# Supplemental Online Content

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

## eMethods

Select individual items from 26-item Expanded Prostate Cancer Composite Index

In addition to the 26-item Expanded Prostate Cancer Composite Index (EPIC-26) domain scores, we compared selected individual binary EPIC-26 items by treatment.[1] The following items were dichotomized a priori according to whether men answered "moderate or big problem" vs. "no, very small, or small problem": sexual function, urinary function, urinary leakage, burning with urination, frequent urination, bowel function, bloody stools, and bowel urgency. Men who reported "moderate or big problem" for the above items were considered to have a problem, as previously described.[2,3] The quality of erections was also assessed and dichotomized according to whether men answered "firm enough for intercourse" vs. "none, not firm, or firm enough for masturbation and foreplay only". Additionally, the following items were compared post hoc: increased frequency of bowel movements, fecal incontinence, abdomen/pelvic/rectal pain, hot flashes, breast tenderness, feeling depressed, lack of energy, and change in body weight. Multivariable analyses were only performed on the a priori selected individual items if the number of events was sufficient.

Further details on statistical analysis:

Each of the multivariable models included the following covariates: treatment modality, time since treatment, an indicator for any use of androgen deprivation therapy (ADT) within 1 year from primary treatment, age at diagnosis, race, general health scale at baseline, prostate cancer (D'Amico) risk group, Total Illness Burden Index for prostate cancer comorbidity score[4], physical functioning score at baseline, social support score at baseline[5], depression score at baseline[6], participatory decision-making scale at baseline[7], and Surveillance, Epidemiology, and End Results (SEER) site. In addition, the baseline domain score or individual EPIC-26 item was adjusted for each model. The two-way interaction terms of treatment choice and time since treatment, treatment choice, and ADT were also included in each model. The restricted cubic splines with 3 knots for age, time since treatment, and the corresponding baseline EPIC-26 score allowed estimation of their nonlinear associations with the

outcome. To account for potential correlation among multiple records from the same patients, generalized estimating equations were used with the Huber-White method to estimate the variance-covariance matrix robustly.

The validated Medical Outcomes Study 36-Item Short Form (SF-36) through 5 years and 12-Item Short Form (SF-12) at year 10 measured general health-related quality of life[9,10]. SF-12 physical and mental health summary scales were only collected on the 10-year survey, and multivariable linear regression models were fit for these outcomes. SF-36 was used at baseline, and the baseline summary scales (physical health or mental health) was included as a covariate along with the same set of covariates described above, excluding the time since treatment and the interaction terms. Due to the limited number of patients who reported SF-12 outcomes and underwent primary treatment with ADT, we excluded the ADT patients in these analyses.

As mentioned in the methods section, missing values for covariates were imputed using the multiple imputation chained equations procedure. No covariates had ≥ 5% data missing, and the missing-at-random assumption was valid in all instances based on the distribution of missingness across treatment groups. Power analysis was conducted in the original research proposal but is no longer applicable since we have analyzed data in favorable and unfavorable- prognosis disease groups separately[8]. Estimates of odds ratios are not adjusted for multiplicity, and the confidence intervals may not be used in place of hypothesis testing.

eFigure 1: Adjusted Expanded Prostate Cancer Index Composite functional domain scores for men with favorable-prognosis prostate cancer through 10 years.

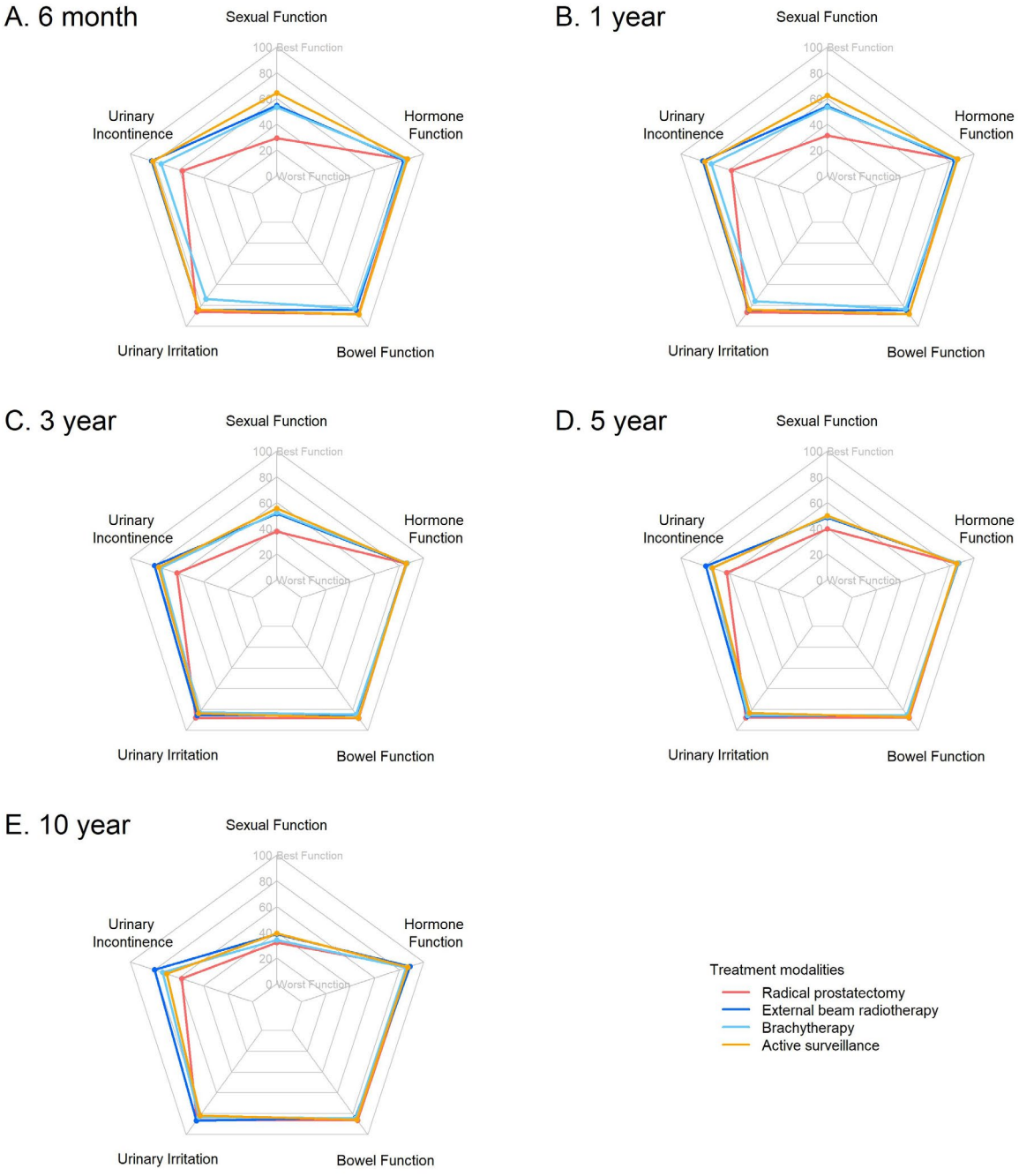


Figure legend: Radar plots of adjusted Expanded Prostate Cancer Index Composite functional domain scores. The center of each figure represents the worst function and the outermost line represents best function (score from 0 to 100). The minimum clinically important difference for sexual function is 10-12; urinary incontinence domain 6-9; urinary irritation domain, 5-7; and bowel and hormonal function domains, 4-6.

eFigure 2: Adjusted Expanded Prostate Cancer Index Composite functional domain scores for men with unfavorable-prognosis prostate cancer through 10 years.

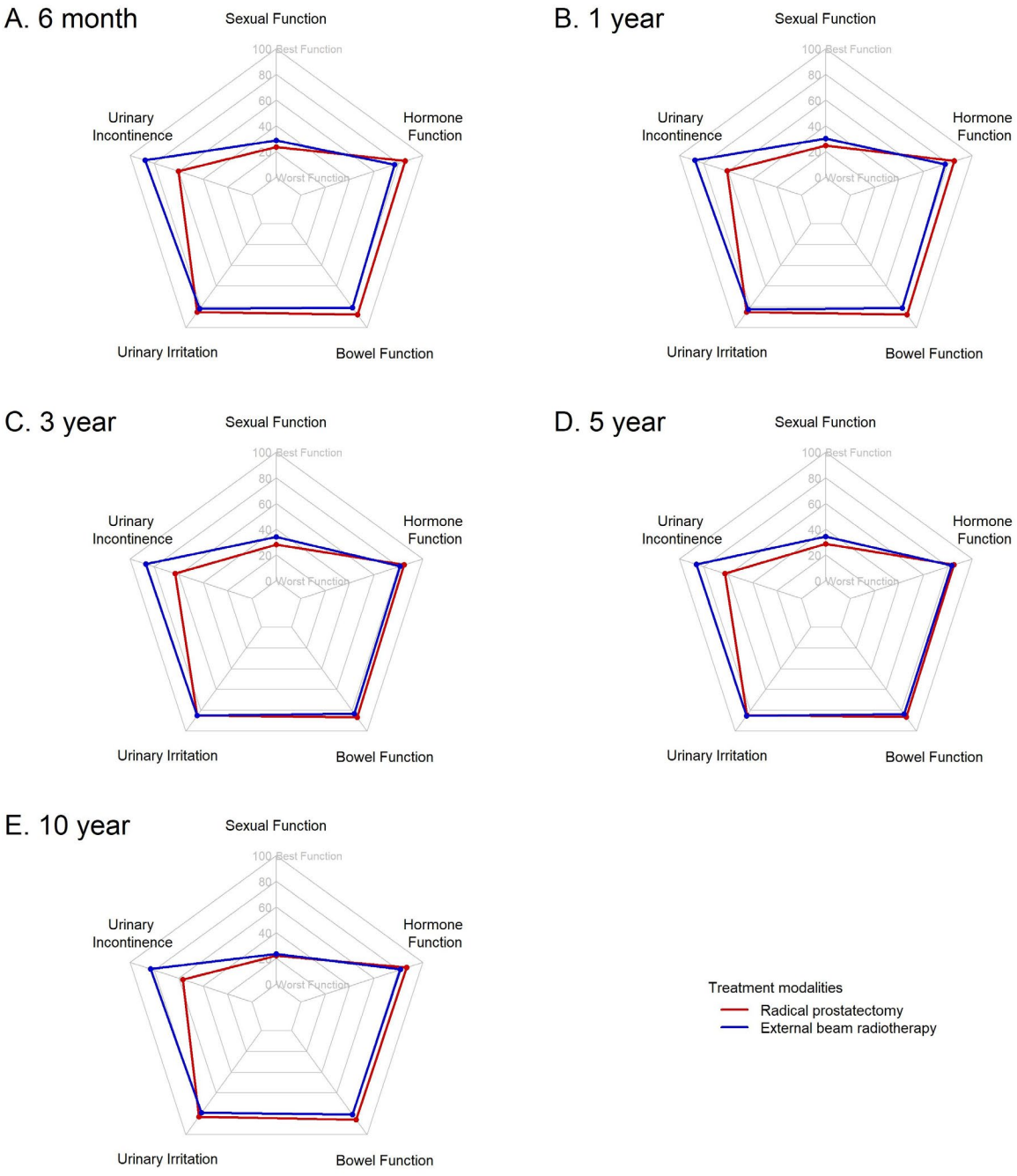


Figure legend: Radar plots of adjusted Expanded Prostate Cancer Index Composite functional domain scores. The center of each figure represents the worst function and the outermost line represents best function (score from 0 to 100). The minimum clinically important difference for sexual function is 10-12; urinary incontinence domain 6-9; urinary irritation domain, 5-7; and bowel and hormonal function domains, 4-6.

eFigure 3: Adjusted-mean differences in functional outcomes of men with favorable-prognosis prostate cancer through 10 years.

