

# Less is More: Risk Factors and Survival Outcomes of Overtreatment for Early-Stage Colorectal Cancer

Daniel R. S. Habib BA<sup>1</sup>, Matthew Shou BA<sup>1</sup>, James L. Rogers BS<sup>1</sup>, Kevin Sun BS<sup>1</sup>, Chen Chia Wang BS<sup>1</sup>, Aimal Khan MD<sup>2</sup>

<sup>1</sup> Vanderbilt University School of Medicine, <sup>2</sup> Vanderbilt University Medical Center

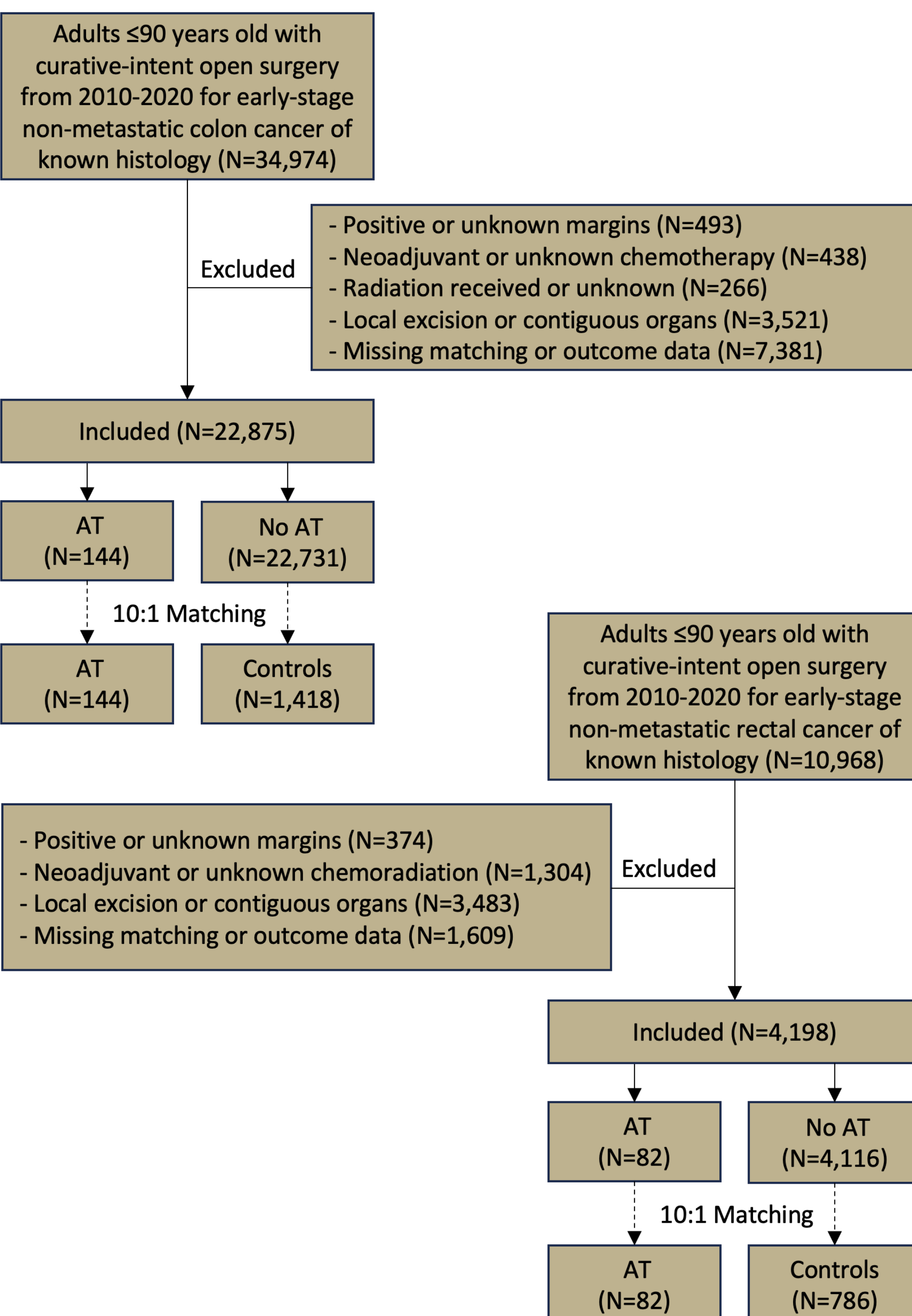


## Introduction

- After cT1-2N0M0 colorectal cancer (CRC) surgery without upstaging, observation is recommended while adjuvant therapy (AT) constitutes overtreatment.
- Guideline-discordant treatment exhibits worse outcomes,<sup>1</sup> but no study has assessed CRC overtreatment in the past decade.<sup>2,3</sup>
- Aim:** Determine risk factors and overall survival (OS) impact of AT in early-stage CRC

