

Comparative Analyses of Costs and Survival Between Radical Cystectomy and Trimodal Therapy

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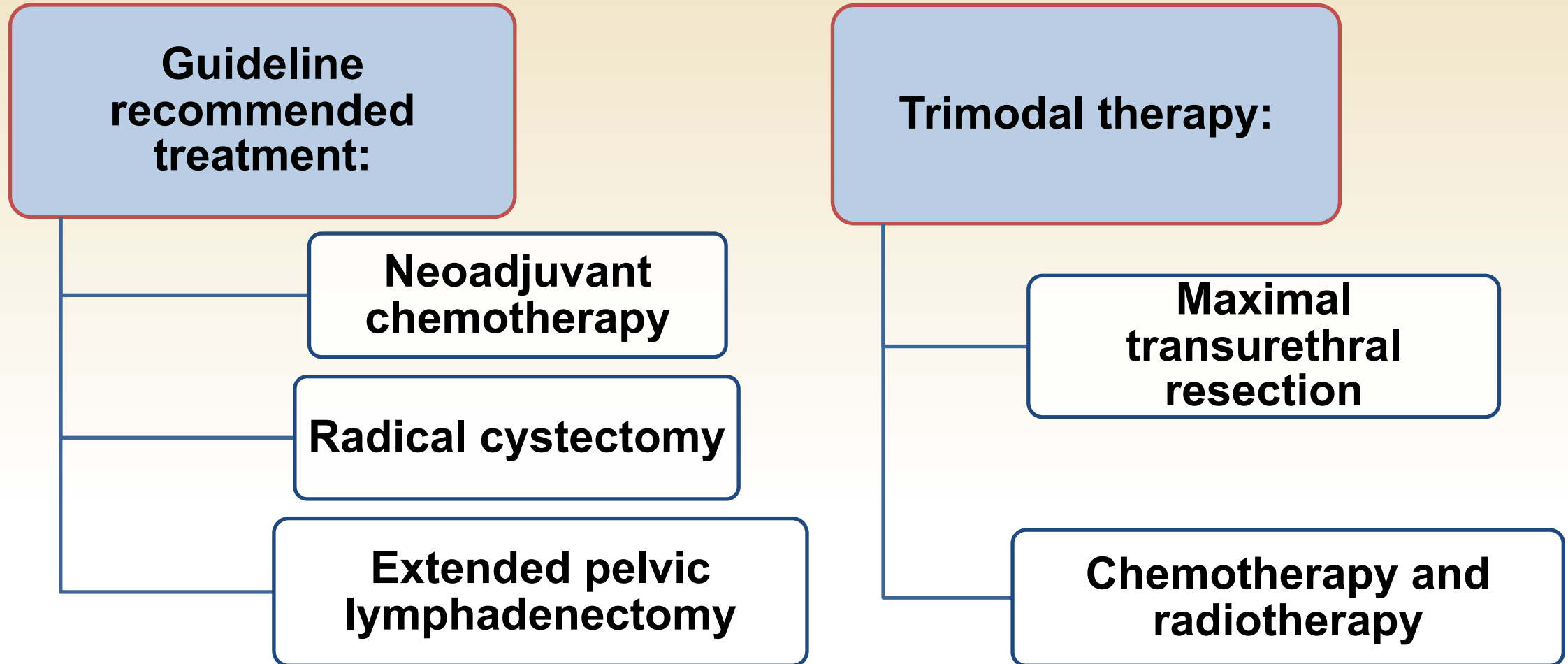
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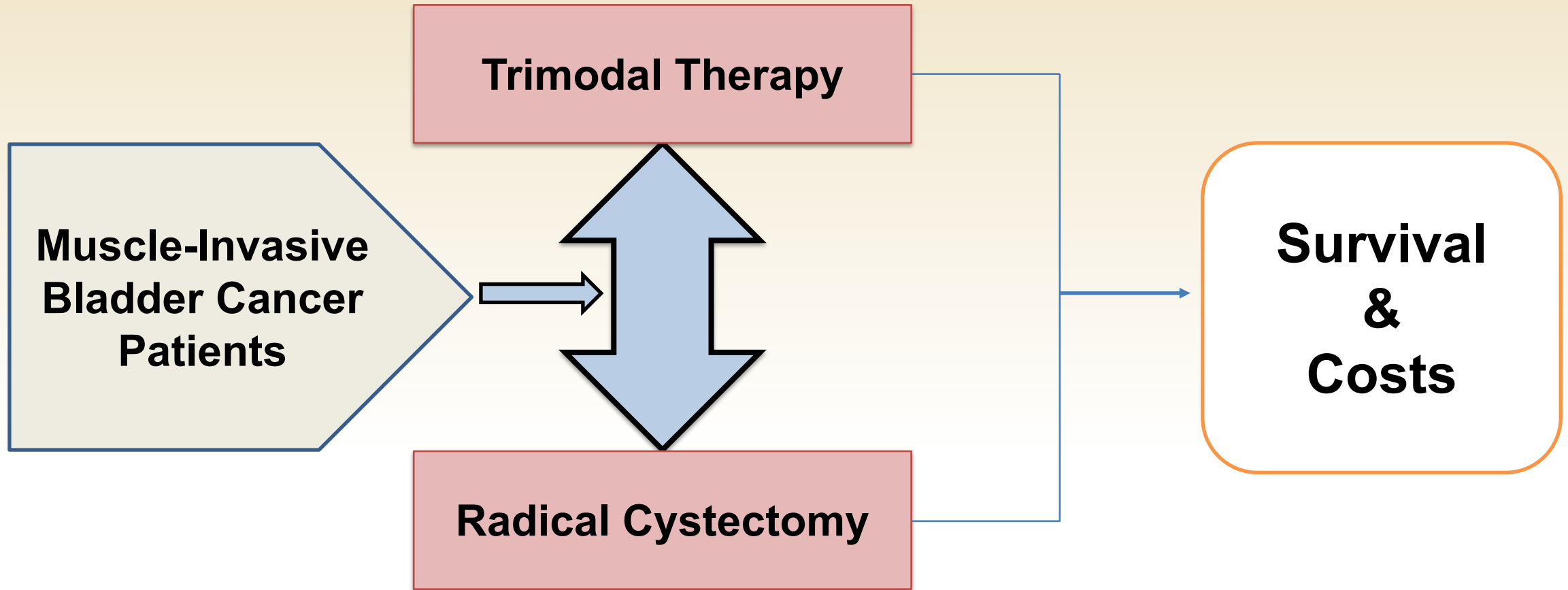
Galveston, TX

