

Supplementary Online Content

Williams SB, Shan Y, Ray-Zack MD, et al. Comparison of costs of radical cystectomy vs trimodal therapy for patients with localized muscle-invasive bladder cancer. *JAMA Surg*. Published online June 5, 2019. doi:10.1001/jamasurg.2019.1629

eFigure 1. Median Cumulative Medicare Costs within One Year of Bladder Cancer Diagnosis

eFigure 2. Adjusted Kaplan-Meier Curves of Overall (A) and Cancer-Specific (B) Survival According to Treatment

eTable 1. International Classification of Diseases–Version 9 (ICD-9) and Common Procedural Terminology (CPT) Codes Used to Identify Patients with Bladder Cancer

eTable 2. Mean \pm SD Medicare Costs (USD) Associated with Radical Cystectomy and Trimodal Therapy Following Bladder Cancer Diagnosis

eTable 3. Calculation of One-Year Medicare Costs (USD) Using the Medical Component of Consumer Price Index and Gross Domestic Product Implicit Price Deflator Methods

eTable 4. Median Medicare Costs (USD) within One-Year from Clinical Diagnosis According to Clinical Stage

eTable 5. Costs (USD) According to Categories of Clinical Services Associated with Bladder Cancer Diagnosis within One-Year of Diagnosis

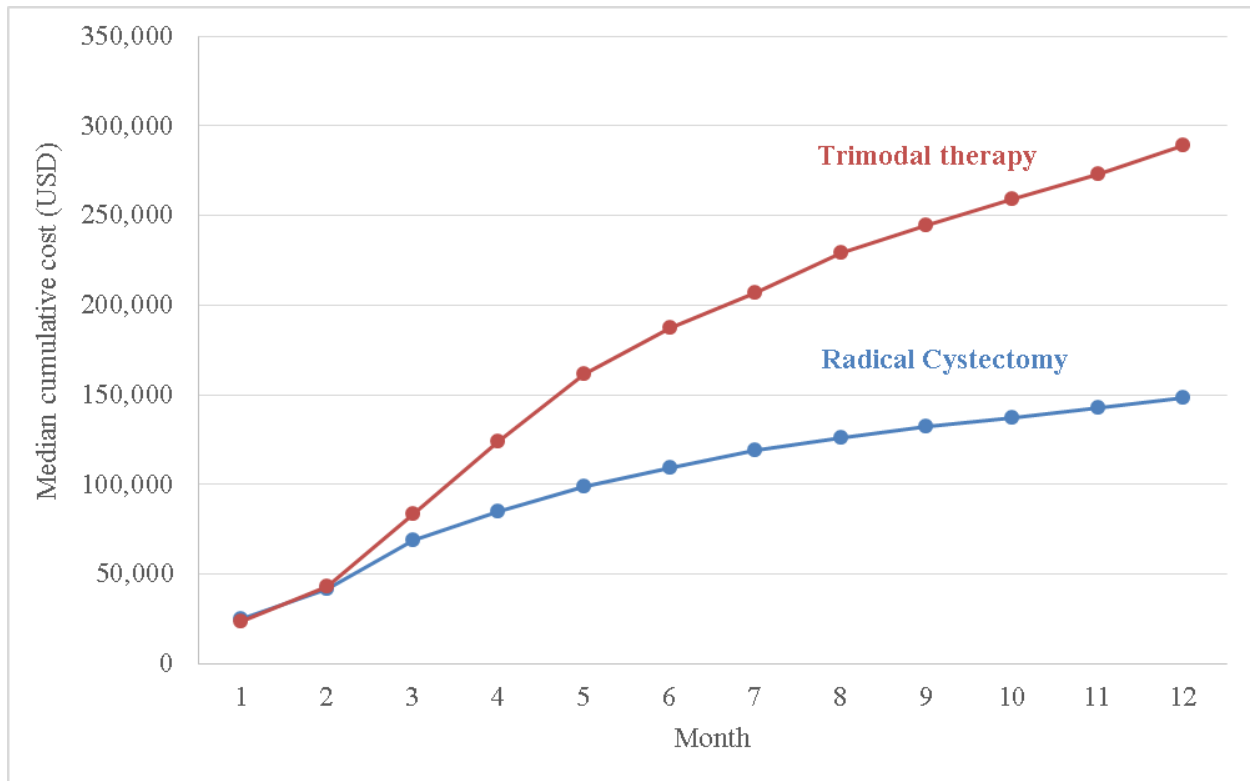
eTable 6. One-Year Medicare Costs (USD) among Patients who Received Neoadjuvant Chemotherapy and Radical Cystectomy versus Trimodal Therapy

eTable 7. One-Year Medicare Costs (USD) among Patients Continuously Enrolled in Medicare Part A + B, Medicare Part D, and Out-of-Pocket Prescription Drugs (Part of Medicare Part D)

eTable 8. Proportional Hazards Regression Model of Predictors for Overall and Cancer-Specific Survival According to Clinical Stage and Total number of radiotherapy fractions received