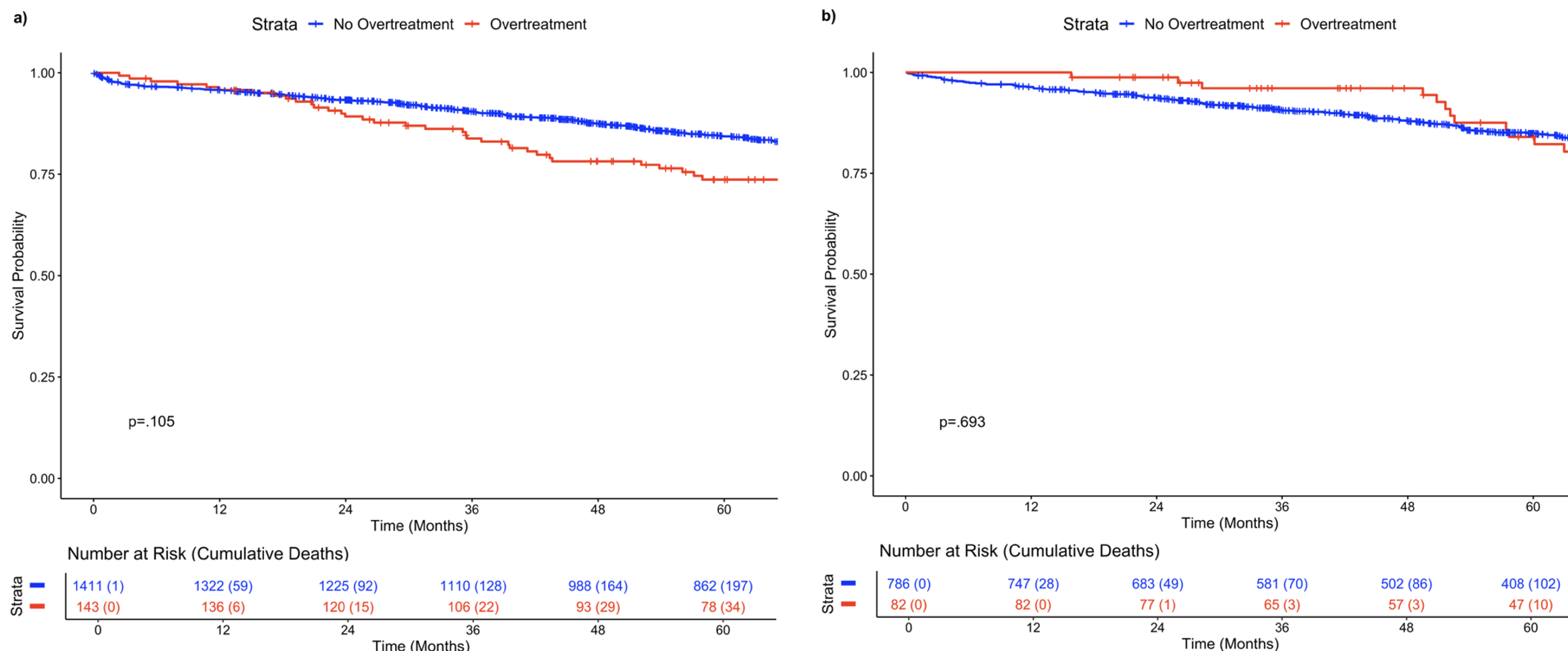
## Methods

- Population:** National Cancer Database (NCDB) CRC patients
- Statistical Analysis:** Multivariable logistic regression of risk factors; 10:1 propensity score matching, Kaplan-Meier analysis, and Cox regressions of patients with and without AT
- Covariates:** Age, sex, race, insurance, income, Charlson-Deyo Comorbidity Index, facility type, facility case volume, grade, histology, pathologic T stage



## Results

**Figure 1. Kaplan Meier Survival Analyses by Overtreatment for (a) Colon and (b) Rectal Cancer**



Overtreatment was not associated with worse OS for rectal cancer but exhibited a non-significant trend to worse OS for colon cancer.

**Table 1. Multivariable Logistic Regressions by Overtreatment**

Variable	Colon		Rectum	
	aOR (95% CI)	P Value	aOR (95% CI)	P Value
Age (1 Year Increase)	<b>0.96 (0.95-0.98)</b>	<b>&lt;.001</b>	1.00 (0.97-1.02)	.770
Female Sex (vs Male)	0.73 (0.52-1.02)	.063	0.88 (0.56-1.38)	.565
Race (vs White)				
Black	<b>1.94 (1.26-2.99)</b>	<b>.002</b>	1.35 (0.60-3.01)	.471
Other	<b>2.04 (1.06-3.95)</b>	<b>.034</b>	0.75 (0.23-2.42)	.630
Private Insurance	0.87 (0.58-1.30)	.488	1.10 (0.62-1.95)	.743
Above Median Income	0.71 (0.51-1.00)	.050	0.83 (0.53-1.33)	.443
Any Comorbidity				
(vs No Comorbidity)	0.83 (0.57-1.20)	.311	0.71 (0.41-1.23)	.225
Research/Academic Facility	0.78 (0.51-1.19)	.246	0.69 (0.40-1.20)	.194
Top Quartile Facility				
Case Volume	0.80 (0.51-1.25)	.325	0.95 (0.54-1.68)	.857
Poor/Undifferentiated (vs Well/Moderately Differentiated)	1.58 (0.95-2.64)	.080	<b>2.61 (1.44-4.76)</b>	<b>.002</b>
High-Risk Histology (vs Nonmucinous Adenocarcinoma)	1.76 (0.98-3.15)	.057	<b>3.20 (1.22-8.40)</b>	<b>.018</b>
pT2 (vs pT1)	<b>1.66 (1.19-2.33)</b>	<b>.003</b>	<b>2.58 (1.59-4.19)</b>	<b>&lt;.001</b>