USA

Background—Treatment of MIBC



Objective



What We Did – Outline

First Study (Published 2018)

- Propensity Score Matching
- Kaplan-Meier and Cox models
- Fine and Gray's model

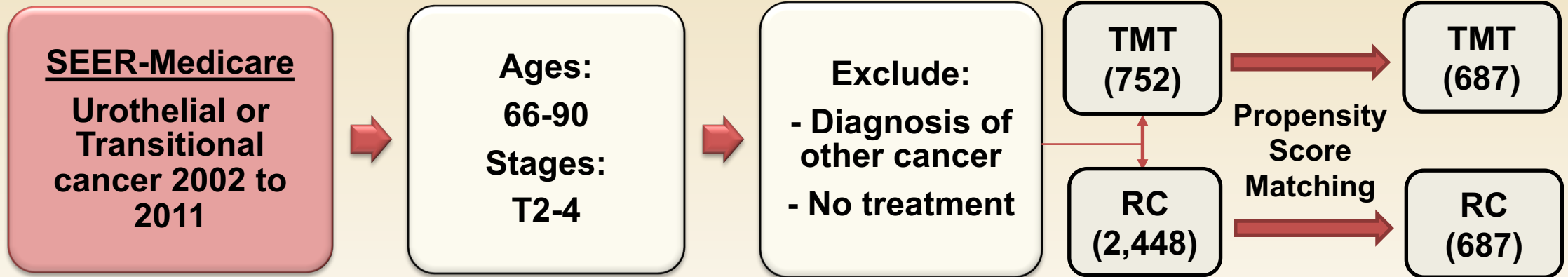
- Characteristics Before and After Match
- Overall and Cancer-Specific Survival
- Median Costs at 30, 90, 180 Days