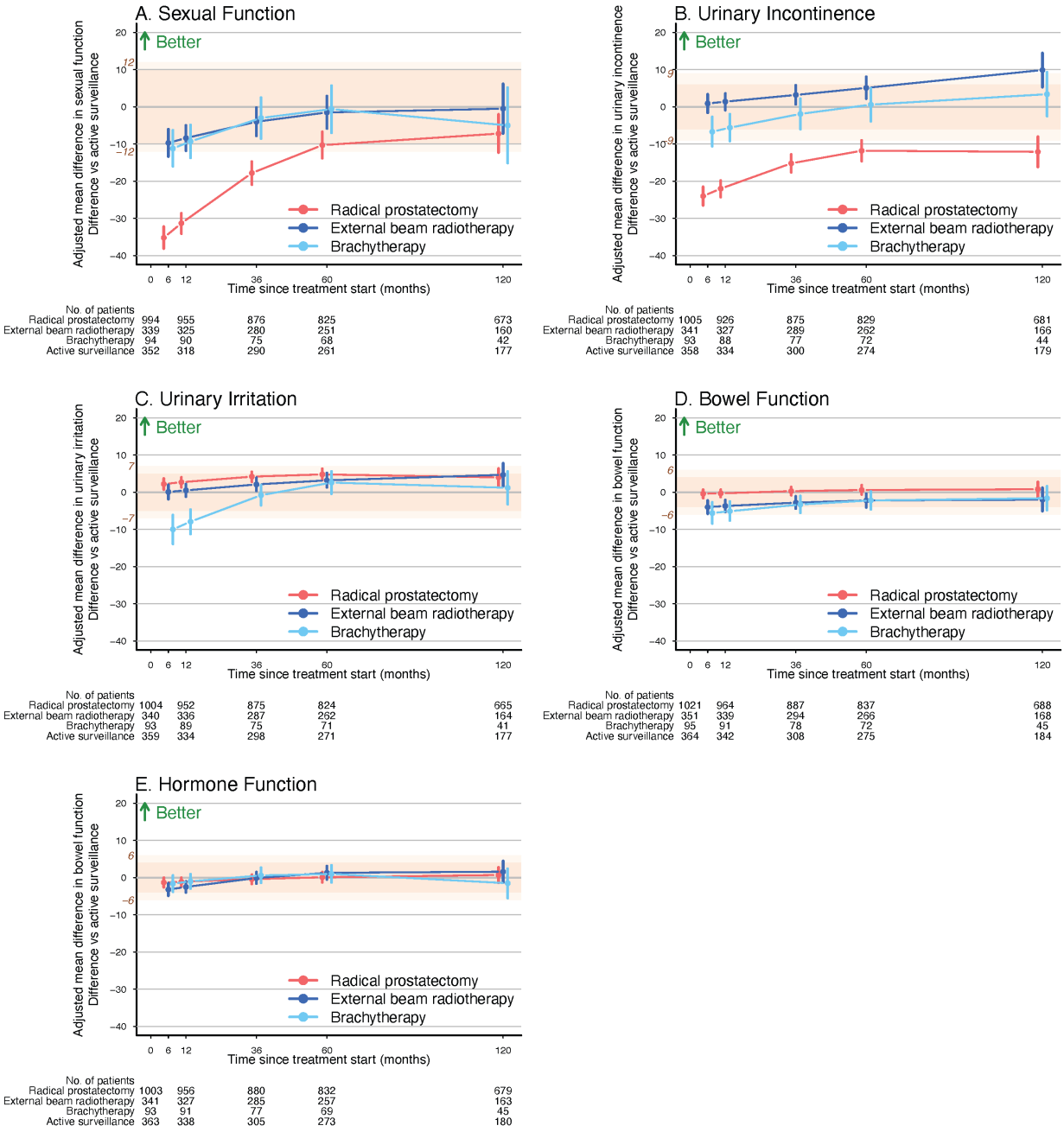


Figure legend: Adjusted-mean difference in Expanded Prostate Cancer Index Composite functional domain scores compared to active surveillance through 10 years. The range of minimum clinically important differences is shaded for each functional domain. The minimum clinically important difference for the sexual function domain is 10-12; urinary incontinence domain, 6-9; urinary irritation domain, 5-7; and bowel and hormonal function domains, 4-6. Error bars represent 95% confidence intervals.

eFigure 4: Adjusted-mean differences in functional outcomes of men with unfavorable-prognosis prostate cancer through 10 years.

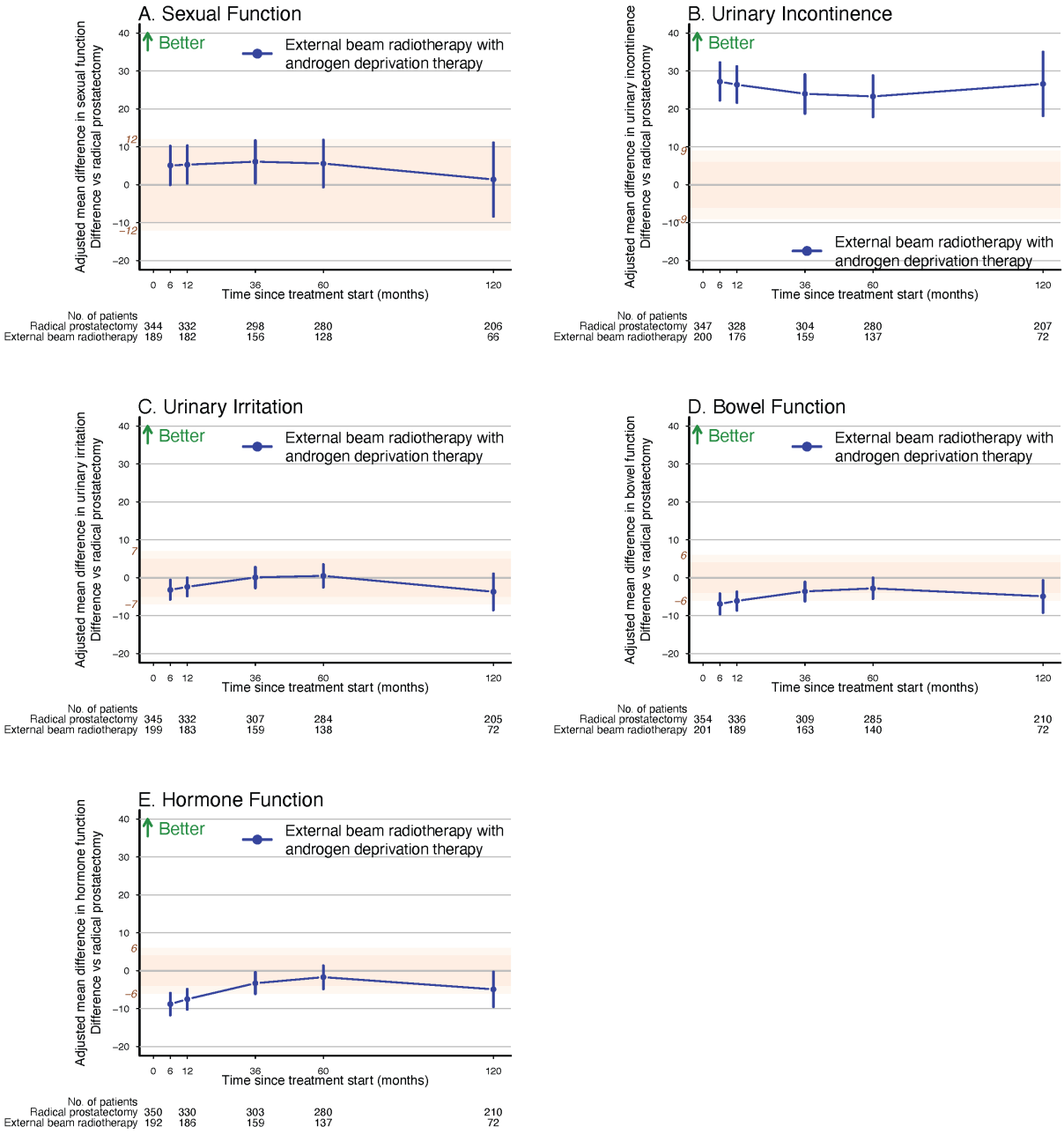


Figure legend: Adjusted-mean difference in Expanded Prostate Cancer Index Composite functional domain scores for men who underwent external beam radiotherapy with androgen deprivation treatment compared to radical prostatectomy through 10 years. The range of minimum clinically important differences is shaded for each functional domain. The minimum clinically important difference for the sexual function domain is 10-12; urinary incontinence domain, 6-9; urinary irritation domain, 5-7; and bowel and hormonal function domains, 4-6. Error bars represent 95% confidence intervals

eFigure 5: Unadjusted functional outcomes of men with favorable-prognosis prostate cancer through 10 years.

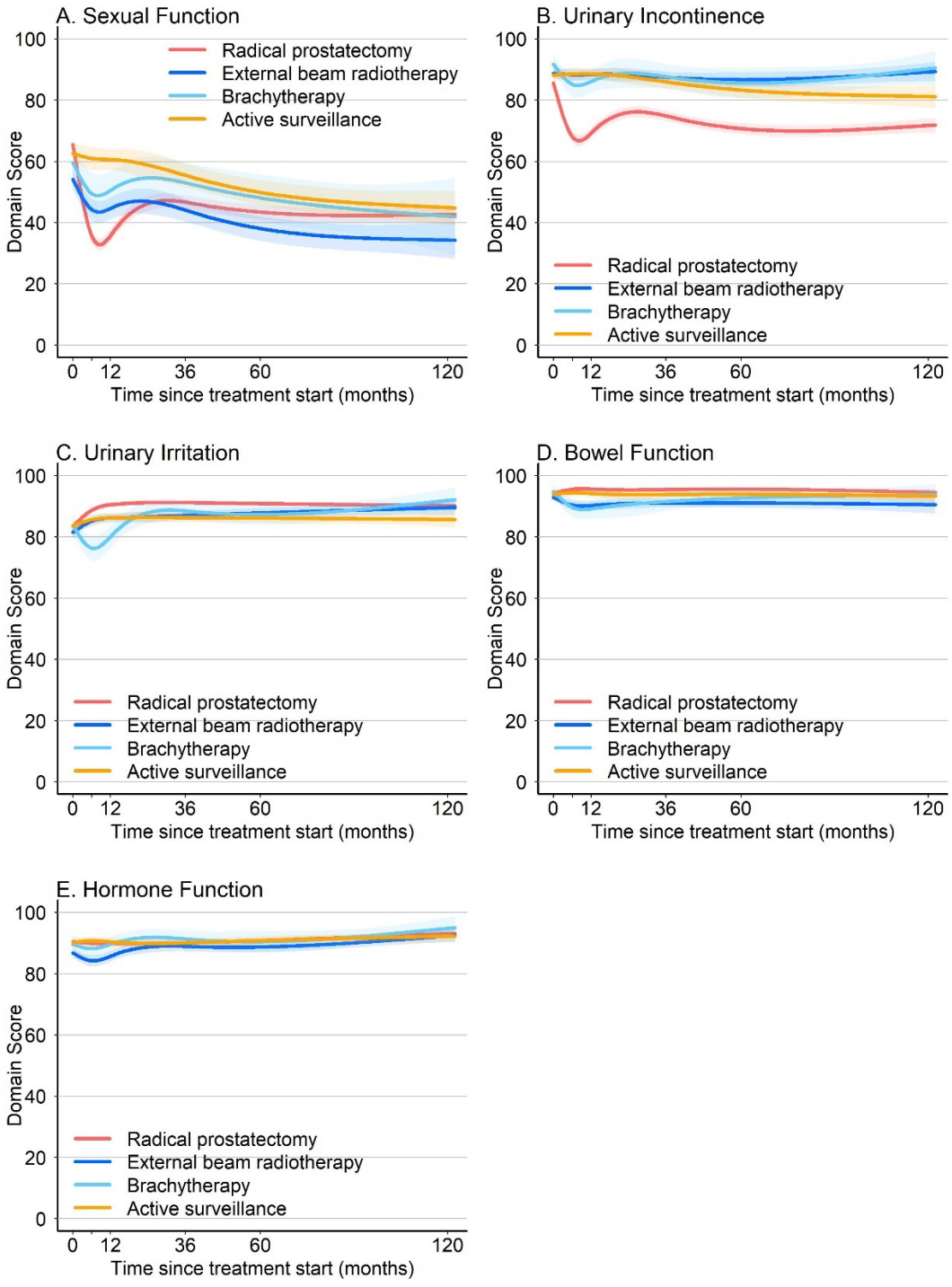


Figure legend: Unadjusted mean functional outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores.

eFigure 6: Unadjusted sexual function outcomes of men with favorable and unfavorable-prognosis prostate cancer through 10 years stratified by baseline function.