**Colon cancer** overtreatment was associated with younger age non-white race, and pathologic stage T2 vs T1.

- Non-significant trends for male sex, low income, poor/undifferentiated grade, and high-risk histology

**Rectal cancer** overtreatment was associated with pathologic stage T2 vs T1, poor/undifferentiated grade, and high-risk histology.

**Table 2. Multivariable Cox Regressions for Overall Survival**

Variable	Colon		Rectum	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age (1 Year Increase)	<b>1.06 (1.05-1.07)</b>	<b>&lt;.001</b>	<b>1.07 (1.05-1.09)</b>	<b>&lt;.001</b>
Female Sex (vs Male)	<b>0.76 (0.61-0.95)</b>	<b>.014</b>	0.85 (0.62-1.18)	.336
Race (vs White)				
Black	<b>1.35 (1.02-1.79)</b>	<b>.034</b>	<b>1.86 (1.14-3.05)</b>	<b>.014</b>
Other	0.70 (0.39-1.25)	.230	0.60 (0.22-1.64)	.318
Private Insurance	0.75 (0.57-1.00)	.052	0.91 (0.61-1.37)	.664
Above Median Income	0.91 (0.73-1.14)	.423	0.76 (0.56-1.03)	.073
Any Comorbidity				
(vs No Comorbidity)	<b>1.71 (1.38-2.12)</b>	<b>&lt;.001</b>	<b>1.47 (1.06-2.02)</b>	<b>.019</b>
Research/Academic Facility	<b>1.33 (1.02-1.74)</b>	<b>.037</b>	0.73 (0.47-1.16)	.182
Top Quartile Facility				
Case Volume	0.76 (0.56-1.02)	.071	0.87 (0.54-1.40)	.556
Poor/Undifferentiated (vs Well/Moderately Differentiated)	0.91 (0.65-1.27)	.587	1.02 (0.66-1.57)	.934
High-Risk Histology (vs Nonmucinous Adenocarcinoma)	1.21 (0.82-1.78)	.338	<b>2.20 (1.10-4.40)</b>	<b>.025</b>
pT2 (vs pT1)	1.01 (0.81-1.25)	.954	1.14 (0.79-1.66)	.480
Overtreatment	<b>1.40 (1.01-1.93)</b>	<b>.042</b>	1.05 (0.66-1.68)	.844

**Colon cancer** overtreatment was independently associated with worse OS.

**Rectal cancer** overtreatment was not independently associated with worse OS.

## Discussion

- Our study aligns with previous work<sup>2</sup> yet is unique in assessing current colon cancer data and is the first to assess rectal cancer overtreatment.
- Younger and non-white patients exhibit worse CRC outcomes,<sup>4,5</sup> which might explain why they are more likely to be overtreated.
- The results highlight the importance of guideline adherence since systemic toxicity risk outweighs potential survival benefit.
- Limitations:**
  - Small overtreatment sample
  - Limited NCDB surgical outcomes
  - Might not capture all factors that influence treatment decisions

## Conclusion

- Overtreatment of early-stage colon (0.6%) and rectal cancer (2.0%) is rare.
- Patient and tumor characteristics were associated with increased odds of overtreatment depending on cancer type.
- Overtreatment was significantly associated with worse OS in colon cancer but not rectal cancer

## References

- Boland GM, Chang GJ, Haynes AB, et al. Association between adherence to National Comprehensive Cancer Network treatment guidelines and improved survival in patients with colon cancer. *Cancer*. 2013;119:1593-1601.
- Kneuert PJ, Chang GJ, Hu C-Y, et al. Overtreatment of Young Adults With Colon Cancer. *JAMA Surg*. 2015;150:402.
- Chaggar R, Xing Y, Chiang Y-J, et al. Adherence to Stage-Specific Treatment Guidelines for Patients With Colon Cancer. *J Clin Oncol*. 2012;30:972-979.
- You YN. Young-Onset Colorectal Cancer: Is It Time to Pay Attention? *Arch Intern Med*. 2012;172:287.
- Alexander DD, Waterbor J, Hughes T, et al. African-American and Caucasian disparities in colorectal cancer mortality and survival by data source: An epidemiologic review. *Cancer Biomarkers*. 2007;3:301-313.

**Daniel R. S. Habib**  
 Website: danielrshabib.github.io  
 ✉ Daniel.r.habib@vanderbilt.edu  
 @danielrshabib

