**Table E2. Key Question 2: Included studies**

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Abdollah,  2012[12](#_ENREF_12)  Retrospective Cohort  Medium | US  1988-2006 | Radical cystectomy for non-  metastatic transitional cell carcinoma of the urinary bladder | Unknown tumor stage or  grade | A: Cystectomy with extended lymph node  dissection (≥10 lymph nodes removed and examined)  B: Cystectomy with limited lymph node dissection (<10 lymph nodes removed and examined)  C: Cystectomy without pelvic lymph node dissection | Not reported |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Abdollah,  2012[12](#_ENREF_12)  Retrospective Cohort  Medium | A+B: 8394  C: 2789 | A+B vs. C  Age (mean): 67.1 vs. 68.8, p<0.001  Male: 6285/8394 vs. 2025/2789 , p<0.01  Caucasian:7533/8394 vs. 2508/2789  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: Ta/Tis:159/8394 vs.  161/2789  T1: 807/8394 vs. 4332789  T2: 3191/8394 vs. 1193/2789  T3: 2578/8394 vs. 495/2789  T4: 1659/8394 vs. 507/2789;  p<0.001  Grade: G1/G2: 599/8394 vs.  326/2789  G3: 4466/8394 vs. 1559/2789  G4: 3329/8394 vs. 904/2789;  p<0.001  Functional status: Not reported | A+B vs. C  HRs adjusted for age, sex, race, tumor stage, tumor grade and year of surgery  10-year cancer-specific mortality: 57.5% vs. 52.5% (log rank p <0.001), HR 1.33 (95% CI:  1.24-1.44)  Ta/Tis: 80.4% vs. 71.9% (p=0.02), HR 2.09 (95% CI 1.16-3.79) T1: 81.7% vs. 70.0% (p<0.001), HR 1.60 (95% CI 1.18-2.17) T2: 71.5% vs. 56.1% (p<0.001), HR 1.68 (95% CI 1.47-1.91) T3: 43.7% vs. 38.8% (p=0.006), HR 1.15 (95% CI 1.01-1.33) T4: 35.1% vs. 32.0% (p=0.1), HR 1.11 (95% CI 0.9-1.28)  10-year overall mortality: 34.1% vs. 27.2% (log rank p<0.001), HR 1.29 (95% CI 1.22-1.37) Ta/Tis:53.4% vs. 48.1% (p=0.07), HR 1.49 (95% CI 1.02-2.17)  T1: 57.7% vs. 41.4% (p=0.001), HR 1.29 (95% CI 1.06-1.57) T2: 44.6% vs. 29.4% (p<0.001), HR 1.44 (95% CI 1.31-1.58) T3: 23.4% vs. 18.5% (p<0.001), HR 1.13 (95% CI 1.01-1.28) T4: 17.5% vs. 11.8% (p<0.001), HR 1.24 (95% CI 1.11-1.39)  A vs. B  10-year cancer-specific mortality: 62.2% vs. 54.0% (log rank p<0.001) Ta/Tis: 70.8% vs. 85.7% (p=0.1)  T1: 85.8% vs. 78.% (p=0.01)  T2: 76.1% vs. 67.7% (p<0.001) T3: 48.7% vs. 39.7% (p<0.001) T4: 38.6% vs. 32.5% (p=0.02)  10-year overall mortality: 39.4% vs. 30.3% (log rank p<0.001) Ta/Tis: 39.1% vs. 63.3% (p=0.05)  T1: 66.7% vs. 51.2% (p<0.001) T2: 50.0% vs. 40.4% (p<0.001) T3: 28.2% vs. 19.7% (p<0.001) T4: 21.5% vs. 14.8% (p<0.001) |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Abdollah,  2012[12](#_ENREF_12)  Retrospective Cohort  Medium | Not reported | Not reported |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Brossner,  2004[13](#_ENREF_13)  Retrospective Cohort  High | Austria and Italy  Two centers  1998-2002 | Patients undergoing radical  cystectomy, American Society of Anesthesiologists grade 2 or 3 | Not reported | A: (Italian Cohort): Cystoprostatectomy in  men or pelvectomy in women, with "extended" lymphadenectomy, including the perivesical, hypogastric, obturator, external iliac, common iliac and aortal lymph nodes, into the region of the inferior mesenteric artery.  