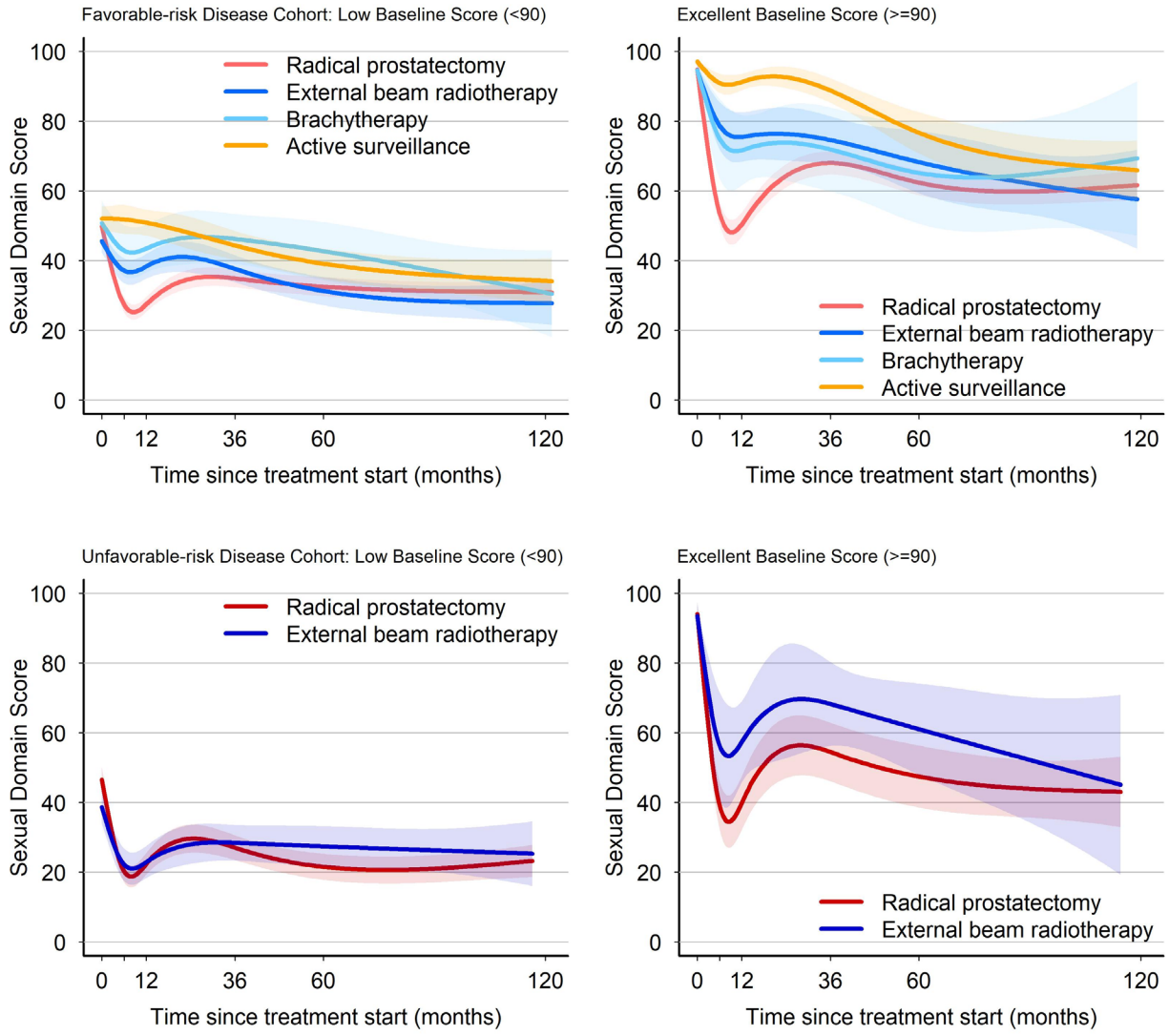


Figure legend: Unadjusted mean sexual function outcomes of men with favorable and unfavorable-prognosis prostate cancer stratified by baseline sexual function (<90 and ≥90) on the Expanded Prostate Cancer Index Composite (EPIC) domain scores.

eFigure 7: Unadjusted hormonal function outcomes of men with favorable-prognosis prostate cancer through 10 years stratified by baseline function.

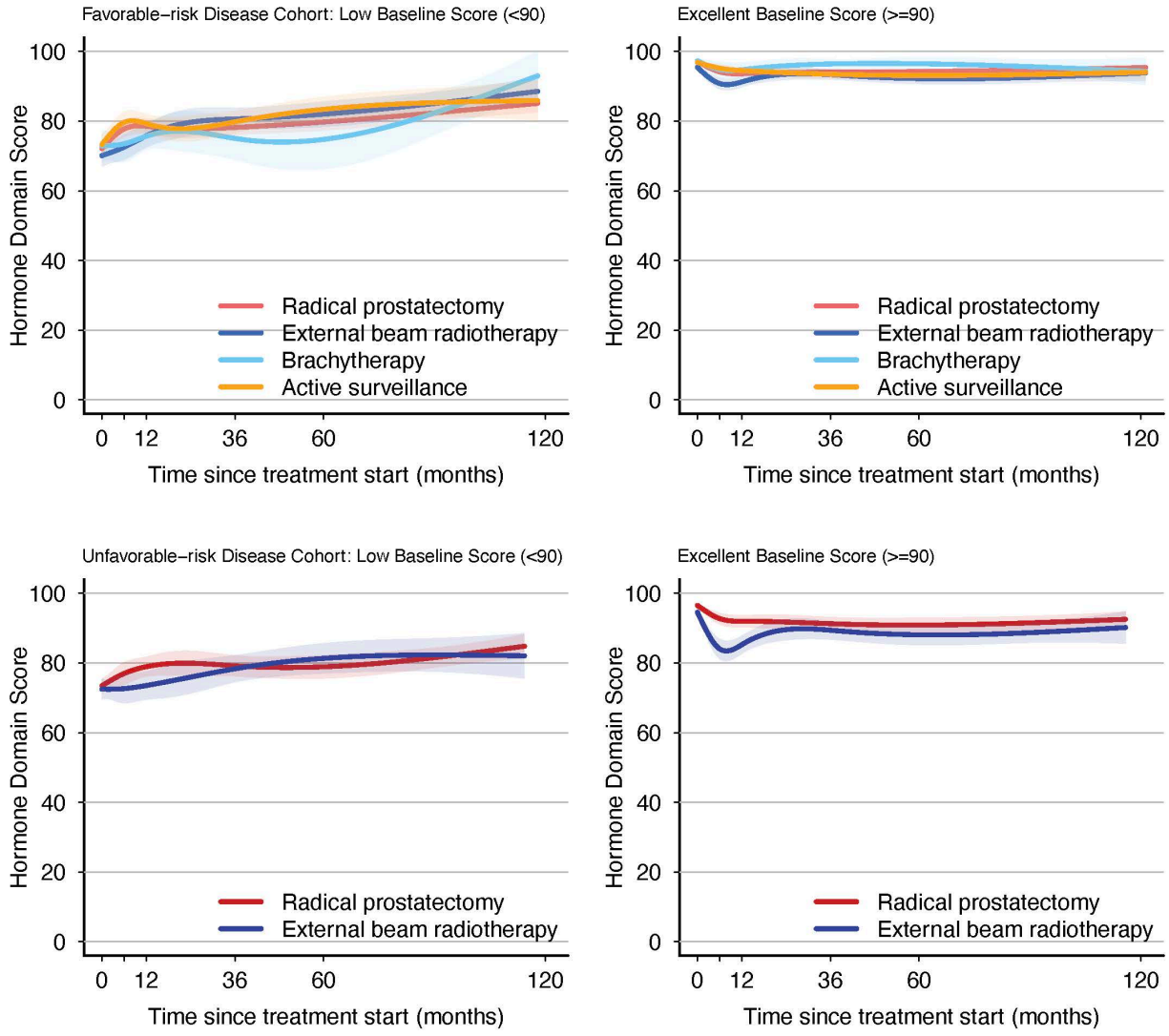


Figure legend: Unadjusted mean hormonal function outcomes of men with favorable and unfavorable-prognosis prostate cancer stratified by baseline sexual function (<90 and ≥90) on the Expanded Prostate Cancer Index Composite (EPIC) domain scores.

eFigure 8: Unadjusted functional outcomes of men with favorable-prognosis prostate cancer treated with external beam raditherapy through 10 years stratified by recepit of androgen deprivation therapy.

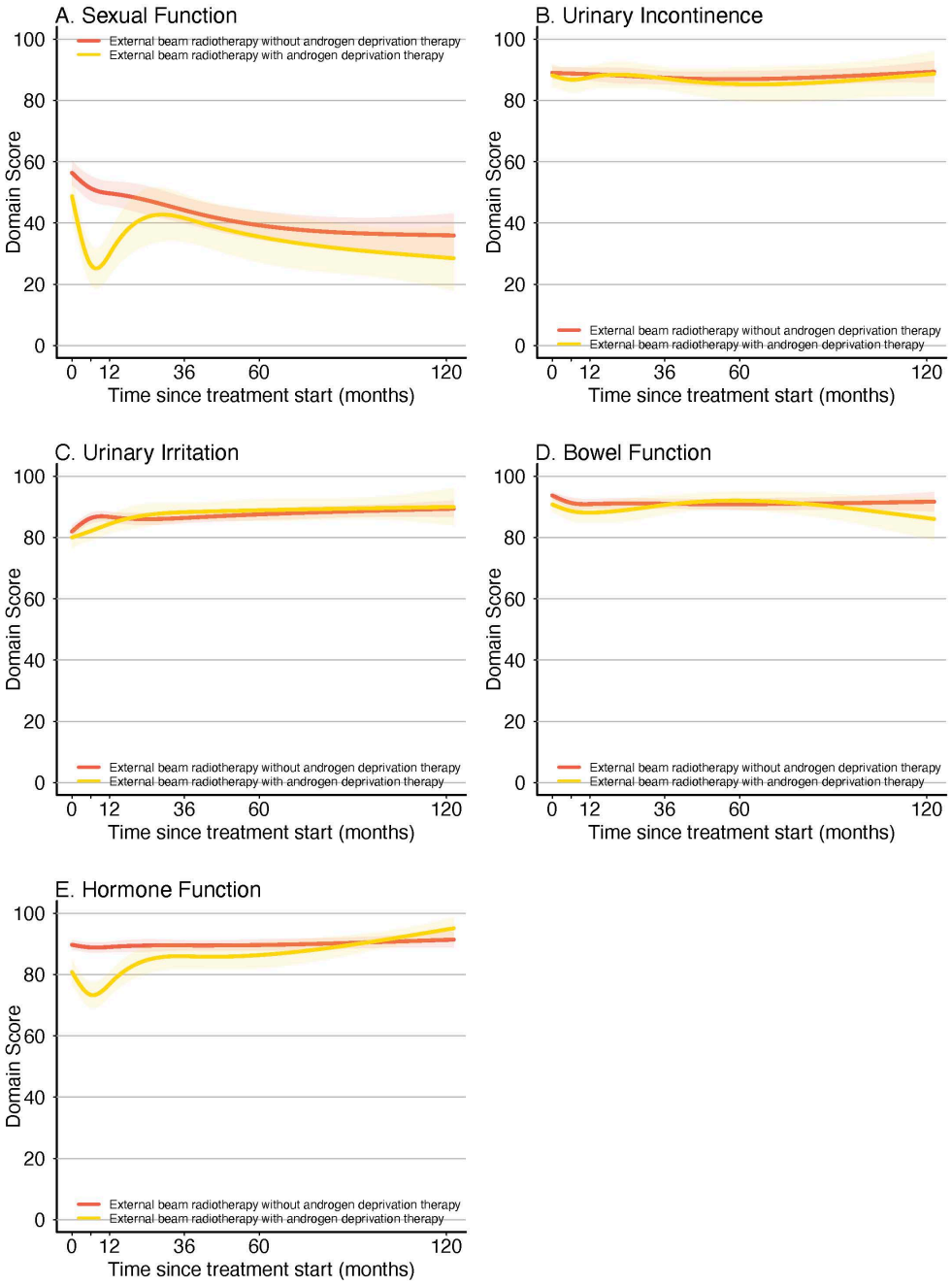


Figure legend: Unadjusted mean hormonal function outcomes of men with favorable-prognosis prostate cancer stratified by receipt of androgen deprivation therapy on the Expanded Prostate Cancer Index Composite (EPIC) domain scores.

eFigure 9: Unadjusted functional outcomes of men with unfavorable-prognosis prostate cancer through 10 years.

