**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 CohortMedium | US1988-2006 | Radical cystectomy for non-metastatic transitional cell carcinoma of the urinary bladder | Unknown tumor stage orgrade | A: Cystectomy with extended lymph nodedissection (≥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 CohortMedium | A+B: 8394C: 2789 | A+B vs. CAge (mean): 67.1 vs. 68.8, p<0.001Male: 6285/8394 vs. 2025/2789 , p<0.01Caucasian:7533/8394 vs. 2508/2789Smoking status: Not reported Recurrent bladder cancer: Not reportedStage: Ta/Tis:159/8394 vs.161/2789T1: 807/8394 vs. 4332789T2: 3191/8394 vs. 1193/2789T3: 2578/8394 vs. 495/2789T4: 1659/8394 vs. 507/2789;p<0.001Grade: G1/G2: 599/8394 vs.326/2789G3: 4466/8394 vs. 1559/2789G4: 3329/8394 vs. 904/2789;p<0.001Functional status: Not reported | A+B vs. CHRs adjusted for age, sex, race, tumor stage, tumor grade and year of surgery10-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. B10-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 CohortMedium | 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 CohortHigh | Austria and ItalyTwo centers1998-2002 | Patients undergoing radicalcystectomy, American Society of Anesthesiologists grade 2 or 3 | Not reported | A: (Italian Cohort): Cystoprostatectomy inmen 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 daysUnclear 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 CohortHigh | A: 46B: 46 | Age (mean): 66.3 vs. 68.2 yearsMale: Not reported Race: Not reported Smoker: Not reportedRecurrent bladder cancer: Not reportedStage: pT1: 4 vs. 6; pT2-3a: 24 vs.18; pT3b-4: 18 vs. 22; Node positive:18 vs. 10Grade: Not reportedFunctional 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 CohortHigh | Median ICU stay (days): 4.5 vs. 5.1, P-value Not reportedMedian hospital stay (days): 16.3 vs. 14.2, P-value Not reportedMedian blood units received during surgery: 0.8 vs. 1.15, P=0.37Median blood units received within 30 days: 0.7 vs. 3.2, P=0.067Complications within 30 days:Overall surgical complications: 20/46 vs. 17/46, P=0.08Perioperative 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=0.28Cardiac arrhythmia: 5/46 vs. 3/46, P=0.16Pulmonary embolus: 1/46 vs. 2/46Pneumonia: 2/46 vs. 7/46, P=0.02Prolonged ileus >6 days: 1/46 vs. 2/46Hydronephrosis: 3/46 vs. 6/46Pyelonephritis: 4/46 vs. 4/46Acute renal failure: 1/46 vs. 0/46Transient 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 CohortMedium | Italy1995-2011 | Radical cystectomy formuscle-invasive or high- grade superficial bladder cancer with curative intent | Neoadjuvant or adjuvantchemotherapy and/or radiation; incomplete clinical, pathological, and followup data | A: Limited template: Cystectomy includingexternal and obturator lymph nodes; or no lymphadenectomyB: Standard template: Cystectomy including external, obturator, internal iliac, and 2 cm common iliac lymph nodes up to the cross with the uretersC: Extended template: Cystectomy including external, obturator, internal iliac, presacral, and complete common iliac lymph nodes up to the aortic bifurcationD: 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 arterySelection of template was based on preference and skills of the surgeons | Mean: 59.2±44.3months |

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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 CohortMedium | A: 116B: 94C: 39D: 23 | Reported for 0-14 lymph nodesremoved (n=128) vs. ≥14 lymph nodes removed (n=154):Age (mean): 69.6±8.4 vs. 667.3±8.1;p=0.010Male: 82.8% vs. 83.1% Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: T0: 23/128 vs. 18/154T1: 21/128 vs. 20/154T2: 24/128 vs. 41/154T3: 37/128 vs. 50/154T4: 23/128 vs. 25/154Tumor Grade: G1-G2: 32/128 vs.34/154G3: 96/128 vs. 120/154Functional 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 CohortMedium | 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 SwitzerlandTwo centers1987-2000 | TCC of bladder (preoperativestage N0M0) who underwent curative intent radical cystectomy | Neoadjuvant treatment,positive pathological margins, stages pTa, pT1, and pT4 cancer | A (Switzerland cohort): Cystectomy withextended 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 yearsA: Every 6 months for2 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: 