B: (Australian cohort): Cystoprostatectomy in men or pelvectomy in women, with "minimal" lymphadenectomy, including perivesical lymph nodes and lymphatic tissue of the obturator fossa, confined laterally by the external iliac vein and medial by the obturator nerve. | 30 days  Unclear method of followup |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Brossner,  2004[13](#_ENREF_13)  Retrospective Cohort  High | A: 46  B: 46 | Age (mean): 66.3 vs. 68.2 years  Male: Not reported Race: Not reported Smoker: Not reported  Recurrent bladder cancer: Not reported  Stage: pT1: 4 vs. 6; pT2-3a: 24 vs.  18; pT3b-4: 18 vs. 22; Node positive:  18 vs. 10  Grade: Not reported  Functional Status: Not reported | Median operative duration (minutes): 330 vs. 227 |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Brossner,  2004[13](#_ENREF_13)  Retrospective Cohort  High | Median ICU stay (days): 4.5 vs. 5.1, P-value Not reported  Median hospital stay (days): 16.3 vs. 14.2, P-value Not reported  Median blood units received during surgery: 0.8 vs. 1.15, P=0.37  Median blood units received within 30 days: 0.7 vs. 3.2, P=0.067  Complications within 30 days:  Overall surgical complications: 20/46 vs. 17/46, P=0.08  Perioperative mortality: 4.3% (2/46) (pneumonia) vs. 2.2% (1/46) (pulmonary embolus), RR 0.50 (95% CI 0.047 to 5.32)  Complications requiring surgery: 5/46 vs. 4/46, P=0.28  Cardiac arrhythmia: 5/46 vs. 3/46, P=0.16  Pulmonary embolus: 1/46 vs. 2/46  Pneumonia: 2/46 vs. 7/46, P=0.02  Prolonged ileus >6 days: 1/46 vs. 2/46  Hydronephrosis: 3/46 vs. 6/46  Pyelonephritis: 4/46 vs. 4/46  Acute renal failure: 1/46 vs. 0/46  Transient cerebrovascular accident: 3/46 vs. 1/46 | Not reported |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Brunocilla,  2013[14](#_ENREF_14)  Retrospective Cohort  Medium | Italy  1995-2011 | Radical cystectomy for  muscle-invasive or high- grade superficial bladder cancer with curative intent | Neoadjuvant or adjuvant  chemotherapy and/or radiation; incomplete clinical, pathological, and followup data | A: Limited template: Cystectomy including  external and obturator lymph nodes; or no lymphadenectomy  B: Standard template: Cystectomy including external, obturator, internal iliac, and 2 cm common iliac lymph nodes up to the cross with the ureters  C: Extended template: Cystectomy including external, obturator, internal iliac, presacral, and complete common iliac lymph nodes up to the aortic bifurcation  D: Super-extended template: Cystectomy including external, obturator, internal iliac, presacral, complete common iliac lymph nodes up to the aortic bifurcation, preaortic and precaval lymph nodes up to inferior mesenteric artery  Selection of template was based on preference and skills of the surgeons | Mean: 59.2±44.3  months |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Brunocilla,  2013[14](#_ENREF_14)  Retrospective Cohort  Medium | A: 116  B: 94  C: 39  D: 23 | Reported for 0-14 lymph nodes  removed (n=128) vs. ≥14 lymph nodes removed (n=154):  Age (mean): 69.6±8.4 vs. 667.3±8.1;  p=0.010  Male: 82.8% vs. 83.1% Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: T0: 23/128 vs. 18/154  T1: 21/128 vs. 20/154  T2: 24/128 vs. 41/154  T3: 37/128 vs. 50/154  T4: 23/128 vs. 25/154  Tumor Grade: G1-G2: 32/128 vs.  34/154  G3: 96/128 vs. 120/154  Functional status: Not reported | Cancer-specific survival, hazard ratio (95%CI)  Univariable:  B vs. A: 0.828 (0.547-1.255) C vs. A: 0.350 (0.221-0.740)  ≥14 lymph nodes removed vs. 0-14 lymph nodes removed: 0.576 (0.382-0.847)  Multivariable:  B vs. A: 0.986 (0.547-1.354) C vs. A: 0.455 (0.365-0.894)  ≥14 lymph nodes removed vs. 0-14 lymph nodes removed: 0.556 (0.282-0.995) |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Brunocilla,  2013[14](#_ENREF_14)  Retrospective Cohort  Medium | Not reported | Not reported |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Dhar, 2008[15](#_ENREF_15)  Retrospective cohort High | US and Switzerland  Two centers  1987-2000 | TCC of bladder (preoperative  stage N0M0) who underwent curative intent radical cystectomy | Neoadjuvant treatment,  positive pathological margins, stages pTa, pT1, and pT4 cancer | A (Switzerland cohort): Cystectomy with  extended lymphadenectomy, with cephalad dissection extended to the crossing of the ureters with the common iliac arteries and removal of all tissue along the lateral and medial portion of internal iliac vessels.  B: (US cohort): Cystectomy with limited lymphadenectomy, with boundaries of the pelvic sidewall between the genitofemoral and obturator nerves, and bifurcation of the iliac vessels to the circumflex iliac vein. | 5 years  A: Every 6 months for  2 years and annually thereafter.  B: 3 and 6 months after surgery, 6-month intervals until 5 years and annually thereafter. |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Dhar, 2008[15](#_ENREF_15)  Retrospective cohort High | A: 322  B: 336 | Age (median): 66.9 vs. 61.6 years,  p<0.001  Male: 78% vs. 79% Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: Not reported  Tumor grade: Not reported  Functional status: Not reported | A vs. B  Lymph Nodes  Number of nodes examined, median (range): 12 (2-31) vs. 22 (10-43) Number of positive nodes, median (range): 1 (1-5) vs. 2 (1-26)  Lymph node positive rate: overall, 13% vs. 26%; pT2, 15/200 vs. 24/150; pT3, 29/136 vs.  59/172  5 year recurrence-free survival (median followup: 25 vs. 40, p<0.001) pT2: 71% vs. 63%, p=0.10  pT3: 19% vs 49%, p<0.0001  5 year overall survival  (median followup: 36 vs. 51, p<0.001)  pT2: 64% vs. 61%, p=0.10 pT3: 22% vs. 42%, p=0.0002  Progression: local or systemic: 55% (184/336) vs. 40% (130/322) RR 0.74 (95% CI 0.63 to  0.87)  Local progression (p for log-rank test)::  pT2: 24% vs 44%, p<0.0001 pT3: 60% vs. 10%, p<0.0001  Systemic progression (includes those with both local and systemic progression):  pT2: 14% vs. 27%, p=0.0048 pT3: 20% vs. 45%, p=0.0012 |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Dhar, 2008[15](#_ENREF_15)  Retrospective cohort High | Not reported | Not reported | Numbers in table do not  correspond to percentages reported in the paper. Percentages are presented here for RFS and OS. Should we do the same for progression. I am unclear as to what denominator was used when calculating p- values. |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Herr, 2002[16](#_ENREF_16)  Retrospective cohort  High | US  Single center  1980-1990 | Bilateral pelvic  lymphadenectomy and radical cystectomy, pathological muscle invasive transitional cell carcinoma, followup greater than 10 years | Preoperative radiation,  neoadjuvant or adjuvant chemotherapy | A: Radical cystectomy with standard  lymphadenectomy, including the distal common iliac, external iliac, hypogastric, obturator,  presacral and perivesical lymph nodes  (n=Not reported)  B: Cystectomy with limited lymphadenectomy, with obturator and perivesical lymph nodes removed en bloc with the bladder. (n=Not reported) | Minimum followup 10  years |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Herr, 2002[16](#_ENREF_16)  Retrospective cohort  High | Not reported,  Overall N=322 | Age: Not reported  Male: Not reported  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: 188 T2, 134 T2-T3  Tumor grade: Not reported  Functional status: Not reported | Local recurrence (uncertain followup):  N0 patients: 5% (7/131) when 8 or more nodes, 24% (31/127) when 1-8 nodes, p=0.001; N+ patients, 9% (3/34) when 11 or more nodes, 30% (10/30) when 1-11 nodes, p=0.002  5-year recurrence-free survival: Stage ≤T3a: 85% vs. 64%, p<0.02; Stage ≥T3b: 27% vs.  39%, p=0.87  10-year survival  N0 patients (n=258): 82% when 8 or more nodes, 63% when 4-7 nodes, 23% when 0-3 nodes, p=0.004.  