Second Study (Published 2019)

- Inverse Probability of Treatment–Weighted Propensity Score Models
- Basu and Manning Method

- Account for Survival and Intensity Effects
- Total Costs Within 1-Year
- Costs Breakdown

Design



Identification of Treatments

- Radical cystectomy +/- pelvic lymph node dissection
- Trimodal: transurethral resection, radiotherapy and chemotherapy

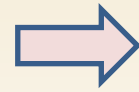
Study Covariates

- Age
- Sex
- Race/ethnicity
- Marital status
- US region
- Socioeconomic Status
- Education level
- Household Median Income
- Comorbidity (Klabunde Modification)

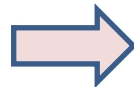
RC = radical cystectomy; TMT = trimodal therapy.

Clinical Characteristics

Treatment Before Matching		
Variable	RC, No. (%)	TMT, No. (%)
All Patients	2,448 (76.5)	752 (23.5)
Stage		
II	966 (39.5)	532 (70.7)
III	761 (31.1)	96 (12.8)
IV	721 (29.5)	124 (16.5)
Grade		
Low	99 (4.0)	30 (4.0)
High	2,288 (93.55)	679 (90.3)
Unknown	61 (2.5)	43 (5.7)



Propensity Matching



Treatment After Matching	
RC, No. (%)	TMT, No. (%)
687 (50.0)	687 (50.0)
Stage	
470 (68.4)	468 (68.1)
98 (14.3)	96 (14.0)
119 (17.3)	123 (17.9)
Grade	
26 (3.8)	28 (4.1)
626 (91.1)	624 (90.8)
35 (5.1)	35 (5.1)

- Patients with high-grade disease more often underwent RC.

- Patients with clinical stage T2 cancer more often underwent TMT.

RC = radical cystectomy; TMT = trimodal therapy.

Results—Survival

Covariate	Cox Regression		
	Overall Survival		
	HR	95% CI	
Treatment			
Radical Cystectomy	ref	-	-
Trimodal Therapy	1.49	1.31	1.69

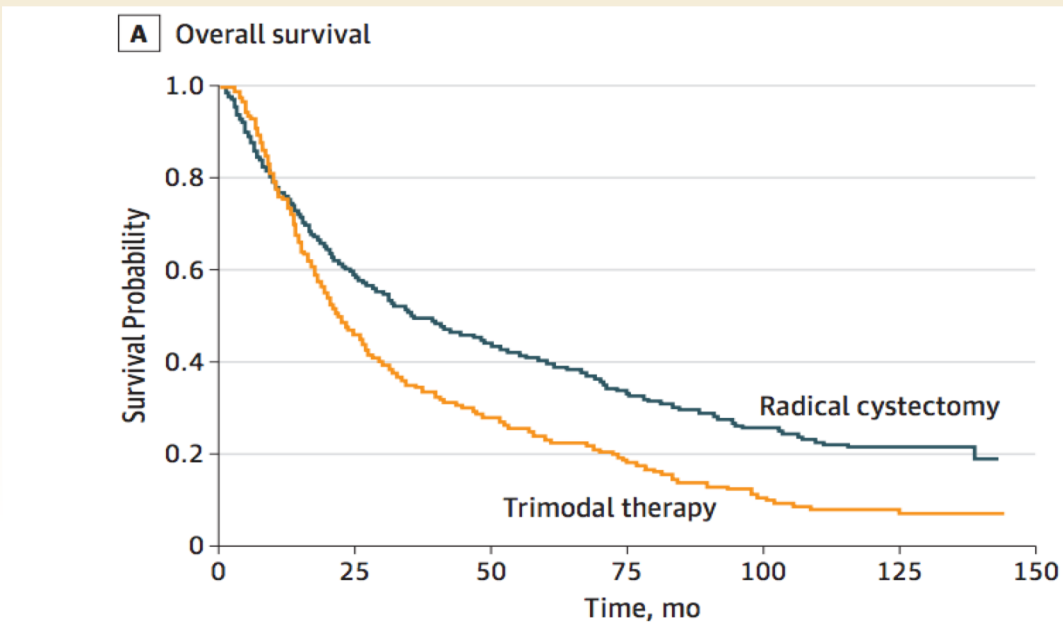
Covariate	Competing Risk Regression		
	Cancer-Specific Survival		
	HR	95% CI	
Treatment			
Radical Cystectomy	ref	-	-
Trimodal Therapy	1.55	1.32	1.83