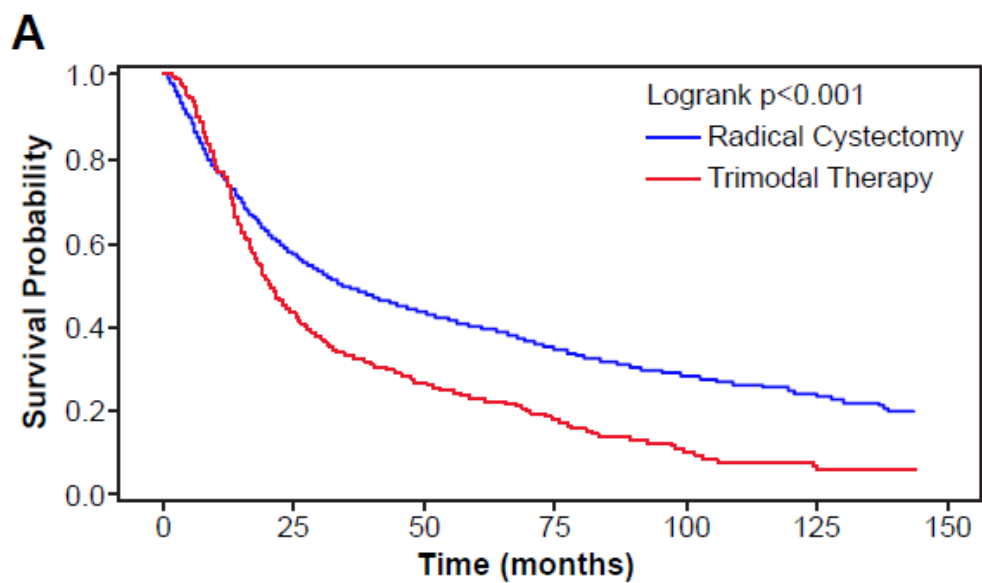
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Median Cumulative Medicare Costs within One Year of Bladder Cancer Diagnosis

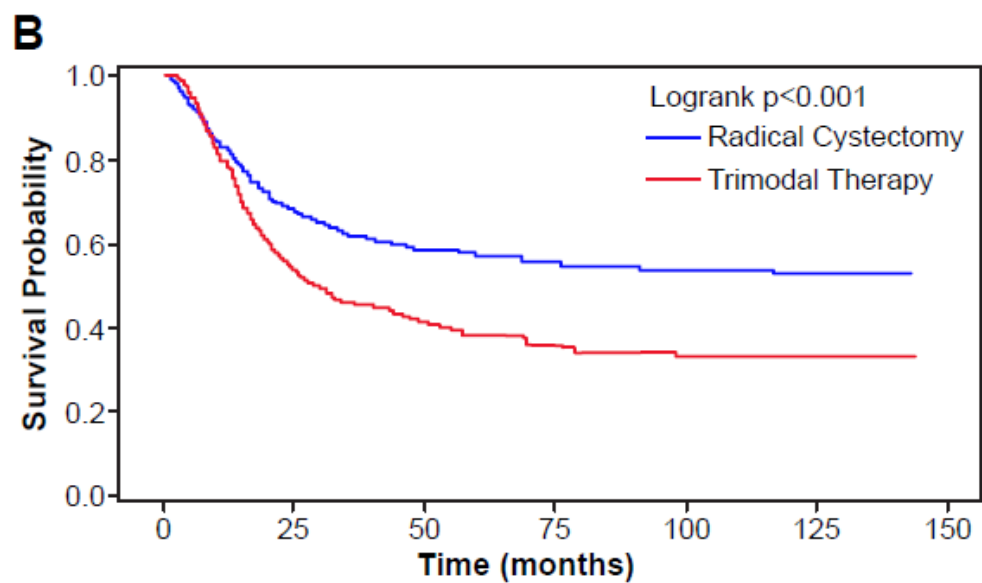


All patients in the study cohort had non-zero costs in 1-year calculations. Medicare costs were similar between patients receiving radical cystectomy versus trimodal therapy for the first three months, corresponding with the interval from time of diagnosis to treatment for most patients.