59% (75/127) ≥ 8 vs. 18% (23/131) <8 lymph nodes  N+ patients (n=64): 45% when > 14 nodes, 39% when 9-14 nodes, 16% when 1-8 nodes, p=0.02.  56% (19/34) ≥ 11 vs. 80% (24/30) for < 11 lymph nodes, p=0.004 |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Herr, 2002[16](#_ENREF_16)  Retrospective cohort  High | Not reported | Not reported |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Herr, 2004[17](#_ENREF_17)  Reanalysis of RCT Medium | US  Multiple centers  1987-1998  Reanalysis of RCT | Muscle invasive bladder  cancer, T2-T4a, N0, M0, candidate for radical cystectomy, SWOG performance status 0-1 | Prior pelvic radiation | A: Cystectomy with standard  lymphadenectomy (n=146), median 15 LN  B: Cystectomy with limited lymphadenectomy (n=98), median 7 LN  C: Cystectomy with no lymphadenectomy  (n=24) | Minimum followup 5  years |
| Konety, 2003[18](#_ENREF_18)  Retrospective cohort Medium | US  Population based study (SEER data)  1988-1996 | primary bladder cancer;  subset with radical cystectomy with or without lymph node dissection | Not reported | Patients with bladder cancer who  underwent cystectomy, number of lymph nodes examined: 0 (n=645), 1-3 (n=203),  4-6 (n=239), 7-9 (n=164), 10-14 (n=163),  15-19 (n=106), ≥20 (n=81), missing data. | Minimum 2 years;  Median in surviving post-cystectomy patients: 63.5 months |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Herr, 2004[17](#_ENREF_17)  Reanalysis of RCT Medium | A: 146  B: 98  C: 24 | Overall characteristics, not reported  by treatment group:  Age: 148/268 <65 years, 120/268 ≥  65 years  Male 81% (216/268) Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: 69% (184/268) T0-T2  31% (84/268) T3-T4  Tumor grade: Not reported  Functional status: 100% SWOG 0 or  1 | A vs. B vs. C  Local Recurrence (no median followup reported):  7/146 (5%) vs. 22/98 (22%) vs.12/24 (50%), p<0.0001  RR 0.21, 95% CI 0.09 to 0.48  ≥10 nodes removed vs. <10 nodes removed: 6% vs. 25%, p<0.0001, multivariate Cox proportional hazards model <10 nodes (HR 0.20, 95% CI 0.07 to 0.56)  5-year overall survival: 60% vs. 46% vs. 33%, p=0.01  ≥10 nodes removed vs. <10 nodes removed: 5-year overall survival: 61% vs. 44%, p=0.0007, multivariate Cox proportional hazards model <10 nodes HR 0.50, 95% CI 0.36 to  0.71  A vs. B  Risk of mortality: 52% (59/146) vs. 64% (63/98), RR 0.94, 95% CI 0.68 to 1.04 |
| Konety, 2003[18](#_ENREF_18)  Retrospective cohort Medium | Cystectomy  subset: N=1923  0 lymph nodes, n=645  ≥1 lymph node, n=956  unknown lymph nodes, n=322 | Age: <35: 70 (3.6%); 35-44: 86  (4.5%); 45-54: 237 (12.3%); 55-64:  476 (24.8%); 65-74: 681 (35.4%); 75-  84: 349 (18.2%); ≥85: 24 (1.3%) Male: 1265/1923 (65.8%)  Race: White: 1698/1923 (93.6%); Black: 117/1923 (6.5%)  Smoking Status: Not reported Recurrent bladder cancer: Not reported  Stage: In situ or 1: 150 (12.9%); Stage 2: 249 (21.4%); Stage 3: 300 (25.8%); Stage 4: 465 (39.9%); missing: 759  Tumor grade: Not reported  Functional status: Not reported | Risk of death by number of lymph nodes examined; Adjusted hazard ratio (95%CI); p-  value:  0: 1 (reference)  1-3: 0.93 (0.69 to 1.27);  4-6: 0.52 (0.36 to 0.76);  7-9: 0.57 (0.39 to 0.81);  10-14: 0.38 (0.25 to 0.57);  15-19: 0.57 (0.39 to 0.85);  ≥20: 0.48 (0.30 to 0.76);  ≥4: 0.53 (0.36 to 0.76) |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Herr, 2004[17](#_ENREF_17)  Reanalysis of RCT Medium | Not reported | SWOG |  |
