Table D-1. Description of study design and selection criteria and treatment (randomized controlled trials)

| **Study** | **Design and Study Enrollment Period** | **Patient Inclusion Criteria** | **Patient Exclusion Criteria** | **Treatment** |
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| Porpiglia et al. 201345 | Single center, single surgeon RCT enrolling 120 men wIth organ confined prostate cancer.  Enrollment Period: January 2010–January 2012 | Males 40 to 75 years of age referred to one institution in Italy with prostate cancer T1 to T2N0M0 clinically staged according to TNM 2009 regardless of prostate size and for whom RP was proposed as a treatment. | Patients with prior radiation therapy, hormonal therapy, and/or transurethral resection of the prostate were excluded. | RARP: Transperitoneal anterograde approach. When indicated unilateral or bilateral neurovascular bundle preservation and extended lymph node dissection were performed.  LRP: Transperitoneal anterograde approach. When indicated unilateral or bilateral neurovascular bundle preservation and extended lymph node dissection were performed. |
| Wilt et al. 201225  Same study as  Wilt et al. 200924  Prostate Intervention Versus Observation Trial (PIVOT) | A multicenter RCT involving 731 men recruited from 52 medical centers (44 Veterans Affairs and 8 National Cancer Institute sites) across the USA.  Enrollment Period: November 1994–January 2002 | Eligible men had to have biopsy proven clinically localized prostate cancer (T1–T2NxM0) of any histologic grade, diagnosed within the past 12 months, prostatic specific antigen (PSA) value ≤50 ng/mL, age ≤75 years, bone scan negative for metastatic disease, an estimated life expectancy of at least 10 years and judged to be medically and surgically fit for radical prostatectomy. | Not reported. | Observation: Men were offered palliative (noncurative) therapy (e.g., TURP for local progression causing urinary obstruction, androgen deprivation and/or targeted radiation therapy for evidence of distant spread).  RP: The technique was at the surgeon’s discretion. Additional interventions were determined by each participant and his physician. |
| Bill-Axelson et al. 201133  Same study as  Johansson et al. 201151,  Holmberg et al. 201234, and  Bill-Axelson et al. 200815  Scandinavian Prostate Cancer Group-4 (SPCG-4) Trial | A multicenter RCT involving 695 men was conducted at 14 centers in Sweden, Finland, and Iceland.  Enrollment Period: October 1989–December 1999 | Men were eligible for inclusion if they were younger than 75 years of age and had a life expectancy of more than 10 years, had no other known cancers, and had a localized tumor T0d (later named T1b), T1, or T2. T1c patients were included in 1994. All patients included in the study were required to have a serum PSA <50 ng/mL and a negative bone scan. | NR | WW: Men who had signs of obstructive voiding disorders were treated with transurethral resection. Metastases detected by bone scan were managed with hormonal therapy.  RP: The surgical procedure started with a lymphadenectomy of the obturator fossa; if no nodal metastases were found in frozen sections, the RP was performed. Radical excision of the tumor was given priority over nerve-sparing surgery. |
| Jones et al. 201143 | A multicenter phase 3 RCT involving 1,979 men was conducted in the USA and Canada.  Enrollment Period: 1994–2001 | Eligible men had to have histologically confirmed prostate cancer stage T1b, T1c, T2a, or T2b, and a PSA ≤20 ng/mL. Other eligibility criteria included a Karnofsky performance score of 70 or more (on a scale of 1 to 100, with higher scores indicating better performance status), an alanine aminotransferase level that was no more than twice the upper limit of the normal range, no evidence of regional lymph node involvement or distant metastatic disease, and no previous chemotherapy, radiotherapy, hormonal therapy, cryosurgery, or definitive surgery for prostate cancer. | NR | EBRT: Radiotherapy was administered in daily 1.8 Gray (Gy) fractions prescribed to the isocenter of the treatment volume, consisted of 46.8 Gy delivered to the pelvis (prostate and regional lymph nodes), followed by 19.8 Gy to the prostate.  EBRT plus short-term ADT: Flutamide at a dose of 250 mg orally three times a day and either monthly subcutaneous goserelin at a dose of 3.6 mg or intramuscular leuprolide at a dose of 7.5 mg for 4 months. Radiotherapy commenced after 2 months of ADT. |