- Trimodal therapy had significantly worse survival.
- These findings persisted across all stages except stage IV.
- Same direction of association in both sensitivity and propensity score analyses.

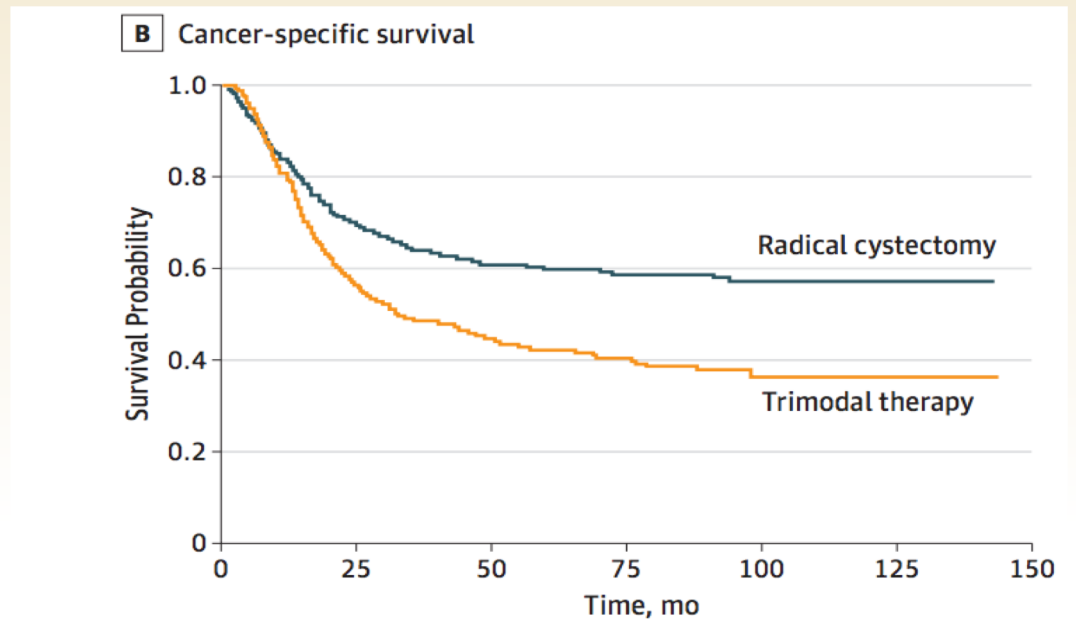
Results—Survival

Overall and Cancer-Specific Survival

- Unadjusted Kaplan-Meier Curves of Overall Survival and Cancer-Specific Survival According to Treatment After Propensity Score Matching.



No. at risk	0	25	50	75	100	125	150
Radical cystectomy	687	406	231	127	61	22	0
Trimodal therapy	687	315	144	66	22	<11	0



No. at risk	0	25	50	75	100	125	150
Radical cystectomy	687	406	231	127	61	22	0
Trimodal therapy	687	315	144	66	22	<11	0

$P < .001$ by the log-rank test for both overall and cancer-specific survival when radical cystectomy is compared with trimodal therapy.