| Konety, 2003[18](#_ENREF_18)  Retrospective cohort Medium | Not reported | Not reported |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Leissner, 2000[19](#_ENREF_19)  retrospective cohort  High | Germany  1986-1997 | Radical cystectomy with  curative intent for pTis, pT1G3, pT2 to pT4 transitional cell carcinoma | previous pelvic  lymphadenectomy or irradiation, preoperative chemotherapy for bladder cancer, pTa bladder cancer | Patients with bladder cancer who  underwent cystectomy, number of lymph nodes examined: 1-5, 6-10, 11-15, 16-20, and >20 | Minimum 2 years;  Mean: 38.7 months |
| Poulsen,  1998[20](#_ENREF_20)  Retrospective cohort  High | Denmark  Single study  1990-1997 | radical cystectomy with  lymphadenectomy | pretreatment of bladder  cancer | A: Radical cystectomy with extended  lymphadenectomy, bounded proximally by bifurcation of the aorta, laterally by the genitofemoral nerve, distally by the circumflex iliac vein and Cloquet's lymph node and posteriorly by the internal ileac vessel, including the presacral nodes and obturator fossa  B: Cystectomy with limited lymphadenectomy, bounded proximally by bifurcation of the common iliac vessels, while the lateral, distal and posterior boundaries were the same as for the extended dissection, including dissection of the obturator fossa. | 4-month intervals for  the first year, then annually. |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Leissner, 2000[19](#_ENREF_19)  retrospective cohort  High | Per group: Not  reported, Overall: 302 | Age: 62.8 years  Male: male: female ratio 4.5:1  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage of disease (for all patients with radical cystectomy): pTis: 15 (3.4%); pT1: 100 (22.4%); pT2a: 88 (19.7%); pT2b: 51(11.4%); pT3: 146 (32.7%); pT4: 47 (10.5%)  Tumor grade: Not reported  Functional status: Not reported | ≥16 nodes removed vs. ≤15 nodes removed :  5-year bladder cancer- specific survival: 65% vs. 51%, p<0.013  Local recurrence: 17% vs. 27%, p<0.01  Distant metastasis: 10.5% vs. 17%, p<0.01 |
| Poulsen,  1998[20](#_ENREF_20)  Retrospective cohort  High | A: n=126  B: n=68 | Age, mean: 61.8 vs. 63.2 years  Male: 102/126 vs. 55/68  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: T0-Ta: 7.1% vs. 5.9%; Tis:  13.5% vs. 5.9%; T1: 12.7% vs. 25%; T2: 10.3% vs. 13.2%; T3a: 13.5%  vs. 16.2%; T3b: 35.7% vs. 29.4%; T4a: 4.0% vs. 1.5%; T4b: 1.6% vs.  1.5%; prostate: 0.8% vs. 1.5%; adenocarcinoma: 0.8% vs. 0% Tumor grade: Not reported Functional status: Not reported | A vs. B:  Median number of nodes removed: 25 (range 9-67) vs. 13 (range 6-30), p<0.0001  5-year recurrence-free survival: 62% vs. 56%, p=0.33  5-year risk of distant metastasis: 29% vs. 30%, p not reported  5-year risk of pelvic metastasis: 10% vs. 10%, p not reported  5-year recurrence-free survival: Stage ≤T3a: 85% vs. 64%, p<0.02; Stage ≥T3b: 27% vs.  39%, p=0.87  5-year survival: Stage ≤T3a,N0: 90% vs. 71%, p<0.02; Stage ≥T3b,N0: 38% vs. 67%, p=0.46 |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Leissner, 2000[19](#_ENREF_19)  retrospective cohort  High | Inverse relationship between number of complications associated with the  lymphadenectomy and the number of lymph nodes removed, data Not reported | Not reported |  |
