

Rafi Kabarriti, MD; N. Patrik Brodin, PhD, Nitin Ohri, MD; Rahul Narang, MD; Renee Huang, MD; Jennifer W. Chuy, MD; Lakshmi N. Rajdev, MD; Shalom Kalnicki, MD; Chandan Guha, MD PhD; Madhur K. Garg, MD  
Albert Einstein College of Medicine-Montefiore Medical Center, Bronx, NY

## Introduction

Human papilloma virus (HPV) is associated with anal cancers.

Whether HPV associated anal cancers have improved overall survival (OS) as well enhanced radiation sensitivity is currently unknown.

### Objective:

To determine if anal cancer patients with HPV positive disease have different overall survival (OS) compared to those with HPV negative disease, and to elucidate any differences in the association between radiation dose and OS.

## Methods

We utilized the National Cancer Database (NCDB) registry to identify a cohort of non-metastatic anal cancer patients treated with curative intent between 2008 – 2015.

Propensity score matching was used to account for potential selection bias between patients with HPV positive and negative disease.

Multivariable Cox regression was used to determine the association between HPV status and OS.

Kaplan-Meier methods were used to compare actuarial survival estimates.

## Results

We identified 5,927 patients with tumor HPV status for this analysis,

3,523 (59.4%) had HPV positive disease and 2,404 (40.6%) had HPV negative disease.

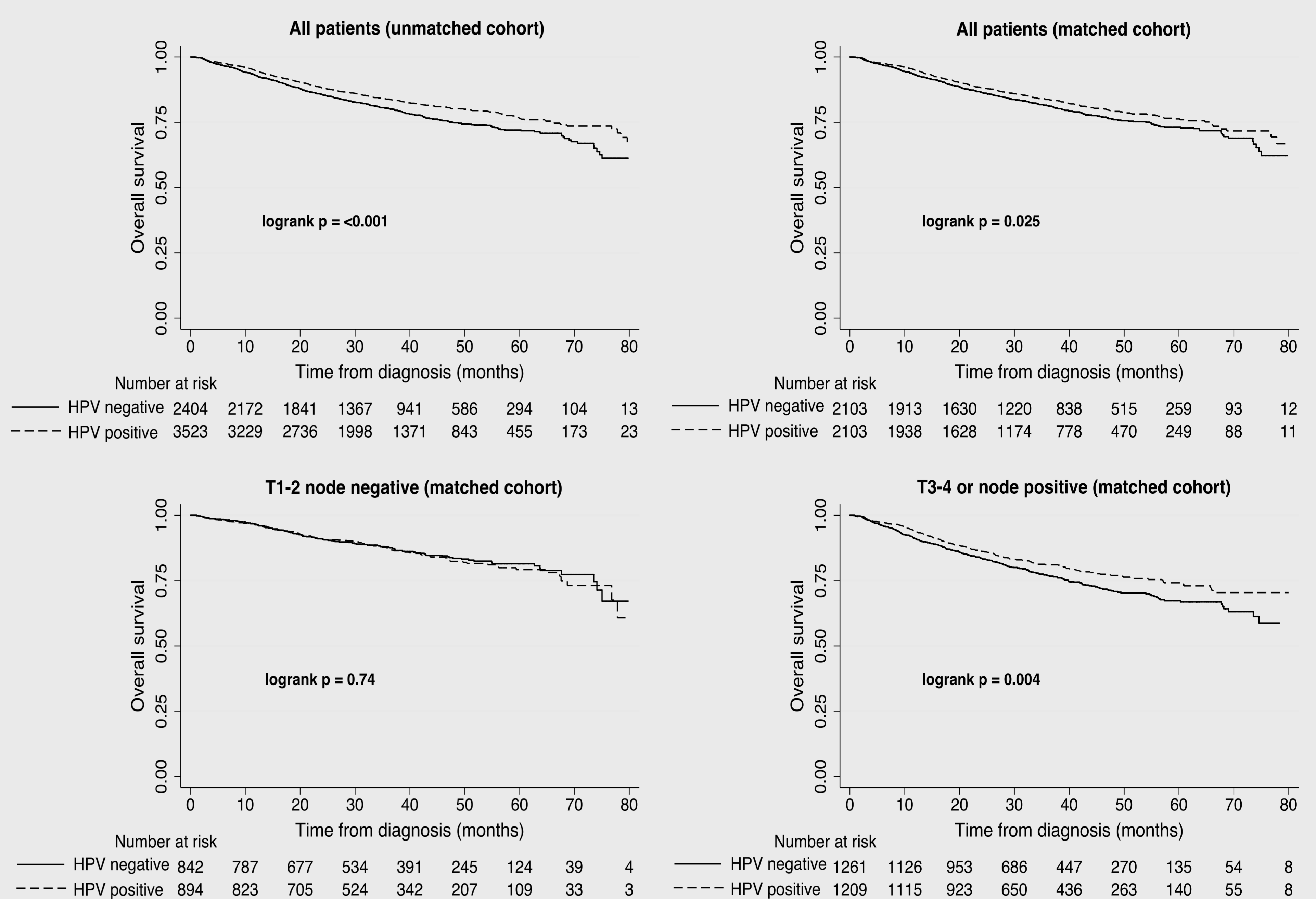
Propensity-matched analysis demonstrated that patients with HPV positive locally advanced (T3-4 or node positive) anal cancer had better OS (HR=0.81 (95%CI: 0.68-0.96), p=0.018).

