to the TNM System. No prediction increment was obtained by adding HPV status to the models in our study population.

Table 1 – Odds ratio of each parameter for each of the built predictive models

Parameter	OR				p			
	All sites	OC	OP	LA	All sites	OC	OP	LA
Age	1.04	1.03	1.1	1.05	0.0003	0.0095	0.0002	0.0256
Clinical volume [≥3cm3]	-	-	-	4.66	-	-	-	0.0001
Clinical volume [≥5cm3]	1.12	-	1.73	-	<0.0001	-	0.0388	-
Clinical volume [≥25cm3]	-	4.45	-	-	-	0.0001	-	-
Lymph node[yes]	1.49	1.68	9.85	2.36	0.0380	0.0461	<0.0001	0.0477
Sex[M]	2.71	2.62	6.3	-	0.0005	0.0039	0.0029	-

OR: odds ratio; OC: oral cavity; OP: oropharynx; LA: larynx; M: male

Table 2 – Discrimination per site

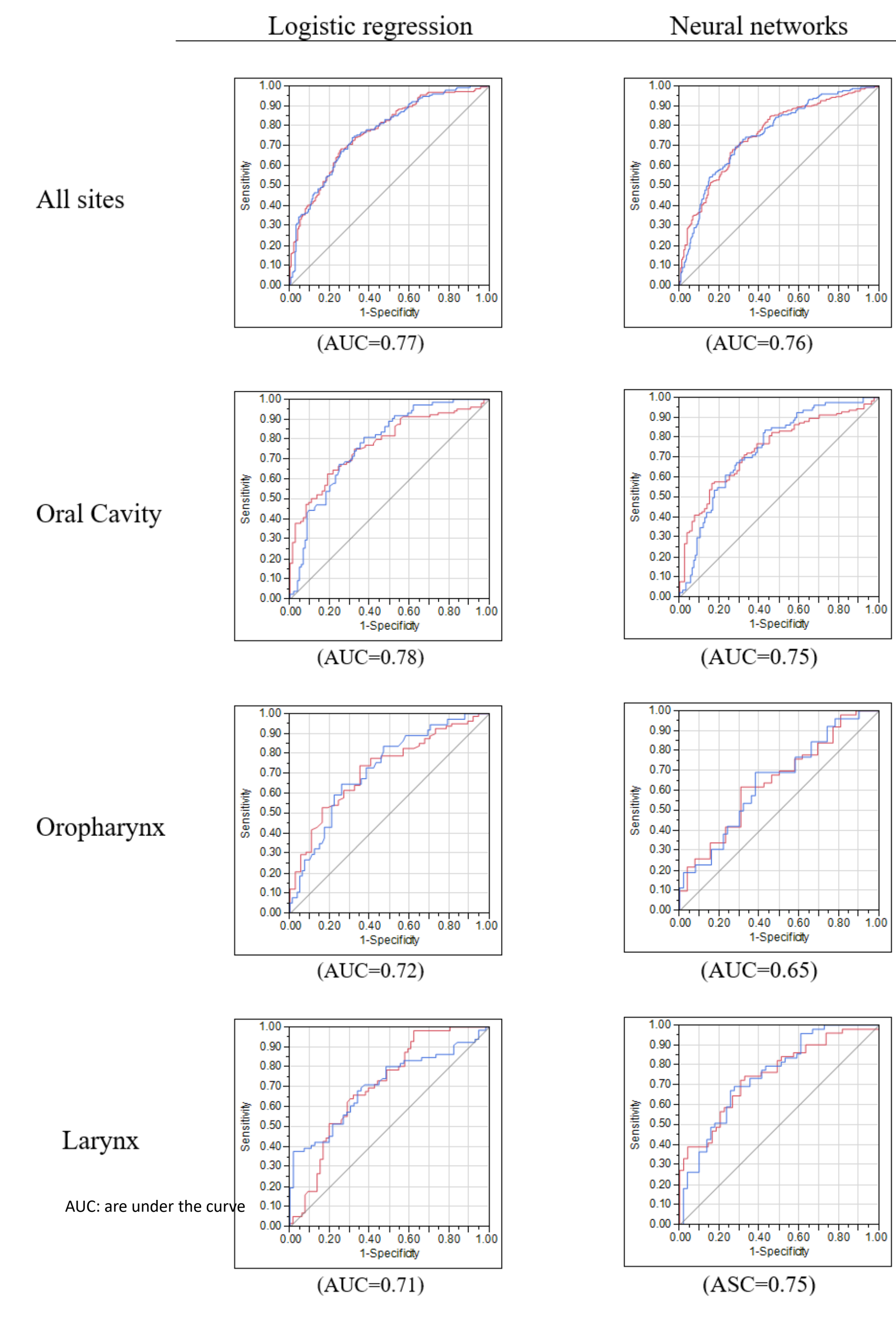


Table 3 – Survival curves – all sites

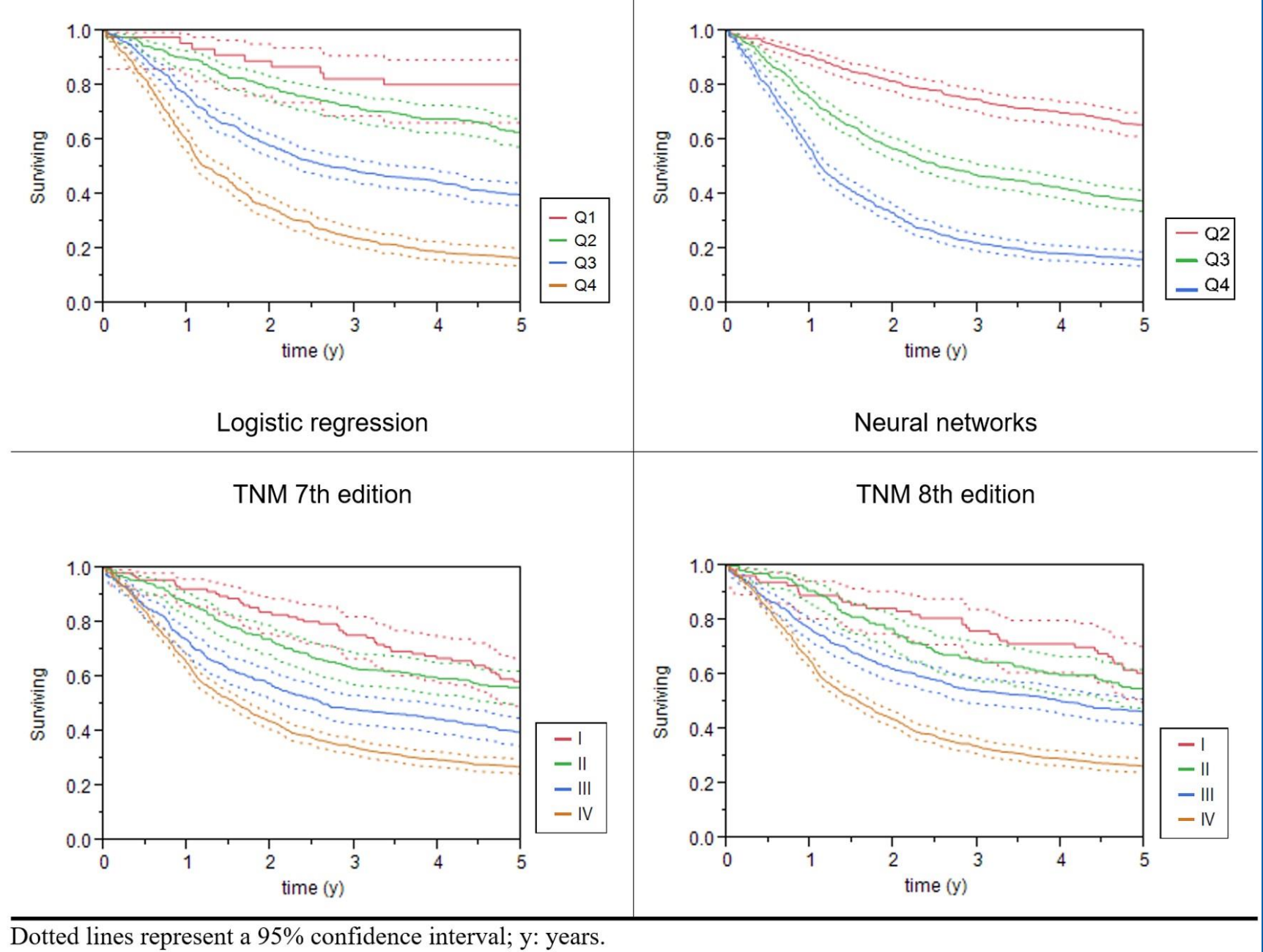


Table 5 – Survival curves – oropharynx

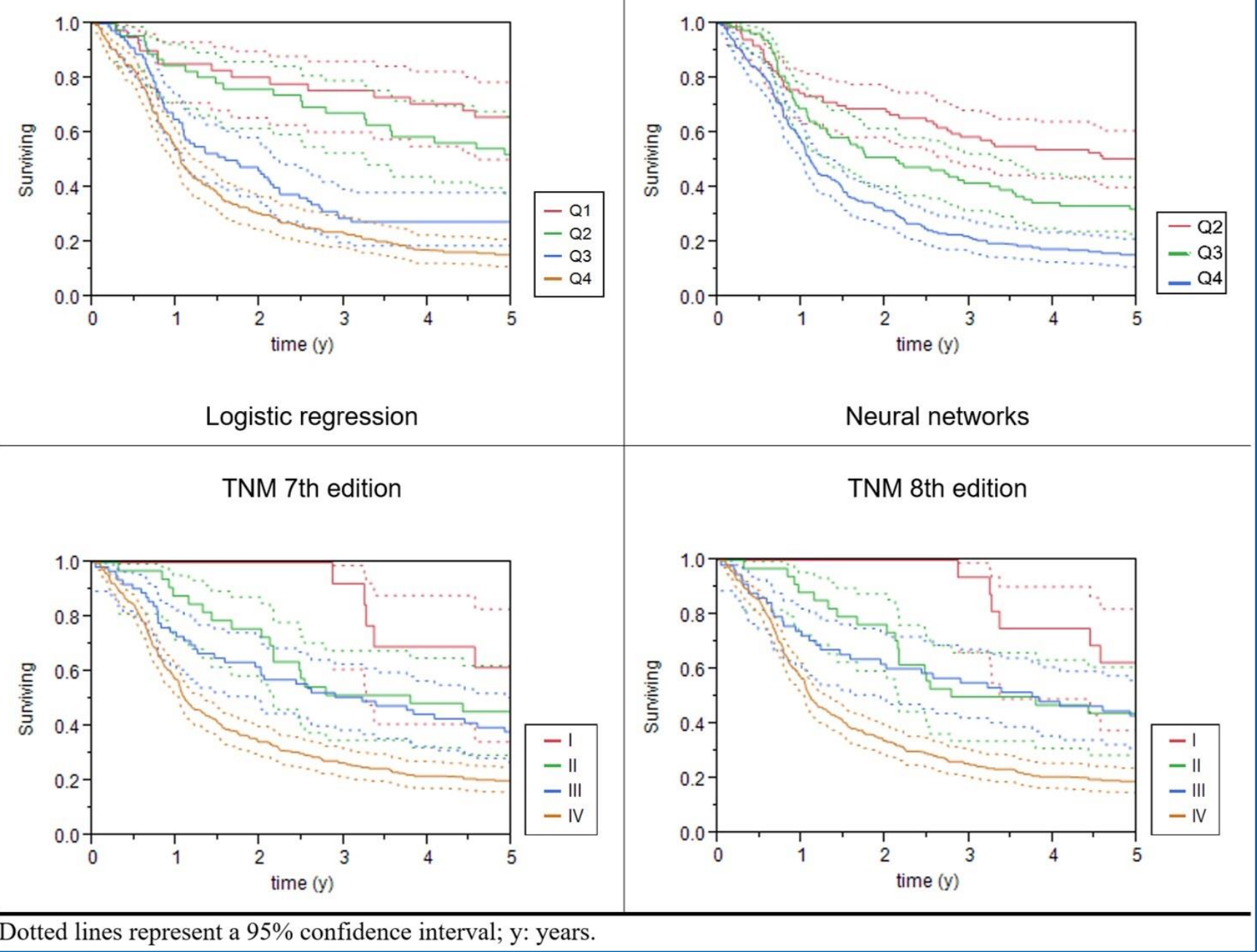


Table 4 – Survival curves – oral cavity

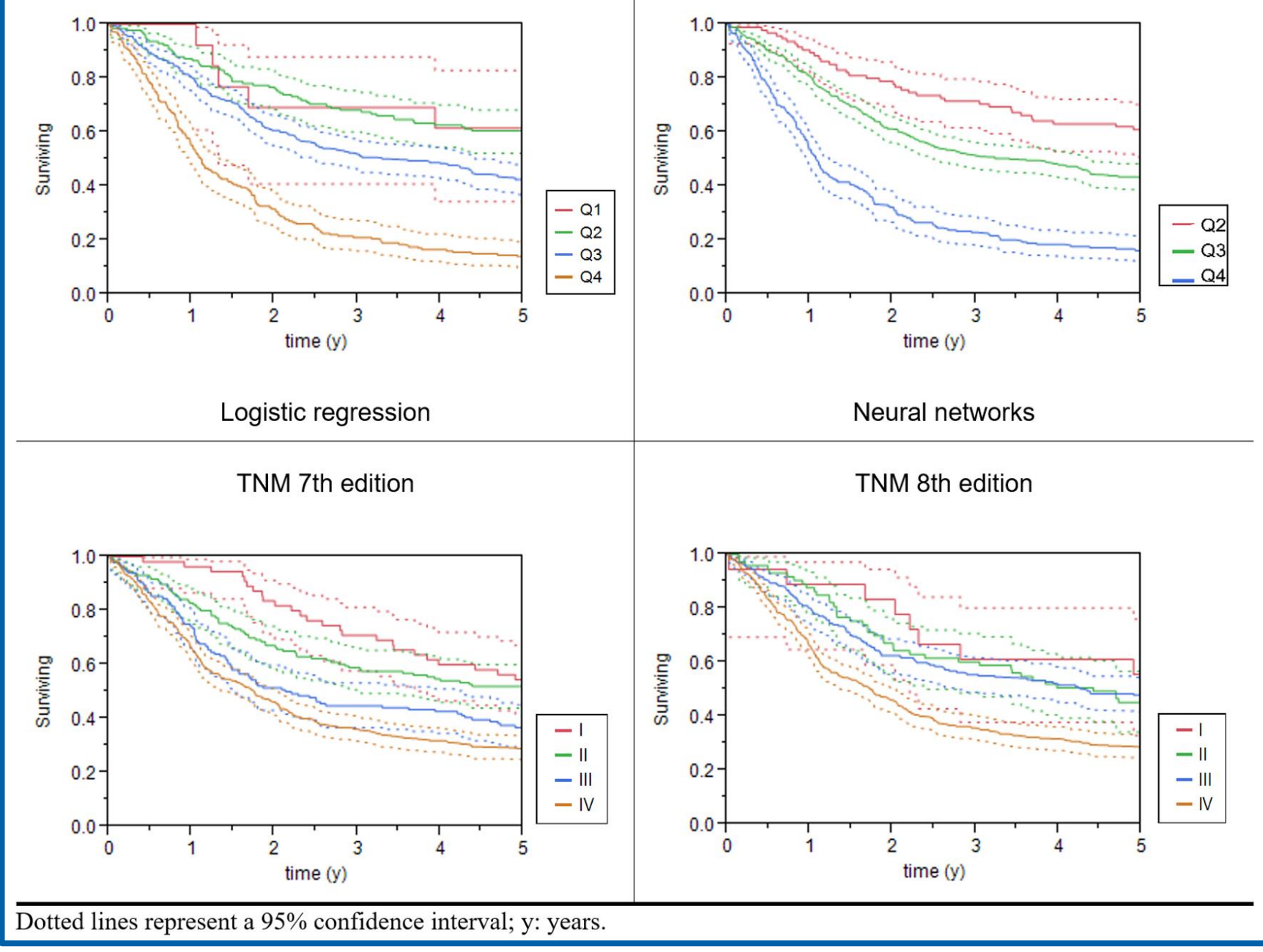
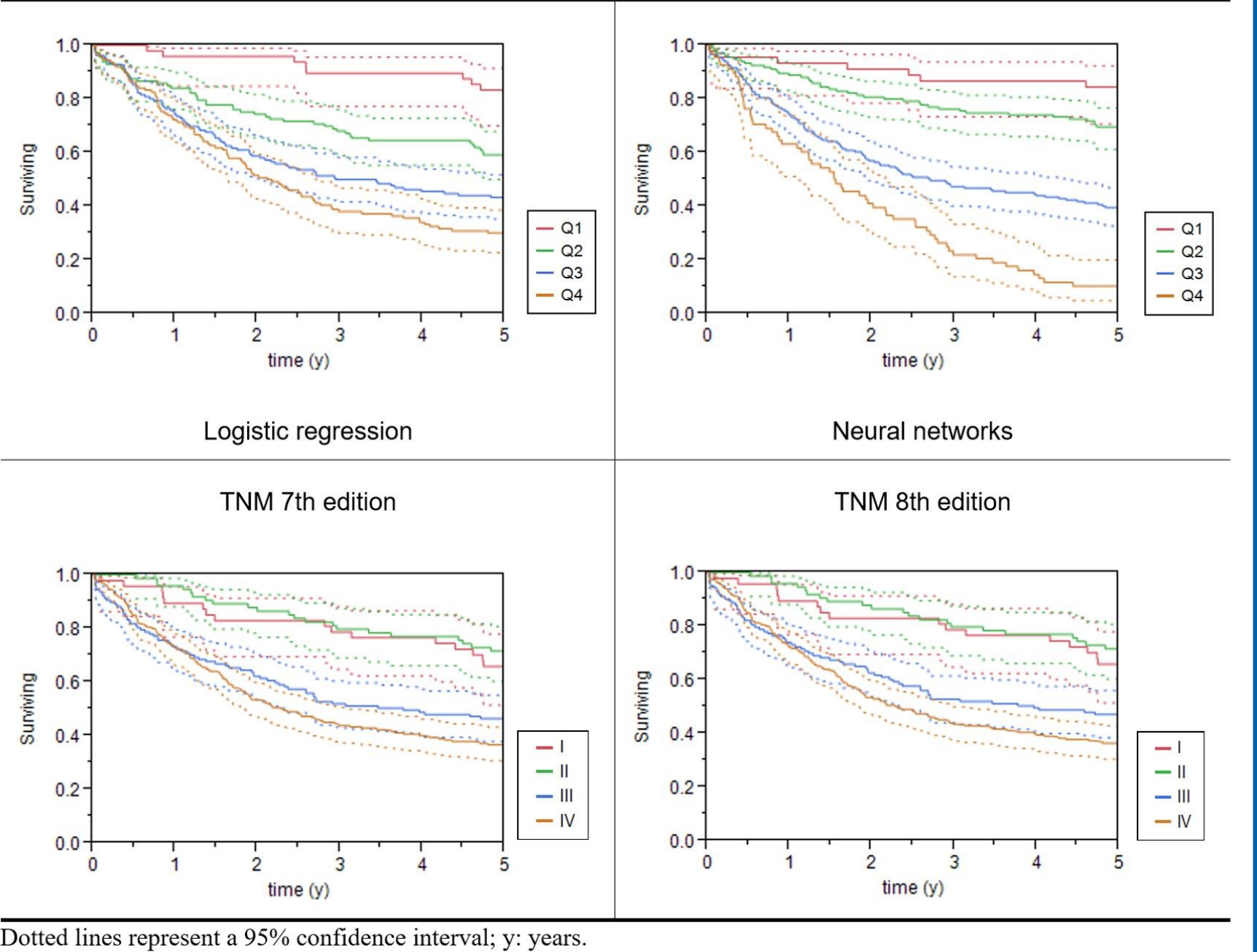


Table 6 – Survival curves – larynx



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Key findings

- We identified parameters not covered by the TNM that were significant in predicting the risk of death in five years for patients with head and neck squamous cell carcinoma.
- We created more accurate prediction models than TNM for the oral cavity, oropharynx and larynx. In addition, we created a model independent of the primary tumor site.
- We evaluated the increase in HPV status in models of predicting the risk of death within five years regardless of the primary tumor site and in patients with oropharyngeal tumors and found no improvement in the performance of the models.