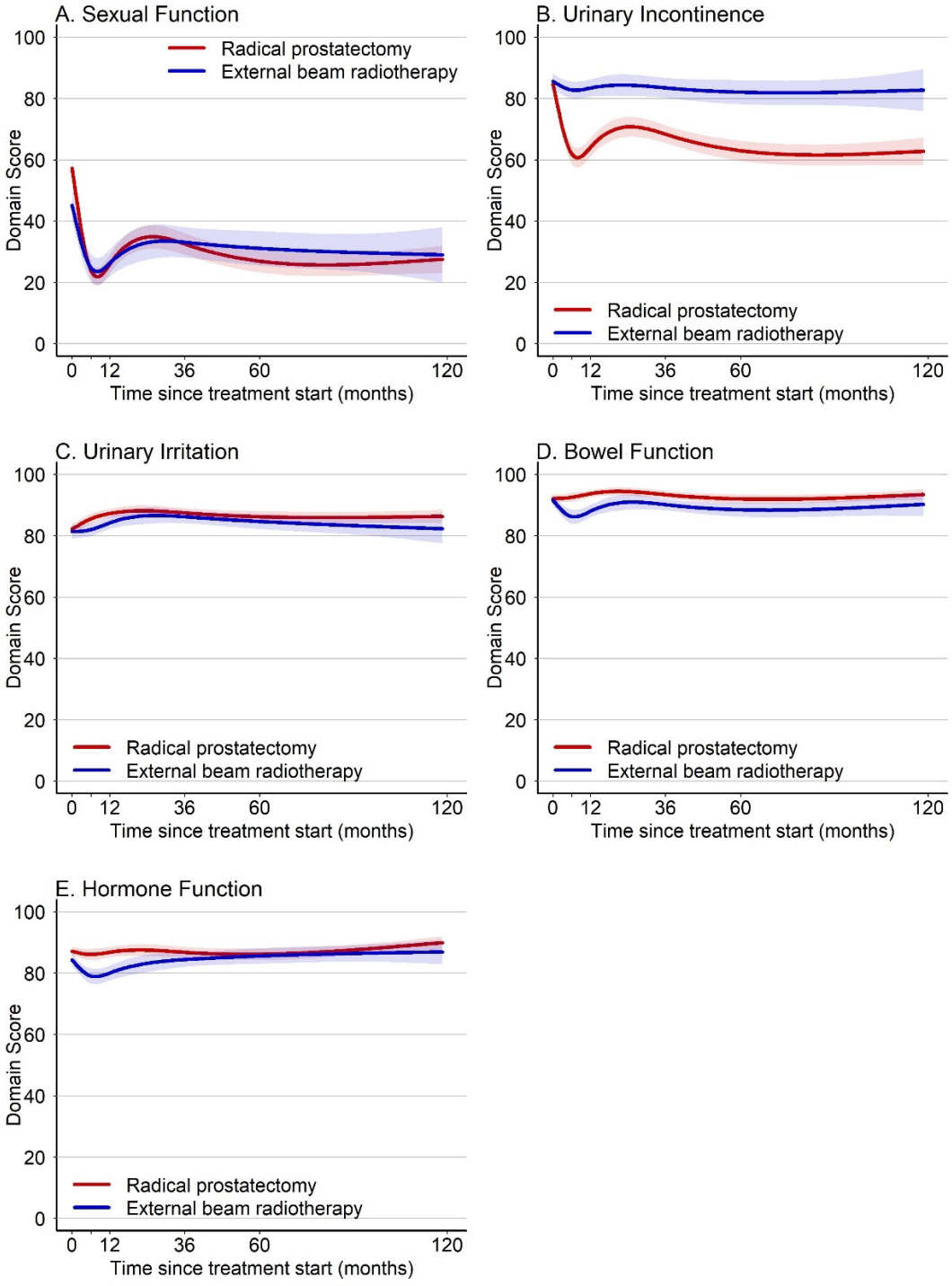


Figure legend: Unadjusted mean functional outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores

eFigure 10: Unadjusted probabilites of seclect individual items of men with favorable-prognosis prostate cancer through 10 years.

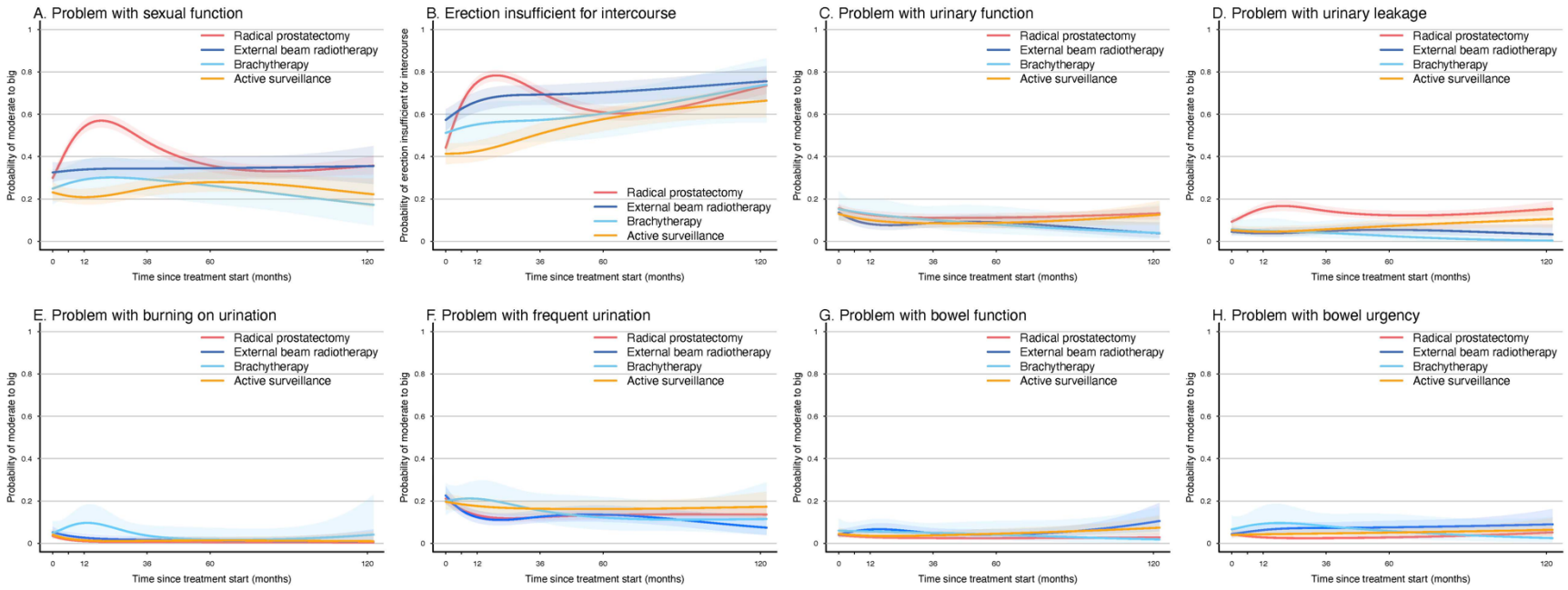


Figure legend: Probabilites of men reporting a moderate or big problem for the individual items are shown. Error bars represent 95% confidence intervals.

eFigure 11: Unadjusted probabilites of seclect individual items of men with unfavorable-prognosis prostate cancer through 10 years.

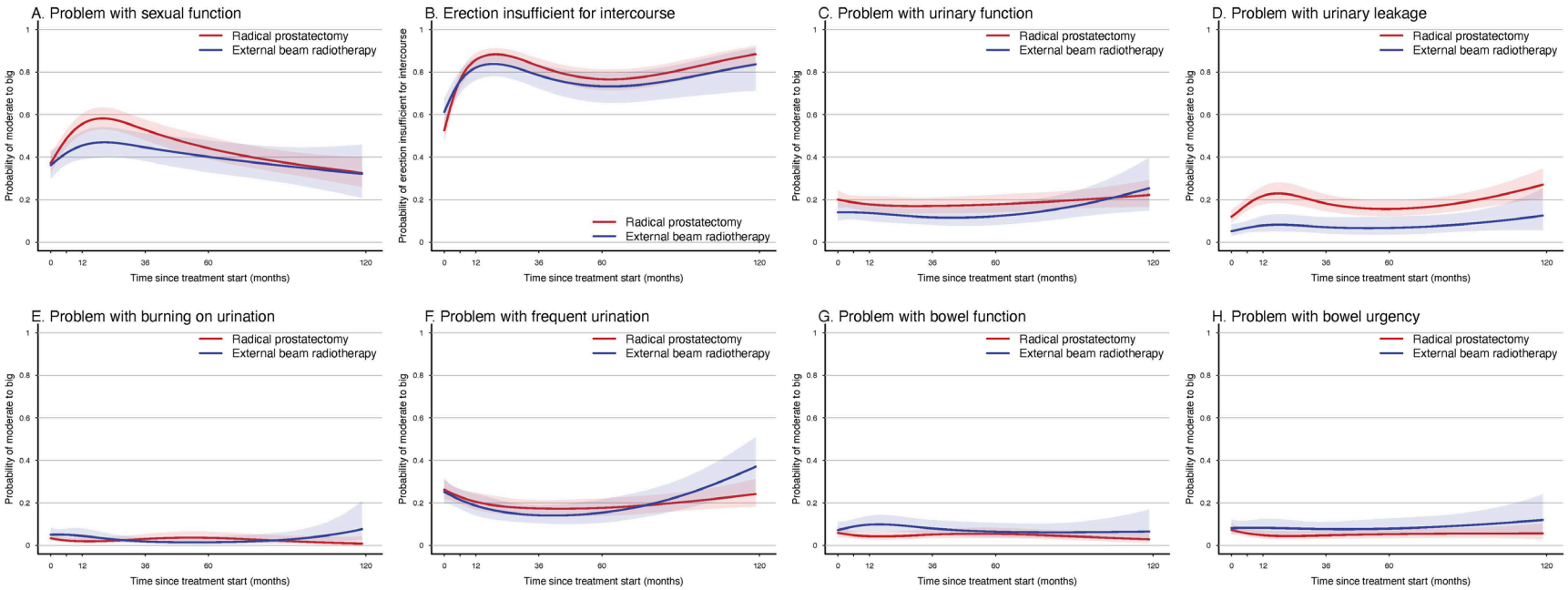


Figure legend: Probabilites of men reporting a moderate or big problem for the individual items are shown. Error bars represent 95% confidence intervals.

eFigure 12: Additional selected individual functional items in men with favorable-prognosis prostate cancer through 10 years.