| Donnelly et al. 201047  Same study as Robinson et al. 200952 | A single-center RCT involving 244 men was conducted in Canada.  Enrollment Period: December 1997–February 2003 | Men T2 or T3, no evidence of lymph node or distant metastases and a pretreatment PSA level ≤20 ng/mL | Clinically bulky T3 tumor, received prior pelvic radiation, received previous ADT at any time, and undergone TURP within the previous 3 months | EBRT: Standard 4-field box technique (2 Gy daily, 5 days per week). The prescribed radiation dose was 68 Gy. The dose was increased to 70 Gy in early 2000 and finally to 73.5 Gy in late 2000 and finally to 73.5 Gy in late 2002.  Cryotherapy: Thermo sensor monitoring, urethral warming, and saline injection were routinely applied to separate anterior rectal wall from the prostate, and 2 freeze-thaw cycles were used in all cases. |
| Giberti et al. 200944 | A single center RCT involving 200 men was conducted in Italy.  Enrollment Period: May 1999–October 2002 | Study included only Caucasian men with low risk prostate cancer (clinical stage T1c or T2a, PSA value ≤10 ng/mL and Gleason sum ≤6) | Previous pelvic irradiation, large median lobes, uroflow-Q max lower than 10 mL/s, history of multiple pelvic surgeries, previous transurethral resection of prostate, prostate volume greater than 60 mL and positive seminal vesicles biopsy. | RRP: Bilateral nerve sparing RRP, in accordance with Walsh’s principles, and standard lymph node dissection were performed on all the patients by a single surgeon.  BT: BT was performed by a team, which included a urologist, a radiation therapist and a primary care physician, through a transperitoneal template-guided peripheral loading real-time technique and seeds of iIodine125. A D90 >140 Gy was considered the cut-off value in order to predict a good quality implant. |
| D’Amico et al. 200849  Same study as  D’Amico et al. 200835 and Nguyen et al. 201053 | A single center RCT involving 206 men was conducted in USA.  Enrollment Period: December 1, 1995–April 15, 2001 | Study included men with prostate cancer clinical stage T1b to T2bN0M0 who had at least a 10-year life expectancy excluding death from prostate cancer and an Eastern Cooperative Oncology Group performance status 0 to 1. | Patients with a history of a prior malignancy except for nonmelanoma skin cancer or prior pelvic radiation therapy or ADT. | EBRT: Daily dose of 1.8 Gy for initial 25 treatments, totaling 45 Gy, and 2.0 Gy for final 11 treatments, totaling 22 Gy.  EBRT plus ADT: EBRT plus ADT which consisted of a luteinizing hormone-releasing agonist, leuprolide or goserelin and antiandrogen flutamide. Leuprolide was delivered intramuscularly each month at a dose 7.5 mg or 22.5 mg every 3 months. Goserelin was administered subcutaneously each month at a dose of 3.6 mg or 10.8 mg every 3 months. Flutamide was taken orally at a dose of 250 mg every 8 hours and starting 1 to 3 days before leuprolide. |
| Martis et al. 200746 | A single center RCT involving 200 men was conducted in Italy.  Enrollment Date: January 1997–December 2004 | Study included men with clinically localized prostate cancer (T1–T2). | For the perineal prostatectomy group, authors reported an exclusion of patients with a prostate weight >80 g, a prominent median lobe and inability to place the patient in an exaggerated lithotomy position because of hip arthrosis, ankylosis, and/or severe coxarthrosis. | Bilateral nerve sparing RP performed by the retropubic or perineal approach by a single surgeon. |

**Abbreviations:** ADT=androgen deprivation therapy, BT=brachytherapy, D90=minimum dose covering 90% of the prostate volume, EBRT=external beam radiation therapy, LRP=laparoscopic radical prostatectomy, NR=not reported, PSA=prostate specific antigen, RARP=robot assisted radical prostatectomy, RCT=randomized controlled trial, RP=radical prostatectomy, RRP=radical retropubic prostatectomy, TURP=transurethral resection of the prostate