eFigure 2. Adjusted Kaplan-Meier Curves of Overall (A) and Cancer-Specific (B) Survival According to Treatment



| | | | | | | | |
|--------------------|------|------|------|-----|-----|-----|---|
| Radical Cystectomy | 2957 | 1701 | 1009 | 613 | 329 | 120 | 0 |
| Trimodal Therapy | 3020 | 1322 | 627 | 297 | 117 | 27 | 0 |



| | | | | | | | |
|--------------------|------|------|------|-----|-----|-----|---|
| Radical Cystectomy | 2957 | 1701 | 1009 | 613 | 329 | 120 | 0 |
| Trimodal Therapy | 3020 | 1322 | 627 | 297 | 117 | 27 | 0 |

eTable 1. International Classification of Diseases–Version 9 (ICD-9) and Common Procedural Terminology (CPT) Codes Used to Identify Patients with Bladder Cancer

| Setting | ICD-9 Procedure Codes | CPT Codes |
|-----------------------|--|---|
| Radical cystectomy | 57.71, 57.79, 68.8 | 51570, 51575, 51580, 51585, 51590, 51595, 51596, 51597 |
| Lymph node dissection | | 38770, 51595 |
| Radiation therapy | 92.2, 92.20–92.27, 92.29, 92.3, 92.30–92.39, 92.4, 92.41 | 77371–77373, 77401–77525, 77761–77799, G0174, G0251, G0339, G0340, G0173, 0082T, 61793, 0182T |
| Chemotherapy | | J6360, J9000, J9001, J9060, J9062, J9201, J9250, J9260, J9000, J9001, J9010, J9250, J9260, J9360, J9070, J9080, J9090, J9091, J9092, J9093, J9094, J9095, J9096, J9097, J9098, J9201, J9265, J9170, J9208, J9999, J9045 |

eTable 2. Mean \pm SD Medicare Costs (USD) Associated with Radical Cystectomy and Trimodal Therapy Following Bladder Cancer Diagnosis

| | Radical Cystectomy | | | Trimodal Therapy | | |
|----------|-----------------------|---------------------|-----------------------|-----------------------|---------------------|-----------------------|
| | Total | Inpatient | Outpatient | Total | Inpatient | Outpatient |
| 90 Days | 77,808 \pm 60,606 | 30,387 \pm 36,898 | 47,420 \pm 50,334 | 97,116 \pm 132,835 | 13,051 \pm 37,972 | 84,065 \pm 130,213 |
| 180 Days | 133,710 \pm 107,358 | 47,224 \pm 45,094 | 86,486 \pm 100,758 | 206,884 \pm 234,475 | 21,101 \pm 54,791 | 185,783 \pm 230,450 |
| 365 Days | 190,934 \pm 176,657 | 61,497 \pm 56,230 | 129,438 \pm 163,294 | 323,608 \pm 367,675 | 32,345 \pm 77,452 | 291,263 \pm 359,185 |

Abbreviations: CI, Confidence Interval; SD, Standard Deviation; USD, US Dollar

eTable 3. Calculation of One-Year Medicare Costs (USD) Using the Medical Component of Consumer Price Index and Gross Domestic Product Implicit Price Deflator Methods

| | Radical Cystectomy (N =2,235) | | Trimodal Therapy (N =728) | | H-L, Median (95% CI) |
|--------------|--------------------------------|------------------|------------------------------|------------------|-------------------------|
| | Median [IQR] | Mean ±SD | Median [IQR] | Mean ±SD | |
| M-CPI | 128,593 [74,843-128,593] | 166,191 ±154,433 | 250,260 [172,499-361,993] | 280,972 ±318,074 | 95,356 (86,252-104,460) |
| GDP Deflator | 127,547 [73,769-217,800] | 164,729 ±153,510 | 247,261 [170,310-362,115] | 278,272 ±314,933 | 94,545 (85,494-103,595) |