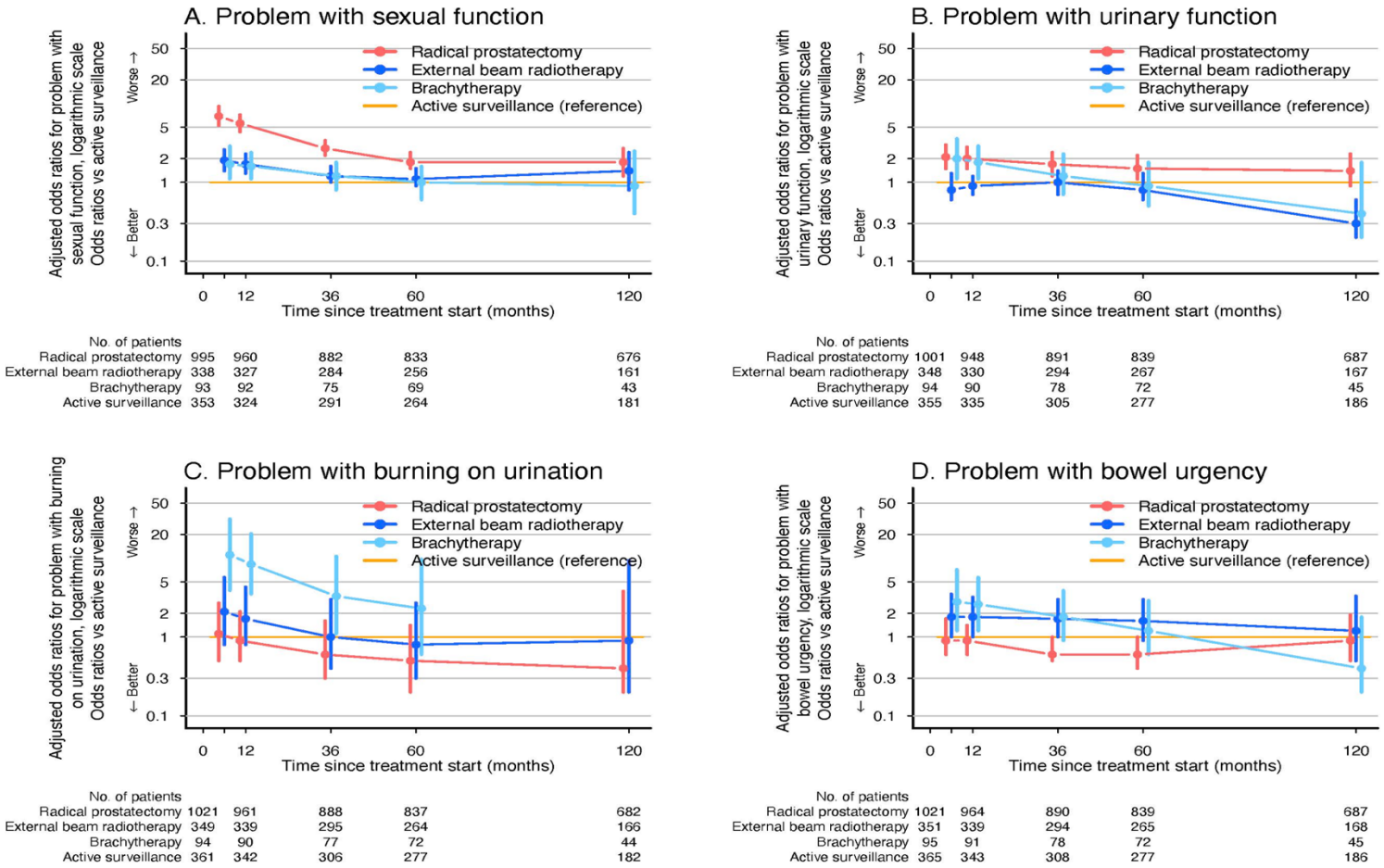


Figure legend: The adjusted odds ratios of men reporting a moderate or big problem for the individual items are shown on a logarithmic scale relative to active surveillance through 10 years. The line at Y=1 shows active surveillance (reference). The whiskers indicate 95% confidence intervals. The regression models were adjusted for baseline domain score, age, race/ethnicity, comorbidities, cancer characteristics (tumor stage, grade group, and prostate-specific antigen level), physical function, social support, depression, medical decision-making style, and accrual site. The table at the bottom indicates the total number of men who reported whether the indiviudal item was a moderate/big problem vs no/very small/small.

eFigure 12: Additional selected individual functional items in men with unfavorable-prognosis disease through 10 years.

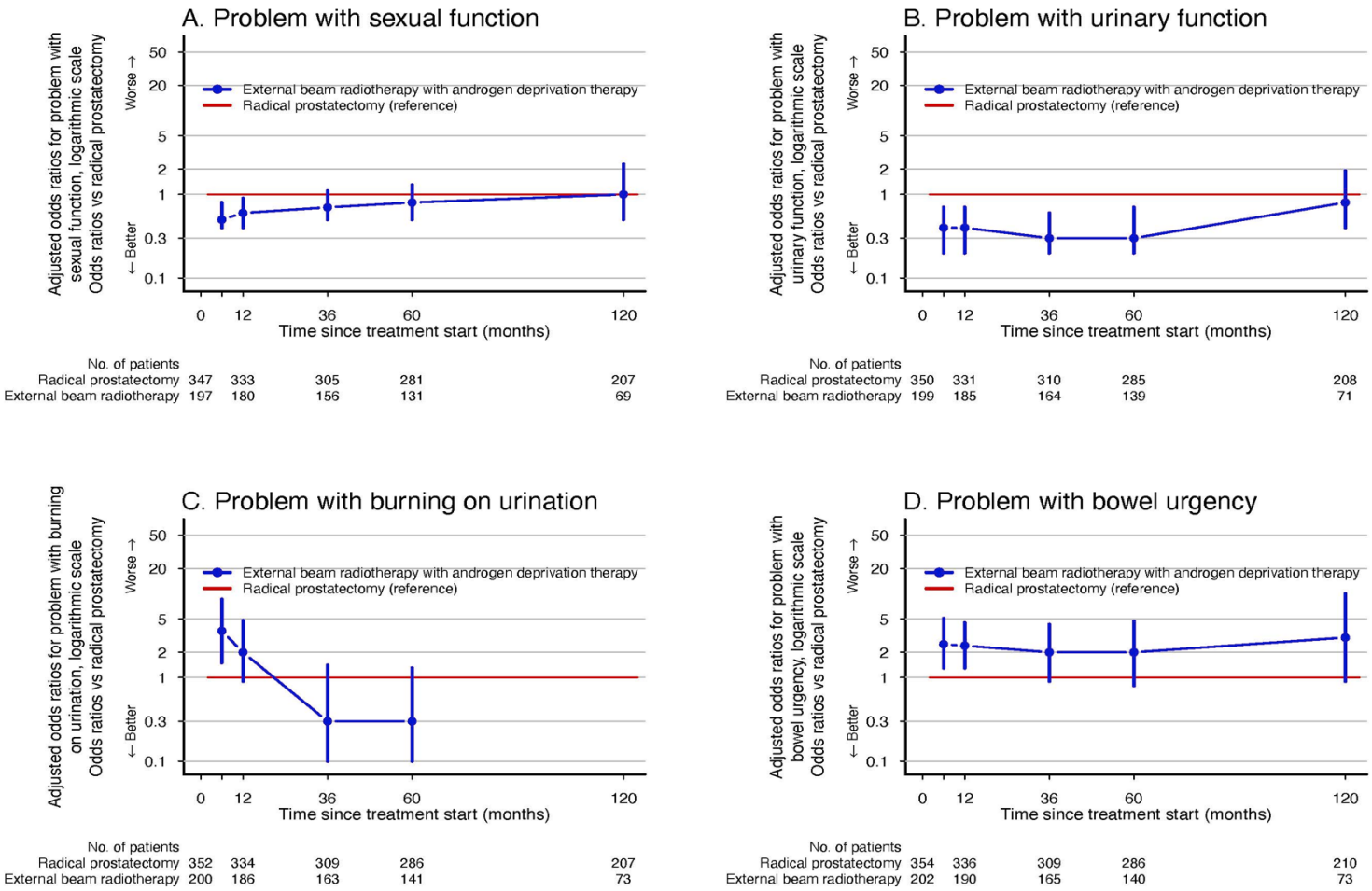


Figure legend: The adjusted odds ratios of men reporting a moderate or big problem for the individual items are shown on a logarithmic scale relative to active surveillance through 10 years. The line at Y=1 shows active surveillance (reference). The whiskers indicate 95% confidence intervals. The regression models were adjusted for baseline domain score, age, race/ethnicity, comorbidities, cancer characteristics (tumor stage, grade group, and prostate-specific antigen level), physical function, social support, depression, medical decision-making style, and accrual site. The table at the bottom indicates the total number of men who reported whether the individual functional item was a moderate/big problem vs no/very small/small or erections insufficient for intercourse

eTable 1: Overall and prostate cancer-specific survival by treatment.

| | Favorable-prognosis prostate cancer | | | | Unfavorable-prognosis prostate cancer | |
|---|---|---|---|---|---|---|
| | Active surveillance (n=379) | Radical prostatectomy (n=1043) | EBRT (n=359) | Brachytherapy (n=96) | Radical prostatectomy (n=362) | EBRT (n=206) |
| Median follow up, year [interquartile range] | 9.4 [9.1, 9.8] | 9.5 [9.3, 9.8] | 9.5 [9.0, 9.8] | 9.3 [8.3, 9.6] | 9.5 [9.1, 9.8] | 9.3 [7.5, 9.8] |
| All cause death, n (%) | 58/365 (16%) | 67/1027 (7%) | 76/350 (22%) | 20/92 (22%) | 37/355 (10%) | 75/203 (37%) |
| 10-year overall survival, % [95% CI][a] | 81.8 [77.0, 86.8] | 91.6 [89.1, 94.1] | 78.1 [73.6, 82.8] | 78.7 [70.6, 87.7] | 88.1 [83.7, 92.8] | 59.6 [52.2, 67.9] |
| Prostate cancer deaths, n (%) | 1/365 (0%) | 5/1026 (0%) | 2/346 (1%) | 0/90 (0%) | 13/354 (4%) | 14/201 (7%) |
| 10-year prostate cancer-specific survival, % [95% CI] [a] | 99.7 [99.1, 100.0] | 99.5 [99.0, 99.9] | 99.3 [98.3, 100.0] | 100 [100.0, 100.0] | 96.4 [94.4, 98.4] | 91.7 [87.6, 96.0] |

Abbreviations: ADT, androgen deprivation therapy; CI, confidence interval; EBRT, external beam radiotherapy. The cause of death is ascertained from by each cancer registry.
[a]Survival probability was calculated using the Kaplan-Meier method.

eTable 2: Number of missing data in study covariates

| Covariate | **Number missing (%)** |
|---|---|
| **Age at diagnosis** | 0 (0%) |
| **Race/ethnicity** | 4 (0%) |
| **Comorbidity score** | 116 (5%) |
| **Damico Risk Groups** | 0 (0%) |
| **Receipt of androgen deprivation therapy in year one** | 60 (2%) |
| **Study site** | 0 (0%) |
| **Social support scale** | 17 (1%) |
| **Depression scale** | 67 (3%) |
| **Participatory decision-making scale** | 47 (2%) |
| **EPIC 26 baseline scores** | |
| Sexual function | 133 (5%) |
| Urinary incontinence | 101 (4%) |
| Urinary irritation | 105 (4%) |
| Bowel function | 59 (2%) |
| Hormonal function | 103 (4%) |
| **EPIC 26 individual item at baseline** | |
| Sexual function bother | 122 (5%) |
| Erection insufficient for penetration | 108 (4%) |
| Urinary function | 98 (4%) |
| Urinary leakage | 62 (3%) |
| Burning on urination | 68 (3%) |
| Frequent urination | 63 (3%) |
| Bowel function bother | 68 (3%) |
| Bowel urgency | 57 (2%) |
| **SF-36 baseline scores** | |
| Physical functioning | 97 (4%) |
| Emotional well-being | 61 (2%) |
| Energy and fatigue | 58 (2%) |
| General health scale | 6 (0%) |

eTable 3: Baseline characteristics of men in the CEASAR study by response to the 10-year survey.