322B: 336 | Age (median): 66.9 vs. 61.6 years,p<0.001Male: 78% vs. 79% Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: Not reportedTumor grade: Not reportedFunctional status: Not reported | A vs. BLymph NodesNumber 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.59/1725 year recurrence-free survival (median followup: 25 vs. 40, p<0.001) pT2: 71% vs. 63%, p=0.10pT3: 19% vs 49%, p<0.00015 year overall survival(median followup: 36 vs. 51, p<0.001)pT2: 64% vs. 61%, p=0.10 pT3: 22% vs. 42%, p=0.0002Progression: local or systemic: 55% (184/336) vs. 40% (130/322) RR 0.74 (95% CI 0.63 to0.87)Local progression (p for log-rank test)::pT2: 24% vs 44%, p<0.0001 pT3: 60% vs. 10%, p<0.0001Systemic 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 notcorrespond 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 cohortHigh | USSingle center1980-1990 | Bilateral pelviclymphadenectomy and radical cystectomy, pathological muscle invasive transitional cell carcinoma, followup greater than 10 years | Preoperative radiation,neoadjuvant or adjuvant chemotherapy | A: Radical cystectomy with standardlymphadenectomy, 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 10years |

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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 cohortHigh | Not reported,Overall N=322 | Age: Not reportedMale: Not reportedRace: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: 188 T2, 134 T2-T3Tumor grade: Not reportedFunctional 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=0.0025-year recurrence-free survival: Stage ≤T3a: 85% vs. 64%, p<0.02; Stage ≥T3b: 27% vs.39%, p=0.8710-year survivalN0 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 nodesN+ 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 cohortHigh | 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 | USMultiple centers1987-1998Reanalysis of RCT | Muscle invasive bladdercancer, T2-T4a, N0, M0, candidate for radical cystectomy, SWOG performance status 0-1 | Prior pelvic radiation | A: Cystectomy with standardlymphadenectomy (n=146), median 15 LNB: Cystectomy with limited lymphadenectomy (n=98), median 7 LNC: Cystectomy with no lymphadenectomy(n=24) | Minimum followup 5years |
| Konety, 2003[18](#_ENREF_18)Retrospective cohort Medium | USPopulation 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 whounderwent 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: 146B: 98C: 24 | Overall characteristics, not reportedby treatment group:Age: 148/268 <65 years, 120/268 ≥65 yearsMale 81% (216/268) Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: 69% (184/268) T0-T231% (84/268) T3-T4Tumor grade: Not reportedFunctional status: 100% SWOG 0 or1 | A vs. B vs. CLocal Recurrence (no median followup reported):7/146 (5%) vs. 22/98 (22%) vs.12/24 (50%), p<0.0001RR 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 to0.71A vs. BRisk 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 | Cystectomysubset: N=19230 lymph nodes, n=645≥1 lymph node, n=956unknown 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 reportedStage: In situ or 1: 150 (12.9%); Stage 2: 249 (21.4%); Stage 3: 300 (25.8%); Stage 4: 465 (39.9%); missing: 759Tumor grade: Not reportedFunctional 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 cohortHigh | Germany1986-1997 | Radical cystectomy withcurative intent for pTis, pT1G3, pT2 to pT4 transitional cell carcinoma | previous pelviclymphadenectomy or irradiation, preoperative chemotherapy for bladder cancer, pTa bladder cancer | Patients with bladder cancer whounderwent 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 cohortHigh | DenmarkSingle study1990-1997 | radical cystectomy withlymphadenectomy | pretreatment of bladdercancer | A: Radical cystectomy with extendedlymphadenectomy, 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 fossaB: 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 forthe 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 cohortHigh | Per group: Notreported, Overall: 302 | Age: 62.8 yearsMale: male: female ratio 4.5:1Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage 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 reportedFunctional status: Not reported | ≥16 nodes removed vs. ≤15 nodes removed :5-year bladder cancer- specific survival: 65% vs. 51%, p<0.013Local recurrence: 17% vs. 27%, p<0.01Distant metastasis: 10.5% vs. 17%, p<0.01 |