Abbreviations: CI, Confidence Interval; GDP, Gross Domestic Product; H-L, Hodges-Lehmann difference estimate; IQR, Interquartile Range; M-CPI, Medical Component of Consumer Price Index; SD, Standard Deviation; USD, US Dollar

eTable 4. Median Medicare Costs (USD) within One-Year from Clinical Diagnosis According to Clinical Stage

| Stage 2 | | | | | | | | |
|---|---------------------------|------------|------------------|-------------------|-------------------------|------------|------------------|-------------------|
| | Radical Cystectomy | | | | Trimodal Therapy | | | |
| | Total | IQR | Inpatient | Outpatient | Total | IQR | Inpatient | Outpatient |
| 90 days* | 65,140 | 53,626 | 22,089 | 36,671 | 73,297 | 74,170 | 4,372 | 64,414 |
| 180 days** | 98,933 | 93,351 | 33,181 | 53,161 | 166,189 | 108,507 | 7,472 | 153,479 |
| *Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: 0.030, <0.001 and <0.001, respectively. **Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: all <0.001, respectively. IQR: Interquartile Range | | | | | | | | |
| Stage 3 | | | | | | | | |
| | Radical Cystectomy | | | | Trimodal Therapy | | | |
| | Total | IQR | Inpatient | Outpatient | Total | IQR | Inpatient | Outpatient |
| 90 days* | 67,612 | 47,159 | 27,814 | 34,758 | 96,588 | 83,162 | 8,768 | 81,786 |
| 180 days** | 105,023 | 98,272 | 38,964 | 51,681 | 194,530 | 142,099 | 19,021 | 167,991 |
| *Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: 0.144, <0.001 and 0.002, respectively. **Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: 0.009, <0.001 and <0.001, respectively. | | | | | | | | |
| Stage 4 | | | | | | | | |
| | Radical Cystectomy | | | | Trimodal Therapy | | | |
| | Total | IQR | Inpatient | Outpatient | Total | IQR | Inpatient | Outpatient |
| 90 days* | 73,874 | 62,346 | 28,042 | 36,739 | 89,475 | 87,923 | 9,786 | 76,411 |
| 180 days** | 136,201 | 118,523 | 43,205 | 73,411 | 207,925 | 157,322 | 21,216 | 186,098 |

*Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: 0.08, <0.001 and 0.001, respectively.

**Radical Cystectomy vs. Trimodal Therapy Total, Inpatient and Outpatient p-values: 0.003, <0.001 and <0.001, respectively.

eTable 5. Costs (USD) According to Categories of Clinical Services Associated with Bladder Cancer Diagnosis within One-Year of Diagnosis

| Service Category | Total Cost | Radical Cystectomy | Trimodal Therapy | H-L Median difference ^a | H-L 95% CI | | P-Value |
|--|------------|--------------------|------------------|------------------------------------|------------|---------|---------|
| | | | | | | | |
| Administered drugs, including chemotherapy drugs | 36,269 | 13,013 | 49,587 | 19,762 | 17,360 | 22,163 | <.0001 |
| Allergy | 241 | 464 | 241 | -363 | -966 | 241 | 0.364 |
| Anesthesia | 757 | 1,070 | 416 | -602 | -637 | -566 | <.0001 |
| Cardiovascular | 1,769 | 1,657 | 1,937 | 124 | 5 | 243 | 0.986 |
| Consultations | 1,203 | 1,093 | 1,262 | 134 | 51 | 217 | 0.075 |
| Emergency Room/Critical Care | 804 | 734 | 866 | 66 | 5 | 128 | 0.304 |
| Immunizations/Injections | 426 | 235 | 2,856 | 391 | 141 | 641 | 0.010 |
| Inpatient Visits | 2,303 | 2,289 | 2,334 | -2 | -198 | 193 | 0.782 |
| Office Visits | 3,460 | 1,952 | 5,586 | 2,658 | 2,350 | 2,966 | <.0001 |
| Ophthalmology | 228 | 238 | 224 | -7 | -28 | 14 | 0.827 |
| Pathology/Laboratory | 20,350 | 15,535 | 26,966 | 8,262 | 6,658 | 9,867 | 0.001 |
| Physical Medicine | 745 | 639 | 845 | 58 | -100 | 216 | 0.465 |
| Preventive Visits | 63 | 24 | 103 | 53 | 0 | 107 | 0.901 |
| Psychiatry & Biofeedback | 211 | 224 | 174 | -31 | -88 | 26 | 0.489 |
| Radiology | 25,346 | 7,476 | 60,599 | 56,747 | 53,815 | 59,678 | <.0001 |
| Surgery | 10,883 | 12,158 | 9,256 | -3,260 | -3,838 | -2,683 | 0.038 |
| Other Professional Services | 16,294 | 5,349 | 27,102 | 12,153 | 10,676 | 13,630 | <.0001 |
| Ambulance | 1,729 | 1,656 | 1,779 | 80 | -84 | 244 | 0.279 |
| Durable medical equipment/Prosthetics/Supplies | 1,639 | 1,447 | 1,820 | 208 | 65 | 351 | 0.381 |
| Unclassified | 11,883 | 5,415 | 21,335 | 11,270 | 10,154 | 12,387 | <.0001 |
| Hospitalization | 36,532 | 44,014 | 25,577 | -19,778 | -21,879 | -17,678 | <.0001 |
| Skilled nursing facilities | 10,735 | 10,664 | 11,406 | 1,009 | -813 | 2,831 | 0.925 |