| | | Did not respond | Responded | p value |
|---|---|---|---|---|
| | | (n=1061) | (n=1384) | |
| **Age at diagnosis, median (Quartiles) [n], year** | | 66 (60, 72) [1061] | 63 (58, 68) [1384] | <0.001 |
| **Race/ethnicity, n (%)** | Non-Hispanic White | 710 (67%) | 1087 (79%) | <0.001 |
| | Non-Hispanic Black | 195 (18%) | 155 (11%) | |
| | Hispanic | 97 (9%) | 87 (6%) | |
| | Asian | 38 (4%) | 39 (3%) | |
| | Other | 17 (2%) | 16 (1%) | |
| **Marital status, n (%)** | Not married | 236 (24%) | 225 (17%) | <0.001 |
| | Married | 744 (76%) | 1108 (83%) | |
| **Education, n (%)** | Less than high school | 167 (17%) | 81 (6%) | <0.001 |
| | High school graduate | 249 (25%) | 237 (18%) | |
| | Some college | 229 (23%) | 287 (21%) | |
| | College graduate | 181 (18%) | 334 (25%) | |
| | Graduate/professional school | 159 (16%) | 397 (30%) | |
| **Comorbidity score, n (%)** | 0-2 | 222 (22%) | 458 (34%) | <0.001 |
| | 3-4 | 379 (38%) | 577 (43%) | |
| | 5 or more | 390 (39%) | 303 (23%) | |
| **Employment, n (%)** | Full time | 343 (33%) | 693 (50%) | <0.001 |
| | Part time | 79 (8%) | 115 (8%) | |
| | Retired | 565 (54%) | 504 (37%) | |
| | Unemployed | 62 (6%) | 63 (5%) | |
| **Risk Groups, n (%)** | Low risk | 460 (43%) | 687 (50%) | 0.003 |
| | Favorable intermediate risk | 319 (30%) | 411 (30%) | |
| | Unfavorable intermediate risk | 97 (9%) | 100 (7%) | |
| | High risk | 185 (17%) | 186 (13%) | |
| **Receipt of androgen deprivation treatment in year one, n (%)** | No | 815 (80%) | 1241 (91%) | |
| | Yes | 202 (20%) | 127 (9%) | |
| **Nerve sparing surgery** | None | 35 (12%) | 56 (8%) | 0.092 |
| | Unilateral | 41 (14%) | 73 (11%) | |
| | Bilateral | 225 (75%) | 544 (81%) | |
| **PSA at diagnosis, median (Quartiles) [n], year** | | 6 (4, 8) [1061] | 5 (4, 7) [1384] | <0.001 |
| **Clinical tumor stage n (%)** | T1 | 805 (77%) | 1067 (77%) | 0.72 |
| | T2 | 247 (23%) | 316 (23%) | |
| **Biopsy grade group, n (%)** | 1 | 526 (50%) | 784 (57%) | <0.001 |
| | 2 | 295 (28%) | 379 (27%) | |
| | 3 | 117 (11%) | 114 (8%) | |
| | 4-5 | 123 (12%) | 105 (8%) | |
| **Positive cores at biopsy, median (Quartiles) [n]** | | 3 (1, 5) [818] | 2 (1, 5) [1128] | 0.14 |
| **Study site n (%)** | Utah | 92 (9%) | 120 (9%) | <0.001 |
| | Atlanta | 165 (16%) | 150 (11%) | |
| | Los Angeles | 325 (31%) | 411 (30%) | |
| | Louisiana | 343 (32%) | 419 (30%) | |
| | New Jersey | 136 (13%) | 284 (21%) | |
| **EPIC 26 baseline scores, median (QUARTILES)[b] [n]** | Sexual function | 60 (22, 85) [987] | 80 (45, 95) [1325] | <0.001 |
| | Urinary incontinence | 100 (73, 100) [1003] | 100 (85, 100) [1341] | <0.001 |
| | Urinary irritation | 88 (69, 94) [1004] | 88 (75, 100) [1336] | <0.001 |
| | Bowel function | 100 (88, 100) [1029] | 100 (96, 100) [1357] | <0.001 |
| | Hormonal function | 90 (80, 100) [1004] | 95 (85, 100) [1338] | <0.001 |
| **SF-36 baseline scores, median (QUARTILES)[c] [n]** | Physical functioning | 90 (68, 100) [1015] | 100 (85, 100) [1333] | <0.001 |
| | Emotional well-being | 84 (64, 92) [1029] | 84 (72, 92) [1355] | 0.001 |
| | Energy and fatigue | 70 (55, 85) [1031] | 80 (65, 90) [1356] | <0.001 |
| | General health scale | 60 (60, 80) [1057] | 80 (60, 100) [1382] | <0.001 |
| **Social support scale, median (QUARTILES)[d] [n]** | | 95 (65, 100) [1052] | 95 (75, 100) [1376] | 0.002 |
| **Depression scale, median (QUARTILES)[e] [n]** | | 19 (7, 37) [1027] | 11 (4, 26) [1351] | <0.001 |
| **Participatory decision-making median (QUARTILES)[f] [n]** | | 79 (64, 93) [1034] | 86 (71, 96) [1364] | <0.001 |

Abbreviations: ADT, androgen deprivation therapy; EBRT, external beam radiotherapy; PSA, prostate-specific antigen.

[a] Total Illness Burden Index score measures the severity of comorbidities (score range 0-23), higher values indicate worse comorbid illnesses.

[b] Expanded Prostate Cancer Index Composite (EPIC) scores (score range 0-100), higher scores indicate better function.

[c] Medical Outcomes Short-Form Health Survey 36 (SF-36) domain scores (score range 0 to100), higher scores indicate better function or less disability.

[d] the social support scale is a modified domain score created using five questions from the Medical Outcomes Study Social Support Scale (score range 0-100), higher scores indicating greater support.

[e] Epidemiologic Studies Depression Scale was used to derive the depression score (scores were scaled to 100), higher scores indicating more severe depressive symptoms.

[f] Seven items were scored to determine participatory decision-making (score range 0 to 100), higher scores indicating increased patient control, responsibility, and choice

eTable 4: Treatment techniques used in men with favorable and unfavorable-prognosis prostate cancer[a]

| | Favorable-prognosis | Unfavorable- prognosis |
|---|---|---|
| **Radical prostatectomy** | | |
| Robot-assisted radical prostatectomy, n (%) | 672/854 (79%) | 212/290 (73%) |
| Open radical prostatectomy, n (%) | 182/854 (21%) | 78/290 (27%) |
| **Radiation therapy** | | |
| Intensity-modulated radiation therapy, n (%) | 278/353 (79%) | 177/199 (89%) |
| Image-guided radiation therapy, n (%) | 273/328 (83%) | 170/192 (89%) |
| Proton beam, n (%) | 20/328 (6%) | 3/189 (2%) |
| EBRT radiation dose, median (quartiles), Gy | 7800 (7600, 7920) | 7800 (7600, 7920) |
| Radiation dose/fraction, median (quartiles), Gy | 180 (180, 180) | 180 (180, 180) |
| Brachytherapy dose, median (quartiles), Gy | 145 (125, 145) | - |
| Received pelvic radiation, n (%) | 27/349 (8%) | 72/199 (36%) |

Abbreviations: EBRT, external beam radiotherapy

[a]Proportions are reported for patients with known information (denominator) about treatment technique.

eTable 5: Unadjusted and adjusted sexual function outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. active surveillance) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Active surveillance** | **Radical prostatectomy** | **EBRT** | **Brachytherapy** | | **Radical prostatectomy** | | | **EBRT** | | | **Brachytherapy** | | |
| | Median score (Quartiles) or frequency (%) | | | | p value | Effect | 95% CI | p value | Effect | 95% CI | p value | Effect | 95% CI | p value |
| **Sexual function domain score** | Median (Quartiles) [n] | | | | | Adjusted mean difference | | | | | | | | |
| Baseline | 75 (41, 85) [352] | 80 (43, 95) [994] | 60 (27, 82) [339] | 72 (38, 85) [94] | <0.001 | | | | | | | | | |
| 6 months | 69 (37, 85) [342] | 25 (7, 58) [953] | 47 (10, 75) [327] | 55 (18, 80) [92] | <0.001 | -35.2[b] | [-38.1, -32.2] | <0.001 | -9.7 | [-13.4, -6.0] | <0.001 | -11.2[b] | [-16.0, -6.3] | <0.001 |
| 1 year | 72 (33, 85) [318] | 35 (10, 68) [955] | 43 (12, 73) [325] | 53 (17, 75) [90] | <0.001 | -31.3[b] | [-34.1, -28.6] | <0.001 | -8.4 | [-11.8, -5.0] | <0.001 | -9.3 | [-13.7, -4.9] | <0.001 |
| 3 years | 62 (18, 85) [290] | 38 (12, 75) [876] | 43 (10, 75) [280] | 58 (19, 80) [75] | <0.001 | -17.8[b] | [-20.9, -14.7] | <0.001 | -4.0 | [-7.8, -0.2] | 0.041 | -3.0 | [-8.5, 2.5] | 0.28 |
| 5 years | 53 (18, 80) [261] | 43 (12, 78) [825] | 33 (7, 68) [251] | 51 (22, 75) [68] | 0.002 | -10.3[b] | [-13.8, -6.7] | <0.001 | -1.5 | [-5.8, 2.9] | 0.50 | -0.6 | [-7.0, 5.7] | 0.85 |
| 10 years | 43 (10, 80) [177] | 38 (10, 73) [673] | 25 (7, 64) [160] | 38 (15, 82) [42] | 0.045 | -7.2 | [-12.3, -2.0] | 0.007 | -0.5 | [-7.2, 6.2] | 0.89 | -5.0 | [-15.1, 5.2] | 0.34 |
| **Sexual function bother (individual item)** | frequency (%) | | | | | Adjusted odds ratio | | | | | | | | |
| Baseline | 83 (24%) | 253 (25%) | 104 (31%) | 21 (23%) | 0.12 | | | | | | | | | |
| 6 months | 69 (20%) | 541 (56%) | 118 (35%) | 28 (30%) | 0.001 | 6.9 | [5.2, 9.3] | <0.001 | 1.9 | [1.3, 2.7] | <0.001 | 1.7 | [1.0, 3.0] | 0.043 |
| 1 year | 70 (22%) | 480 (50%) | 115 (35%) | 26 (28%) | 0.001 | 5.6 | [4.3, 7.3] | <0.001 | 1.7 | [1.2, 2.4] | <0.001 | 1.6 | [1.0, 2.5] | 0.052 |
| 3 years | 81 (28%) | 394 (45%) | 89 (31%) | 23 (31%) | 0.001 | 2.7 | [2.1, 3.5] | <0.001 | 1.2 | [0.9, 1.7] | 0.21 | 1.2 | [0.7, 1.9] | 0.58 |
| 5 years | 68 (26%) | 326 (39%) | 94 (37%) | 18 (26%) | 0.001 | 1.8 | [1.4, 2.5] | <0.001 | 1.1 | [0.8, 1.6] | 0.64 | 1.0 | [0.5, 1.7] | 0.89 |
| 10 years | 43 (24%) | 230 (34%) | 55 (34%) | 8 (19%) | 0.013 | 1.8 | [1.1, 2.8] | 0.018 | 1.4 | [0.7, 2.5] | 0.31 | 0.9 | [0.3, 2.6] | 0.79 |
| **Erection insufficient for intercourse (individual item)** | Median (Quartiles) [n] | | | | | Adjusted odds ratio | | | | | | | | |
| Baseline | 144 (41%) | 379 (38%) | 186 (54%) | 44 (47%) | 0.001 | | | | | | | | | |
| 6 months | 150 (43%) | 747 (78%) | 222 (66%) | 54 (57%) | 0.001 | 12.3 | [9.0, 16.8] | <0.001 | 2.3 | [1.6, 3.3] | <0.001 | 2.0 | [1.2, 3.3] | 0.007 |
| 1 year | 140 (43%) | 671 (71%) | 218 (66%) | 50 (56%) | 0.001 | 9.2 | [6.9, 12.3] | <0.001 | 2.1 | [1.6, 2.9] | <0.001 | 1.8 | [1.1, 2.8] | 0.011 |
| 3 years | 148 (51%) | 589 (67%) | 189 (66%) | 41 (55%) | 0.001 | 3.4 | [2.5, 4.5] | <0.001 | 1.5 | [1.1, 2.1] | 0.025 | 1.2 | [0.7, 2.0] | 0.49 |
| 5 years | 158 (60%) | 536 (65%) | 188 (73%) | 44 (63%) | 0.014 | 1.9 | [1.4, 2.6] | <0.001 | 1.2 | [0.8, 1.7] | 0.48 | 1.0 | [0.6, 1.8] | 0.91 |
| 10 years | 117 (65%) | 472 (69%) | 118 (74%) | 29 (69%) | 0.38 | 1.5 | [0.9, 2.3] | 0.095 | 0.8 | [0.4, 1.5] | 0.53 | 1.4 | [0.6, 3.4] | 0.44 |