| Poulsen,  1998[20](#_ENREF_20)  Retrospective cohort  High | Not reported | Mauritzen La Fontaine  Foundation |  |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Shirotake,  2010[21](#_ENREF_21)  Retrospective cohort  Medium | Japan  Single center  1987-2008 | refractory non-muscle-  invasive or muscle-invasive bladder cancer | noncurative surgery,  tumors of nonurothelial origin, unclear medical history | A: Cystectomy with lymphadenectomy  B: Cystectomy without lymphadenectomy  Neoadjuvant chemotherapy, n=16, mostly  T3-4  Adjuvant chemotherapy, n=26, T3-4 or  Node positive | 3-month intervals for 2  years and every 6 months thereafter |
| Simone,  2013[22](#_ENREF_22)  Retrospective cohort  Medium | Italy  Two centers  2002-2010 | high-grade urothelial  carcinoma | neoadjuvant treatment,  salvage cystectomy | A: Cystectomy with extended  lymphadenectomy, dissected nodes up to and, in some cases, above the aortic bifurcation including the presacral nodes  B: Cystectomy with standard lymphadenectomy, dissected nodes with an upper boundary at the iliac bifurcation (not including presacral and common nodes) | followup method, Not  reported |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Shirotake,  2010[21](#_ENREF_21)  Retrospective cohort  Medium | A: 107  B: 62 (includes those without lymphadenectomy or unknown number of  nodes removed) | Age, mean: 67.65 vs. 69.4 years  Male: overall 127/169  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: ≤T2: 52/107 vs. 34/62; T3-4:  55/107 vs. 28/62  Tumor grade: G1-2: 27/107 vs.  28/62; G3: 80/107 vs. 38/62  Functional status: Not reported | Node positive (N+) vs. Node negative (N-) vs. Nodes not removed or unknown (Nx)  5-year Cancer-specific survival: 40.8% vs. 72.3% vs. 73.5%; N+ vs. N-, p=0.0471, Nx vs. N-  , p=0.846  ≥9 nodes removed vs. <9 nodes removed:  5-year Cancer-specific survival, node-positive and node negative patients: 84.3% vs.  52.7%, adjusted HR 3.48 (95%CI 1.50 to 9.31)  Node negative patients: adjusted HR 6.94 (95% CI 1.88 to 38.21) |
| Simone,  2013[22](#_ENREF_22)  Retrospective cohort  Medium | A: 349  B: 584 | Age, mean: 65.4 years vs. 66.9  years  Male: 309/349 vs. 502/584  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: T0, a, is, 1: 94/349 vs.  140/584; T2: 98/349 vs. 131/584;  T3: 108/349 vs. 235/584; T4: 49/349 vs. 78/584  Tumor grade: Not reported  Functional status: Not reported | Number of nodes removed, A vs. B, mean (SD): 32.7 (14.9) vs. 16.6 (11.8), p<0.001  Lymph node invasion found: 111/349 vs. 187/584, p=0.56  Balder cancer specific survival: Adjusted HR 1.80 (95% CI 1.37 to 2.37) |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Shirotake,  2010[21](#_ENREF_21)  Retrospective cohort  Medium | Not reported | Not reported, Authors disclosed  no COI |  |
| Simone,  2013[22](#_ENREF_22)  Retrospective cohort  Medium | Not reported | Not reported, Authors disclosed  no COI | No details on how patients were  selected for the two procedures |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Setting and Study**  **Years** | **Inclusion Criteria** | **Exclusion Criteria** | **Type of Intervention (experimental and control groups, dose, duration of treatment)** | **Duration of Followup and Followup Method** |