Abbreviations: H-L, Hodges-Lehmann; CI, confidence interval; USD, US Dollar

^aHodges-Lehmann median difference in total costs (trimodal therapy minus radical cystectomy).

eTable 6. One-Year Medicare Costs (USD) among Patients who Received Neoadjuvant Chemotherapy and Radical Cystectomy versus Trimodal Therapy

| | NAC + RC (N =252) | | Trimodal Therapy (N = 728) | | H-L, Median (95% CI) |
|----------|------------------------------|------------------|------------------------------|------------------|-----------------------|
| | Median [IQR] | Mean ±SD | Median [IQR] | Mean ±SD | |
| One-Year | 292,930 [215,674-401,904] | 328,946 ±195,483 | 289,142 [197,649-409,655] | 323,608 ±367,675 | 24,897 (5,243-44,551) |

Abbreviations: CI, Confidence Interval; H-L, Hodges-Lehmann difference estimate; IQR, Interquartile Range; NAC, Neoadjuvant Chemotherapy; RC, Radical Cystectomy; SD, Standard Deviation; USD, US Dollar

eTable 7. One-Year Medicare Costs (USD) among Patients Continuously Enrolled in Medicare Part A + B, Medicare Part D, and Out-of-Pocket Prescription Drugs (Part of Medicare Part D)

| | Radical Cystectomy (N =354) | | Trimodal Therapy (N =123) | | H-L Estimate (95% CI) |
|----------------------------------|------------------------------|-----------------------|------------------------------|-----------------------|-------------------------|
| | Median [IQR] | Mean \pm SD | Median [IQR] | Mean \pm SD | |
| Medicare Parts A+B | 178,338 [105,071-270,104] | 214,368 \pm 216,937 | 293,073 [187,655-400,431] | 316,919 \pm 356,974 | 84,943 (58,361-111,525) |
| Medicare Part D | 2,110 [909-3,525] | 3,058 \pm 5,417 | 2,822 [1,545-5,832] | 4,647 \pm 10,895 | 667 (219-1,114) |
| Out-of-Pocket Prescription Drugs | 349 [106-787] | 586 \pm 831 | 400 [77-991] | 833 \pm 2,404 | 15 (-50 - 80) |

Abbreviations: CI, Confidence Interval; H-L, Hodges-Lehmann difference estimate; IQR, Interquartile Range; RC, Radical Cystectomy; SD, Standard Deviation; USD, US Dollar

eTable 8. Proportional Hazards Regression Model of Predictors for Overall and Cancer-Specific Survival According to Clinical Stage and Total number of radiotherapy fractions received

| Covariate | Cox Regression | | | | Competing Risk Regression | | | |
|---------------------------------------|------------------|--------|------|---------|---------------------------|--------|------|---------|
| | Overall Survival | | | | Cancer-Specific Survival | | | |
| | HR | 95% CI | | p Value | HR | 95% CI | | p-Value |
| Stage T2 | | | | | | | | |
| Radical Cystectomy | ref | - | - | - | ref | - | - | - |
| Trimodal Therapy | 1.81 | 1.57 | 2.10 | <0.001 | 1.83 | 1.60 | 2.08 | <0.001 |
| Stage T3 | | | | | | | | |
| Radical Cystectomy | ref | - | - | - | ref | - | - | - |
| Trimodal Therapy | 1.73 | 1.36 | 2.21 | <0.001 | 1.46 | 1.25 | 1.69 | <0.001 |
| Stage T4a | | | | | | | | |
| Radical Cystectomy | ref | - | - | - | ref | - | - | - |
| Trimodal Therapy | 1.03 | 0.86 | 1.24 | 0.755 | 1.24 | 1.10 | 1.39 | <0.001 |
| Radiotherapy fractions <27* | | | | | | | | |
| Radical Cystectomy | ref | - | - | - | N/A | | | |
| Trimodal Therapy | 1.59 | 1.41 | 1.79 | <0.001 | | | | |
| Radiotherapy fractions ≥27* | | | | | | | | |
| Radical Cystectomy | ref | - | - | - | N/A | | | |
| Trimodal Therapy | 1.22 | 1.09 | 1.37 | 0.001 | | | | |

Abbreviations: CI: Confidence interval; HR: Hazard ratio