Results—Costs

	Year	Radical Cystectomy Median	Trimodal Therapy Median	P-Value
30 Days	Total	20,298	29,459	NSD
90 Days	Total	69,181	80,174	<0.001
180 Days	Total	107,017	179,891	<0.001

- **Costs did not statistically differ at 30-d.**
- **TMT had significantly higher 90-d and 180-d costs.**
- **Costs from 2002 to 2011 increased for both treatments at 30-d and 90-d.**
- **In recent years, TMT costs at 180 days plateaued but RC continued to rise.**

RC = radical cystectomy; TMT = trimodal therapy.

Conclusion

- **Trimodal therapy was associated with significantly decreased overall and cancer-specific survival at increased costs compared with radical cystectomy.**
- **Extrapolated nationally, this resulted in excess spending of \$335 million with trimodal therapy for patients in 2011.**
- **Findings have important health policy implications regarding appropriate use of high-value based care among patients who are candidates for either treatment.**

Research

JAMA Surgery | **Original Investigation**

Comparing Survival Outcomes and Costs Associated With Radical Cystectomy and Trimodal Therapy for Older Adults With Muscle-Invasive Bladder Cancer

Stephen B. Williams, MD; Yong Shan, PhD; Usama Jazzar, BS; Hemalkumar B. Mehta, PhD; Jacques G. Baillargeon, PhD; Jinhai Huo, PhD; Anthony J. Senagore, MD; Eduardo Orihuela, MD; Douglas S. Tyler, MD; Todd A. Swanson, MD, PhD; Ashish M. Kamat, MD

JAMA Surg. doi:10.1001/jamasurg.2018.1680

Published online June 27, 2018.

Research

JAMA Surgery | **Original Investigation**

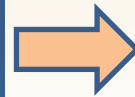
Comparison of Costs of Radical Cystectomy vs Trimodal Therapy for Patients With Localized Muscle-Invasive Bladder Cancer

Stephen B. Williams, MD; Yong Shan, PhD; Mohamed D. Ray-Zack, MBBS; Hogan K. Hudgins, BS; Usama Jazzar, BS; Douglas S. Tyler, MD; Stephen J. Freedland, MD; Todd A. Swanson, MD, PhD; Jacques G. Baillargeon, PhD; Jim C. Hu, MD; Sapna Kaul, PhD; Ashish M. Kamat, MD; John L. Gore, MD; Hemalkumar B. Mehta, PhD

Follow-up

Issues to Address

- Standard methods for handling censored survival data, such as the Kaplan-Meier estimator and Cox regression, do not account for dependent censoring.
- Cumulative cost at survival time is correlated with the cumulative cost at censoring time, even if underlying survival time and censoring time are independent.



Incorporate in Analysis

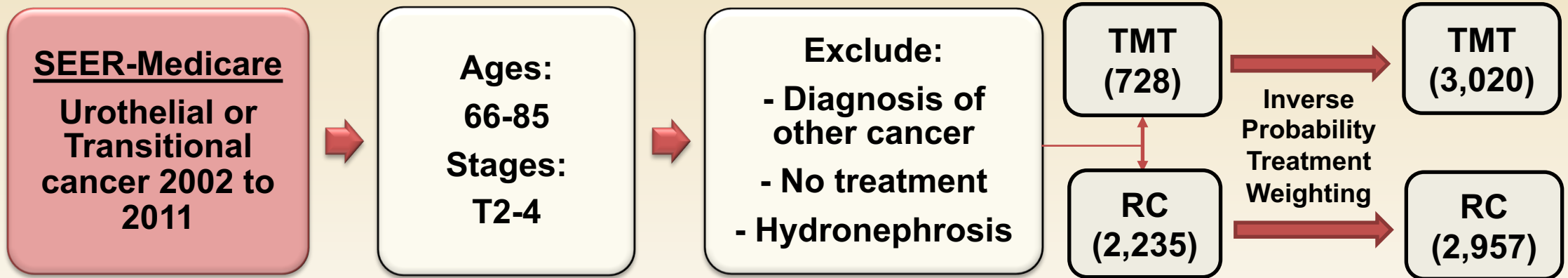
1. Non-linear two-part models for modeling skewed outcomes in presence of censoring.
2. Variable rates of accumulation of costs over time.
3. Spikes in cost-accumulation due to end-of-life care
4. Model consistency in the presence of heavy censoring and covariates affecting survival.