For patients with early stage disease (T1-2 and node negative) there was no difference in OS (HR=1.11 (95%CI:0.86-1.43), p=0.43).

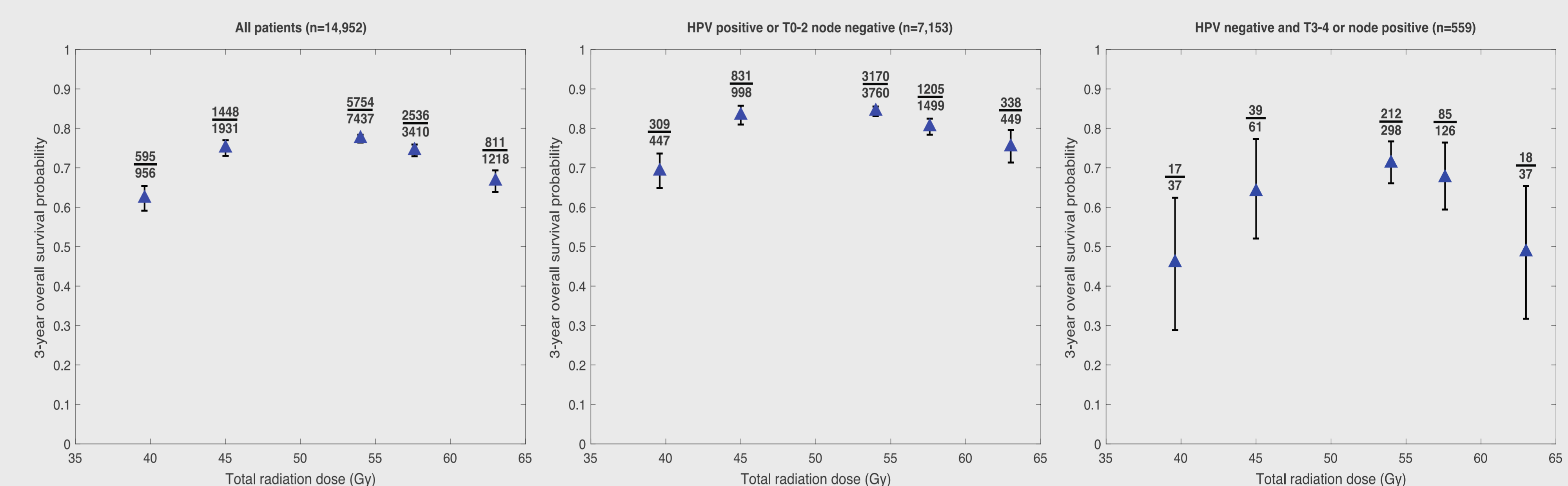
In the unmatched cohort, there was an increase in 3-year OS for patients with HPV positive tumors or early stage disease up to 45-49.9 Gy (p<0.001),

whereas for patients with HPV negative and locally advanced disease, there was an increase in survival from 46% at 30-44.9 Gy, to 64% at 45-49.9 Gy (p=0.093) and further to 71% at 50-54.9 Gy (p=0.005).

## Results (continued)



**Figure 1.** Kaplan-Meier curves showing the difference in overall survival between HPV positive and negative patients with early compared to advanced disease.



**Figure 2.** The 3-year overall survival is shown for the different dose groups with a median total dose of 39.6 Gy, 45 Gy, 54 Gy, 57.6 Gy and 63 Gy, respectively. Uncertainty bars show 95% binomial confidence intervals and numerical indicators show the number of patients alive at 3 years out of the total number of patients in each dose group

## Discussion

Our study utilizing a large cohort of anal cancers with HPV tumor status demonstrated that patients with HPV positive anal cancers had improved OS compared to patients with HPV negative anal cancers.

After propensity score matching, this benefit in OS was most pronounced in the locally advanced anal cancers with T3-T4 or node positive disease but not in the early stage anal cancers.

We also demonstrated a radiation dose-response relationship showing that a total dose >45 Gy was associated with better 3-year OS.

For HPV negative locally advanced anal cancers there was a further increase in survival for doses up to between 50-54.9 Gy.

## Conclusions

We found HPV to be a significant prognostic marker in anal tumors, especially for locally advanced disease.

We further found that higher radiation dose up to 50-55 Gy was associated with better OS, mainly for locally advanced disease in HPV negative patients.

## References

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