| Poulsen,1998[20](#_ENREF_20)Retrospective cohortHigh | A: n=126B: n=68 | Age, mean: 61.8 vs. 63.2 yearsMale: 102/126 vs. 55/68Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: 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<0.00015-year recurrence-free survival: 62% vs. 56%, p=0.335-year risk of distant metastasis: 29% vs. 30%, p not reported5-year risk of pelvic metastasis: 10% vs. 10%, p not reported5-year recurrence-free survival: Stage ≤T3a: 85% vs. 64%, p<0.02; Stage ≥T3b: 27% vs.39%, p=0.875-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 cohortHigh | Inverse relationship between number of complications associated with thelymphadenectomy and the number of lymph nodes removed, data Not reported | Not reported |  |
| Poulsen,1998[20](#_ENREF_20)Retrospective cohortHigh | Not reported | Mauritzen La FontaineFoundation |  |

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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 cohortMedium | JapanSingle center1987-2008 | refractory non-muscle-invasive or muscle-invasive bladder cancer | noncurative surgery,tumors of nonurothelial origin, unclear medical history | A: Cystectomy with lymphadenectomyB: Cystectomy without lymphadenectomyNeoadjuvant chemotherapy, n=16, mostlyT3-4Adjuvant chemotherapy, n=26, T3-4 orNode positive | 3-month intervals for 2years and every 6 months thereafter |
| Simone,2013[22](#_ENREF_22)Retrospective cohortMedium | ItalyTwo centers2002-2010 | high-grade urothelialcarcinoma | neoadjuvant treatment,salvage cystectomy | A: Cystectomy with extendedlymphadenectomy, dissected nodes up to and, in some cases, above the aortic bifurcation including the presacral nodesB: Cystectomy with standard lymphadenectomy, dissected nodes with an upper boundary at the iliac bifurcation (not including presacral and common nodes) | followup method, Notreported |

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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 cohortMedium | A: 107B: 62 (includes those without lymphadenectomy or unknown number ofnodes removed) | Age, mean: 67.65 vs. 69.4 yearsMale: overall 127/169Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: ≤T2: 52/107 vs. 34/62; T3-4:55/107 vs. 28/62Tumor grade: G1-2: 27/107 vs.28/62; G3: 80/107 vs. 38/62Functional 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 cohortMedium | A: 349B: 584 | Age, mean: 65.4 years vs. 66.9yearsMale: 309/349 vs. 502/584Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: 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. 78/584Tumor grade: Not reportedFunctional status: Not reported | Number of nodes removed, A vs. B, mean (SD): 32.7 (14.9) vs. 16.6 (11.8), p<0.001Lymph node invasion found: 111/349 vs. 187/584, p=0.56Balder 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 cohortMedium | Not reported | Not reported, Authors disclosedno COI |  |
| Simone,2013[22](#_ENREF_22)Retrospective cohortMedium | Not reported | Not reported, Authors disclosedno COI | No details on how patients wereselected 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 cohortHigh | US and SwitzerlandTwo centers1985-2005 | Radical cystectomy withlymphadenectomy 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 withlymphadenectomy, 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 presacralspace 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 bifurcationBoth 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 inyear 1, 6-month intervals in year 2, annually thereafter; Median followup: 10.9 yearsB: 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 cohortHigh | A: 554B: 405 | Age, median: 67 vs. 67 yearsMale: 421/554 vs. 314/405Race: Not reportedSmoking status: Not reported Recurrent bladder cancer: Not reportedStage: T2: 253/554 vs. 169/554; T3:301/554 vs. 236/405Tumor grade: G3: 534/554 vs.390/405Functional status: Not reported | Pathologically Node-positive: 195/554 vs. 114/405Recurrence: 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 cohortHigh | 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