2nd Study
(Published 2019)



Design



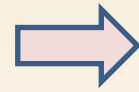
- Identification of Treatments and Study Covariates Consistent with 1st Study.
- Costs subdivided to different categories and calculated for a total of 1 year.

Statistical Analysis:

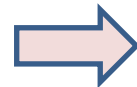
- Incorporate survival (ie, increased costs due to differences in survival between 2 treatments).
- Incorporate Intensity (ie, cost accumulation over time when patients are alive) effects.

Clinical Characteristics

Unweighted before IPTW		
Variable	RC, No. (%)	TMT, No. (%)
All Patients	2,235 (75.4)	728 (24.6)
Stage		
II	903 (40.4)	474 (65.1)
III	689 (30.8)	103 (14.1)
IV	643 (28.8)	151 (20.7)
Grade		
Low	95 (4.3)	25 (3.4)
High	2,082 (93.2)	664 (91.2)
Unknown	58 (2.6)	39 (5.4)



Inverse Probability Treatment Weighting



Weighted after IPTW	
RC, No. (%)	TMT, No. (%)
2,957 (49.5)	3,020 (50.5)
Stage	
1,366 (46.2)	1,341 (44.4)
792 (26.8)	827 (27.4)
799 (27.0)	852 (28.2)
Grade	
120 (4.1)	112 (3.7)
2,736 (92.5)	2,799 (92.7)
101 (3.4)	109 (3.6)

Significantly higher proportion of patients who underwent RC were:

- Younger
- Women
- Had none/fewer comorbidities compared with TMT.

RC = radical cystectomy; TMT = trimodal therapy.