| Zehnder,  2011[23](#_ENREF_23)  Retrospective cohort  High | US and Switzerland  Two centers  1985-2005 | Radical cystectomy with  lymphadenectomy with curative intent for T2-3, clinically N0M0 bladder cancer | Neoadjuvant treatment,  positive soft tissue margins, T1 or T4 bladder cancer | A (US cohort): Cystectomy with  lymphadenectomy, pure intrapelvic template plus removal of lymphatic tissue along the common iliac vessels, the distal vena cava/aorta to the IMA takeoff and complete dissection of the presacral  space from the bifurcation of the aorta into the sacral fossa.  B (Switzerland cohort): Cystectomy with lymphadenectomy, pure intrapelvic template ended proximally at the mid- upper third of the common iliac vessels, included the presacral region medial to the internal iliac vessels but left tissue containing the hypogastric nerves located medial to the retracted ureters and inferior to the aortic bifurcation  Both groups used pure intrapelvic template for lymphadenectomy, with boundaries of the genitofemoral nerve and the pelvic side wall laterally, the circumflex iliac vein and Cloquet's node distally, the obturator fossa with full exposure of the intrapelvic course of the obturator nerve and the internal iliac vessels posteriorly, and the tissue medial to these vessels. | A: 4-month intervals in  year 1, 6-month intervals in year 2, annually thereafter; Median followup: 10.9 years  B: 3, 6, 12 months postoperatively, annually thereafter; Median followup: 9.9 years |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Number of Subjects Per Group** | **Population Characteristics by Treatment Group (age, sex, race, smoking status, recurrent bladder cancer, stage of disease, tumor grade, functional status)** | **Results** |
| Zehnder,  2011[23](#_ENREF_23)  Retrospective cohort  High | A: 554  B: 405 | Age, median: 67 vs. 67 years  Male: 421/554 vs. 314/405  Race: Not reported  Smoking status: Not reported Recurrent bladder cancer: Not reported  Stage: T2: 253/554 vs. 169/554; T3:  301/554 vs. 236/405  Tumor grade: G3: 534/554 vs.  390/405  Functional status: Not reported | Pathologically Node-positive: 195/554 vs. 114/405  Recurrence: 38% (210/554) vs. 38% (154/405), RR 1.0 (95% CI 0.85 to 1.17) Recurrence-free survival: ~58% in each group (p=0.75)  Overall survival: ~17% in WACH group (p=0.45) |

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| **Author, Year Study**  **Name**  **Study Design**  **Risk of Bias** | **Adverse Events and Withdrawals due to Adverse Events** | **Sponsor** | **Comments** |
| Zehnder,  2011[23](#_ENREF_23)  Retrospective cohort  High | Not reported | Not reported |  |

CI, Confidence Intervals; COI, Conflict of interest;; G1, Grade 1; G2, Grade 2; G3, Grade 3; HR, Hazard Ratio; ICU, Intensive Care Unit; IMA, inferior mesenteric artery; M0, Metastasis stage 0; N, Nodes; N-, Node positive; N+, Node negative; N0, Node stage 0; NR, Not reported; Nx, Nodes not removed or unknown; OS, overall survival;pT1, Tumor stage 1 determined by pathology; pT2, Tumor stage 2 determined by pathology; pT3, Tumor stage 3 determined by pathology; pT4, Tumor stage 4 determined by pathology; pTa, Tumor stage a determined by pathology; pTis, Tumor stage *in situ* determined by pathology;RFS, Recurrance free survival; RR, relative risk; SD, Standard deviation; SEER, Surveillance, Epidemiology and End Results program; T0, Tumor stage 0; T1, Tumor stage 1; T2, Tumor stage 2; T3, Tumor stage 3; T3a, Tumor stage 3a; T3b, Tumor stage 3b; T4, Tumor stage 4; T4a, Tumor stage 4a; T4b, Tumor stage 4b; Ta, Tumor stage a; TCC, Transitional cell carcinoma; Tis, carcinoma in situ; USA, United States of America