Abbreviations: EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (10-12 points) for sexual function.

eTable 6: Pair-wise comparisons of adjusted functional outcomes of men with favorable-prognosis prostate cancer by treatment.[a]

| | Radical prostatectomy vs EBRT | | | Radical prostatectomy vs Brachytherapy | | | EBRT vs Brachytherapy | | |
|---|---|---|---|---|---|---|---|---|---|
| | Adjusted mean difference or odds ratio | 95% CI | p value | Adjusted mean difference or odds ratio | 95% CI | p value | Adjusted mean difference or odds ratio | 95% CI | p value |
| **Sexual function** | | | | | | | | | |
| Sexual function domain score, mean adjusted difference [95% CI] | | | | | | | | | |
| 6 months | -25.5[b] | [-28.9, -22.1] | <0.001 | -24.0[b] | [-28.7, -19.3] | <0.001 | 1.5 | [-3.8, 6.7] | 0.58 |
| 1 year | -22.9[b] | [-26.1, -19.7] | <0.001 | -22.0[b] | [-26.4, -17.7] | <0.001 | 0.9 | [-4.0, 5.7] | 0.72 |
| 3 years | -13.9[b] | [-17.3, -10.4] | <0.001 | -14.8[b] | [-20.1, -9.5] | <0.001 | -1.0 | [-6.7, 4.8] | 0.75 |
| 5 years | -8.8 | [-12.5, -5.0] | <0.001 | -9.6 | [-15.6, -3.6] | 0.002 | -0.9 | [-7.4, 5.6] | 0.80 |
| 10 years | -6.7 | [-12.1, -1.2] | 0.017 | -2.2 | [-11.6, 7.3] | 0.65 | 4.5 | [-5.8, 14.8] | 0.39 |
| Sexual function bother, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 3.7 | [2.8, 4.9] | <0.001 | 4.0 | [2.4, 6.6] | <0.001 | 1.1 | [0.6, 1.9] | 0.75 |
| 1 year | 3.3 | [2.5, 4.3] | <0.001 | 3.5 | [2.3, 5.5] | <0.001 | 1.1 | [0.7, 1.7] | 0.74 |
| 3 years | 2.2 | [1.7, 2.9] | <0.001 | 2.3 | [1.5, 3.8] | <0.001 | 1.1 | [0.6, 1.8] | 0.79 |
| 5 years | 1.7 | [1.2, 2.3] | <0.001 | 1.9 | [1.1, 3.3] | 0.022 | 1.1 | [0.6, 2.1] | 0.67 |
| 10 years | 1.3 | [0.8, 2.1] | 0.31 | 2.0 | [0.7, 5.8] | 0.18 | 1.6 | [0.5, 4.8] | 0.42 |
| Erection insufficient for penetration, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 5.2 | [3.7, 7.3] | <0.001 | 6.1 | [3.7, 10.0] | <0.001 | 1.2 | [0.7, 2.0] | 0.57 |
| 1 year | 4.4 | [3.2, 5.9] | <0.001 | 5.2 | [3.3, 8.0] | <0.001 | 1.2 | [0.7, 1.9] | 0.47 |
| 3 years | 2.3 | [1.7, 3.2] | <0.001 | 2.8 | [1.7, 4.6] | <0.001 | 1.2 | [0.7, 2.1] | 0.43 |
| 5 years | 1.7 | [1.2, 2.4] | 0.005 | 1.9 | [1.1, 3.2] | 0.026 | 1.1 | [0.6, 2.0] | 0.72 |
| 10 years | 1.8 | [1.1, 3.1] | 0.028 | 1.0 | [0.5, 2.4] | 0.92 | 0.6 | [0.2, 1.5] | 0.24 |
| **Urinary function** | | | | | | | | | |
| Urinary incontinence domain score, mean adjusted difference [95% CI] | | | | | | | | | |
| 6 months | -24.9[b] | [-27.6, -22.2] | <0.001 | -17.3[b] | [-21.4, -13.3] | <0.001 | 7.6[b] | [3.5, 11.7] | <0.001 |
| 1 year | -23.4[b] | [-25.9, -20.9] | <0.001 | -16.4[b] | [-20.2, -12.6] | <0.001 | 7.0[b] | [3.2, 10.8] | <0.001 |
| 3 years | -18.5[b] | [-21.1, -15.9] | <0.001 | -13.4[b] | [-17.5, -9.2] | <0.001 | 5.1 | [0.9, 9.3] | 0.017 |
| 5 years | -16.9[b] | [-19.7, -14.1] | <0.001 | -12.4[b] | [-16.7, -8.0] | <0.001 | 4.5 | [0.1, 9.0] | 0.046 |
| 10 years | -22.0[b] | [-25.8, -18.3] | <0.001 | -15.5[b] | [-20.8, -10.2] | <0.001 | 6.5[b] | [0.8, 12.1] | 0.025 |
| Urinary irritation domain score, mean adjusted difference [95% CI] | | | | | | | | | |
| 6 months | 2.2 | [0.4, 3.9] | 0.014 | 12.2[b] | [8.4, 16.0] | <0.001 | 10.1[b] | [6.1, 14.1] | <0.001 |
| 1 year | 2.2 | [0.6, 3.7] | 0.006 | 10.6[b] | [7.4, 13.8] | <0.001 | 8.4[b] | [5.1, 11.8] | <0.001 |
| 3 years | 2.1 | [0.6, 3.6] | 0.007 | 5.0[b] | [2.4, 7.5] | <0.001 | 2.9 | [0.2, 5.7] | 0.039 |
| 5 years | 1.6 | [-0.1, 3.2] | 0.059 | 2.2 | [-0.6, 5.0] | 0.12 | 0.7 | [-2.4, 3.7] | 0.68 |
| 10 years | -0.7 | [-3.2, 1.8] | 0.57 | 2.8 | [-1.3, 6.8] | 0.18 | 3.5 | [-1.0, 8.0] | 0.13 |
| Urinary function, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 2.6 | [1.7, 3.9] | <0.001 | 1.1 | [0.6, 1.9] | 0.79 | 0.4 | [0.2, 0.8] | 0.011 |
| 1 year | 2.3 | [1.6, 3.4] | <0.001 | 1.1 | [0.7, 1.9] | 0.61 | 0.5 | [0.3, 0.9] | 0.014 |
| 3 years | 1.8 | [1.2, 2.7] | 0.007 | 1.4 | [0.7, 2.7] | 0.29 | 0.8 | [0.4, 1.6] | 0.52 |
| 5 years | 1.9 | [1.2, 3.0] | 0.009 | 1.8 | [0.8, 3.7] | 0.13 | 0.9 | [0.4, 2.1] | 0.90 |
| 10 years | 5.0 | [2.1, 12.0] | <0.001 | 3.2 | [0.8, 13.5] | 0.11 | 0.6 | [0.1, 3.3] | 0.59 |
| Urinary leakage, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 8.6 | [4.6, 15.8] | <0.001 | 3.0 | [1.4, 6.2] | 0.004 | 0.3 | [0.1, 0.9] | 0.024 |
| 1 year | 7.3 | [4.2, 12.8] | <0.001 | 3.2 | [1.7, 6.2] | <0.001 | 0.4 | [0.2, 1.0] | 0.049 |
| 3 years | 4.4 | [2.6, 7.5] | <0.001 | 4.5 | [1.4, 14.1] | 0.011 | 1.0 | [0.3, 3.5] | 0.97 |
| 5 years | 3.8 | [2.1, 6.8] | <0.001 | 6.9 | [1.7, 27.9] | 0.007 | 1.8 | [0.4, 7.9] | 0.43 |
| 10 years | 7.2 | [2.7, 19.0] | <0.001 | 25.9 | [6.8, 97.9] | <0.001 | 3.6 | [0.7, 17.8] | 0.115 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Burning on urination, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 0.5 | [0.2, 1.2] | 0.11 | 0.1 | [0.0, 0.2] | <0.001 | 0.2 | [0.1, 0.5] | <0.001 |
| 1 year | 0.5 | [0.3, 1.1] | 0.092 | 0.1 | [0.1, 0.2] | <0.001 | 0.2 | [0.1, 0.5] | <0.001 |
| 3 years | 0.6 | [0.2, 1.6] | 0.31 | 0.2 | [0.1, 0.5] | 0.002 | 0.3 | [0.1, 1.0] | 0.052 |
| 5 years | 0.6 | [0.2, 1.9] | 0.38 | 0.2 | [0.0, 0.8] | 0.023 | 0.3 | [0.1, 1.5] | 0.15 |
| 10 years | 0.5 | [0.1, 3.9] | 0.51 | 0.1 | [0.0, 1.2] | 0.072 | 0.2 | [0.0, 3.1] | 0.27 |
| Frequent urination, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 1.5 | [1.1, 2.2] | 0.024 | 0.5 | [0.3, 0.9] | 0.016 | 0.3 | [0.2, 0.6] | <0.001 |
| 1 year | 1.5 | [1.1, 2.0] | 0.023 | 0.5 | [0.3, 0.9] | 0.013 | 0.4 | [0.2, 0.6] | <0.001 |
| 3 years | 1.3 | [0.9, 1.9] | 0.17 | 0.7 | [0.4, 1.4] | 0.33 | 0.6 | [0.3, 1.1] | 0.094 |
| 5 years | 1.3 | [0.9, 2.1] | 0.18 | 0.9 | [0.4, 1.8] | 0.70 | 0.6 | [0.3, 1.4] | 0.28 |
| 10 years | 2.1 | [1.0, 4.3] | 0.041 | 0.9 | [0.3, 3.1] | 0.89 | 0.4 | [0.1, 1.7] | 0.23 |
| **Bowel function** | | | | | | | | | |
| Bowel function domain score, mean adjusted difference [95% CI] | | | | | | | | | |
| 6 months | 3.6 | [1.9, 5.2] | <0.001 | 5.1[b] | [2.3, 8.0] | <0.001 | 1.6 | [-1.6, 4.7] | 0.33 |
| 1 year | 3.5 | [2.0, 4.9] | <0.001 | 4.8[b] | [2.3, 7.3] | <0.001 | 1.3 | [-1.4, 4.1] | 0.35 |
| 3 years | 3.1 | [1.6, 4.6] | <0.001 | 3.6 | [1.4, 5.7] | 0.001 | 0.5 | [-2.0, 3.0] | 0.70 |
| 5 years | 2.9 | [1.3, 4.5] | <0.001 | 2.9 | [0.7, 5.1] | 0.011 | 0.0 | [-2.6, 2.6] | 0.99 |
| 10 years | 2.7 | [0.1, 5.4] | 0.042 | 2.4 | [-0.5, 5.2] | 0.10 | -0.4 | [-4.0, 3.3] | 0.84 |
| Bowel function bother, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 0.7 | [0.4, 1.3] | 0.24 | 0.7 | [0.3, 1.6] | 0.36 | 0.9 | [0.4, 2.3] | 0.88 |
| 1 year | 0.7 | [0.4, 1.2] | 0.24 | 0.7 | [0.3, 1.4] | 0.30 | 0.9 | [0.4, 2.0] | 0.83 |
| 3 years | 0.8 | [0.4, 1.5] | 0.49 | 0.7 | [0.3, 1.9] | 0.51 | 0.9 | [0.3, 2.5] | 0.85 |
| 5 years | 0.7 | [0.4, 1.5] | 0.39 | 0.8 | [0.2, 2.5] | 0.69 | 1.1 | [0.3, 3.7] | 0.92 |
| 10 years | 0.4 | [0.2, 0.9] | 0.027 | 0.9 | [0.1, 9.3] | 0.96 | 2.5 | [0.2, 25.9] | 0.44 |
| Bowel urgency, adjusted odds ratio [95% CI] | | | | | | | | | |
| 6 months | 0.5 | [0.3, 0.9] | 0.03 | 0.3 | [0.1, 0.8] | 0.019 | 0.6 | [0.2, 1.7] | 0.36 |
| 1 year | 0.5 | [0.3, 0.8] | 0.006 | 0.3 | [0.2, 0.7] | 0.006 | 0.7 | [0.3, 1.6] | 0.38 |
| 3 years | 0.4 | [0.2, 0.6] | <0.001 | 0.4 | [0.2, 0.8] | 0.009 | 0.9 | [0.4, 2.1] | 0.89 |
| 5 years | 0.4 | [0.2, 0.7] | 0.001 | 0.5 | [0.2, 1.1] | 0.097 | 1.3 | [0.5, 3.2] | 0.56 |
| 10 years | 0.7 | [0.3, 1.7] | 0.43 | 2.2 | [0.5, 9.7] | 0.31 | 3.1 | [0.6, 15.1] | 0.17 |
| **Hormonal function** | | | | | | | | | |
| Hormonal domain score, mean adjusted difference [95% CI] | | | | | | | | | |
| 6 months | 1.9 | [0.3, 3.5] | 0.02 | 0.3 | [-1.9, 2.4] | 0.81 | -1.6 | [-4.1, 0.8] | 0.18 |
| 1 year | 1.4 | [0.0, 2.8] | 0.056 | -0.1 | [-1.9, 1.8] | 0.94 | -1.5 | [-3.6, 0.6] | 0.18 |
| 3 years | -0.4 | [-1.8, 1.1] | 0.62 | -1.0 | [-3.0, 0.9] | 0.31 | -0.7 | [-2.8, 1.5] | 0.55 |
| 5 years | -1.2 | [-2.8, 0.4] | 0.13 | -0.9 | [-3.1, 1.2] | 0.41 | 0.3 | [-2.1, 2.7] | 0.81 |
| 10 years | -1.0 | [-3.3, 1.4] | 0.43 | 2.2 | [-1.4, 5.8] | 0.22 | 3.2 | [-0.9, 7.3] | 0.13 |