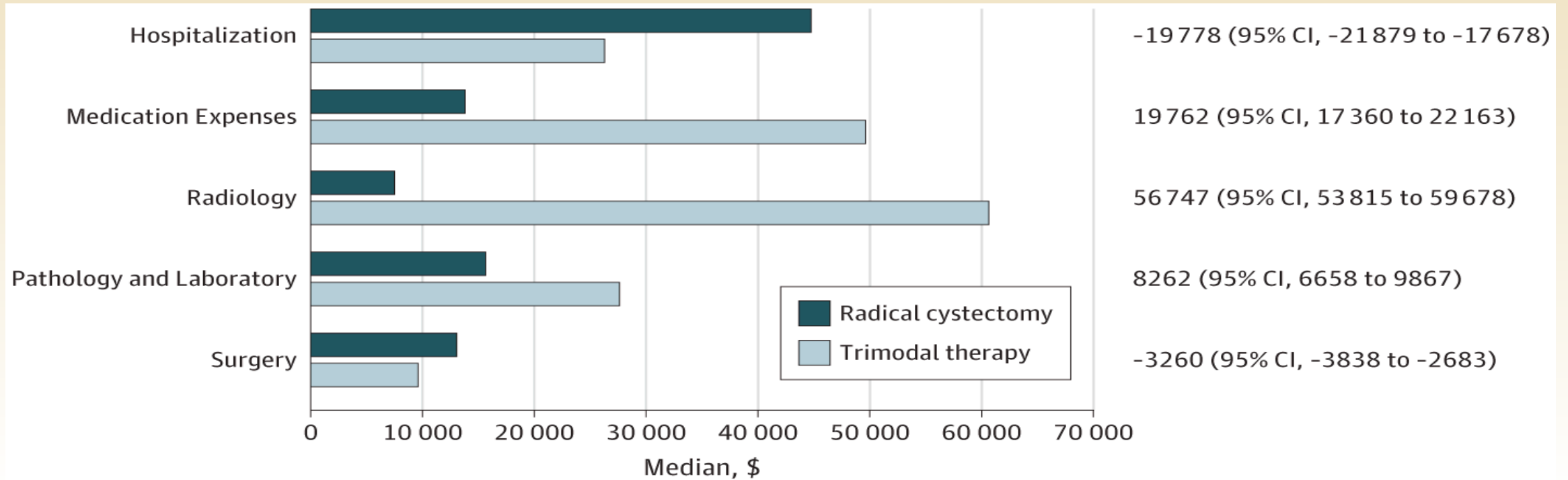
Results—Total Costs

	Radical Cystectomy Median (IQR), \$	Trimodal Therapy Median	Hodges- Lehmann Estimate
90 Days	68,692 (44,912 – 98,871)	83,754 (50,974 – 129,299)	11,805
180 Days	109,078 (71,368 – 170,788)	187,162 (126,905 – 261,817)	62,370
365 Days	148,757 (87,282 – 252,518)	289,142 (197,649 – 409,655)	109,027

- Median total costs associated with TMT were significantly higher at 90, 180, and 365 days.
- Median inpatient costs were significantly higher with RC at all intervals.
- Median outpatient costs were significantly higher with TMT at all intervals.
- Differences between inpatient and outpatient with treatment persisted at all stages.

IQR – Interquartile Range; RC = radical cystectomy; TMT = trimodal therapy.

Results—Costs Categories



- RC associated with significantly higher hospitalization costs (\$44,014 vs. \$25,577).
- TMT had significantly higher medication, radiology, and pathology/laboratory expenses.
- Neoadjuvant chemotherapy followed by RC significantly greater cost than TMT (median, \$292,930 vs \$289,142).

RC = radical cystectomy; TMT = trimodal therapy.

Results—Cumulative Incremental Effects on Total Medicare Costs Within 1 Year

Treatment	Total Medicare Costs, \$			
	Unadjusted Costs, Mean (SD)	Adjusted Incremental Effects (95% CI)		
		Overall	Survival	Intensity
Radical Cystectomy	190,934 (176,657)	1 [Reference]	1 [Reference]	1 [Reference]
Trimodal Therapy	323,608 (367,675)	136,935 (122,131 – 152,115)	7,080 (3,098 – 11,103)	129,854 (115,793 – 145,299)

- TMT associated with significantly higher costs than RC in total 1 year unadjusted analyses.
- Difference persisted after adjusted incremental analyses accounting for survival and intensity.
- Extrapolating findings in 2017 results in excess spending of \$468 million associated with TMT.
- Overall and cancer-specific survival after IPTW were significantly decreased in TMT patients.

RC = radical cystectomy; TMT = trimodal therapy.

Conclusion

- **Trimodal therapy was associated with increased costs and decreased survival compared to radical cystectomy utilizing inverse probability of treatment weighting (supporting first study).**
- **Differences in costs largely attributed to medication and radiology expenses in trimodal therapy.**
- **Accounting for effects of survival and intensity of use using robust statistical analyses revealed a mean excess spending of \$136,935 per patient per year for trimodal therapy.**
- **Extrapolation of mean cost difference resulted in excess spending of \$468 in 2017.**
- **In addition to cost containment for cancer care (in particular anticancer medications), these findings suggest the need for improved survival and quality-of-life years gained to justify using trimodal therapy to manage bladder cancer.**

Limitations

- **65 years and older**
 - **May not be applicable to younger patients.**
- **Retrospective in nature**
 - **Inherent selection bias with inability to control for possible unknown confounders.**
- **SEER-Medicare**
 - **Lacks ability to capture clinician and hospital-level data.**
- **Not a cost-effectiveness study as this would need analysis of quality-of-life years gained.**
- **Costs up to 365 days from diagnosis date and further long-term “global cost of care” assessments needed.**

Thank You!

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