Abbreviations: CI, confidence interval; EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance. A minimally important difference in domain scores is 10-12 points for the sexual function, 6-9 points for the urinary incontinence; 5-7 points for the urinary irritation, 4-6 points for the bowel function, and 4-6 points for the hormonal function.

eTable 7: Summary of sexual function at 10 years according to baseline function.

| | Favorable-prognosis | | | | Unfavorable-prognosis | |
|---|---|---|---|---|---|---|
| | Radical prostatectomy | EBRT | Brachytherapy | Active surveillance | Radical prostatectomy | EBRT |
| **Patient with sufficient erections for intercourse at year 10** | | | | | | |
| Reported erections sufficient for intercourse at baseline, % (n) | 41% (183/449) | 43% (34/79) | 48% (13/27) | 46% (57/123) | 22% (24/109) | 24% (9/38) |
| Reported erections insufficient for intercourse at baseline, % (n) | 9% (20/212) | 8% (6/77) | 0 (0/15) | 8% (4/49) | 6% (6/93) | 11% (3/28) |
| Abbreviations: ADT, androgen deprivation therapy; EBRT, external beam radiotherapy | | | | | | |

eTable 8: Unadjusted and adjusted urinary incontinence function outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. active surveillance) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Active surveillance | Radical prostatectomy | EBRT | Brachytherapy | | Radical prostatectomy | | | EBRT | | | Brachytherapy | | |
| | Median score (Quartiles) or frequency (%) | | | | p value | Effect | 95% CI | p value | Effect | 95% CI | p value | Effect | 95% CI | p value |
| **Urinary incontinence domain score** | Median (Quartiles) [n] | | | | | Adjusted mean difference | | | | | | | | |
| Baseline | 100 (79, 100) [358] | 100 (79, 100) [1005] | 100 (79, 100) [341] | 100 (92, 100) [93] | 0.19 | | | | | | | | | |
| 6 months | 100 (79, 100) [360] | 67 (46, 94) [972] | 100 (79, 100) [346] | 93 (73, 100) [92] | <0.001 | -24.0[b] | [-26.5, -21.5] | <0.001 | 0.9 | [-1.6, 3.4] | 0.48 | -6.7[b] | [-10.6, -2.7] | <0.001 |
| 1 year | 100 (79, 100) [334] | 79 (52, 100) [926] | 100 (79, 100) [327] | 94 (79, 100) [88] | <0.001 | -22.0[b] | [-24.3, -19.8] | <0.001 | 1.4 | [-0.9, 3.6] | 0.24 | -5.6 | [-9.2, -2.0] | 0.002 |
| 3 years | 100 (77, 100) [300] | 79 (54, 100) [875] | 100 (79, 100) [289] | 100 (79, 100) [77] | <0.001 | -15.2[b] | [-17.6, -12.8] | <0.001 | 3.2 | [0.7, 5.8] | 0.012 | -1.9 | [-6.0, 2.2] | 0.37 |
| 5 years | 92 (73, 100) [274] | 77 (54, 100) [829] | 100 (79, 100) [262] | 97 (79, 100) [72] | <0.001 | -11.8[b] | [-14.6, -9.0] | <0.001 | 5.1 | [2.2, 8.1] | <0.001 | 0.6 | [-3.9, 5.0] | 0.80 |
| 10 years | 92 (69, 100) [179] | 79 (52, 100) [681] | 100 (79, 100) [166] | 100 (84, 100) [44] | <0.001 | -12.1[b] | [-16.2, -8.0] | <0.001 | 9.9[b] | [5.3, 14.5] | <0.001 | 3.4 | [-2.5, 9.3] | 0.26 |
| **Urinary leakage (individual item)** | frequency (%) | | | | | Adjusted odds ratio | | | | | | | | |
| Baseline | 20 (5%) | 65 (6%) | 16 (5%) | 3 (3%) | 0.43 | | | | | | | | | |
| 6 months | 14 (4%) | 178 (18%) | 14 (4%) | 10 (11%) | <0.001 | 7.2 | [4.1, 12.8] | <0.001 | 0.8 | [0.4, 1.8] | 0.672 | 2.4 | [1.0, 5.9] | 0.047 |
| 1 year | 18 (5%) | 133 (14%) | 14 (4%) | 2 (2%) | <0.001 | 6.1 | [3.7, 10.0] | <0.001 | 0.8 | [0.4, 1.6] | 0.60 | 1.9 | [0.9, 4.1] | 0.11 |
| 3 years | 17 (6%) | 120 (14%) | 11 (4%) | 2 (3%) | <0.001 | 3.3 | [2.1, 5.1] | <0.001 | 0.8 | [0.4, 1.4] | 0.36 | 0.7 | [0.2, 2.4] | 0.61 |
| 5 years | 21 (8%) | 112 (13%) | 16 (6%) | 3 (4%) | <0.001 | 2.3 | [1.4, 3.7] | <0.001 | 0.6 | [0.3, 1.2] | 0.14 | 0.3 | [0.1, 1.4] | 0.14 |
| 10 years | 18 (10%) | 96 (14%) | 6 (4%) | 0 (0%) | <0.001 | 1.9 | [1.0, 3.5] | 0.055 | 0.3 | [0.1, 0.8] | 0.016 | 0.1 | [0.0, 0.3] | <0.001 |

Abbreviations: EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (6-9 points) for the urinary incontinence.

eTable 9: Unadjusted and adjusted urinary irritation function outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. active surveillance) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Active surveillance | Radical prostatectomy | EBRT | Brachytherapy | | Radical prostatectomy | | | EBRT | | | Brachytherapy | | |
| | Median score (Quartiles) or frequency (%) | | | | p value | Effect | 95% CI | p value | Effect | 95% CI | p value | Effect | 95% CI | p value |
| **Urinary irritation domain score** | | | Median (Quartiles) [n] | | | | | | | | Adjusted mean difference | | | |
| Baseline | 88 (75, 100) [359] | 88 (75, 100) [1004] | 88 (75, 94) [340] | 94 (75, 100) [93] | 0.065 | | | | | | | | | |
| 6 months | 88 (81, 100) [354] | 94 (81, 100) [960] | 88 (81, 97) [343] | 81 (62, 88) [92] | <0.001 | 2.2 | [0.7, 3.7] | 0.004 | 0.1 | [-1.9, 2.0] | 0.95 | -10.0[b] | [-13.9, -6.1] | <0.001 |
| 1 year | 88 (81, 100) [334] | 94 (88, 100) [952] | 88 (81, 94) [336] | 88 (75, 94) [89] | <0.001 | 2.7 | [1.3, 4.0] | <0.001 | 0.5 | [-1.2, 2.2] | 0.57 | -7.9[b] | [-11.2, -4.7] | <0.001 |
| 3 years | 88 (81, 100) [298] | 94 (88, 100) [875] | 88 (81, 100) [287] | 94 (88, 94) [75] | <0.001 | 4.2 | [2.8, 5.5] | <0.001 | 2.1 | [0.4, 3.9] | 0.017 | -0.8 | [-3.5, 1.9] | 0.55 |
| 5 years | 88 (75, 100) [271] | 94 (88, 100) [824] | 94 (81, 100) [262] | 94 (81, 100) [71] | <0.001 | 4.8 | [3.3, 6.3] | <0.001 | 3.2 | [1.3, 5.2] | 0.001 | 2.6 | [-0.4, 5.6] | 0.091 |
| 10 years | 88 (81, 94) [177] | 94 (88, 100) [665] | 94 (86, 100) [164] | 94 (88, 100) [41] | <0.001 | 4.0 | [1.6, 6.4] | <0.001 | 4.7 | [1.6, 7.8] | 0.003 | 1.2 | [-3.2, 5.6] | 0.58 |
| **Urinary function bother (individual item)** | | | Frequency (%) | | | | | | | | Adjusted odds ratio | | | |
| Baseline | 47 (13%) | 137 (14%) | 45 (13%) | 11 (12%) | 0.95 | | | | | | | | | |
| 6 months | 35 (10%) | 159 (16%) | 37 (11%) | 20 (22%) | <0.001 | 2.1 | [1.4, 3.1] | <0.001 | 0.8 | [0.5, 1.4] | 0.45 | 2.0 | [1.0, 3.7] | 0.036 |
| 1 year | 34 (10%) | 111 (12%) | 26 (8%) | 8 (9%) | 0.24 | 2.0 | [1.4, 2.9] | <0.001 | 0.9 | [0.6, 1.3] | 0.52 | 1.8 | [1.0, 3.0] | 0.037 |
| 3 years | 26 (9%) | 98 (11%) | 27 (9%) | 7 (9%) | 0.57 | 1.7 | [1.1, 2.5] | 0.009 | 1.0 | [0.6, 1.5] | 0.84 | 1.2 | [0.6, 2.4] | 0.61 |
| 5 years | 24 (9%) | 98 (12%) | 23 (9%) | 7 (10%) | 0.35 | 1.5 | [1.0, 2.3] | 0.066 | 0.8 | [0.5, 1.4] | 0.44 | 0.9 | [0.4, 1.9] | 0.69 |
| 10 years | 22 (12%) | 87 (13%) | 8 (5%) | 2 (4%) | 0.014 | 1.4 | [0.8, 2.4] | 0.31 | 0.3 | [0.1, 0.7] | 0.007 | 0.4 | [0.1, 1.9] | 0.25 |
| **Burning on urination (individual item)** | | | Frequency (%) | | | | | | | | Adjusted odds ratio | | | |
| Baseline | 15 (4%) | 37 (4%) | 17 (5%) | 3 (3%) | 0.74 | | | | | | | | | |
| 6 months | 6 (2%) | 13 (1%) | 12 (3%) | 8 (9%) | <0.001 | 1.1 | [0.4, 2.8] | 0.92 | 2.1 | [0.7, 5.8] | 0.17 | 11.0 | [3.8, 31.6] | <0.001 |
| 1 year | 4 (1%) | 10 (1%) | 10 (3%) | 10 (11%) | <0.001 | 0.9 | [0.4, 2.2] | 0.85 | 1.7 | [0.7, 4.4] | 0.24 | 8.4 | [3.4, 20.6] | <0.001 |
| 3 years | 5 (2%) | 11 (1%) | 7 (2%) | 1 (1%) | 0.59 | 0.6 | [0.2, 1.7] | 0.31 | 1.0 | [0.3, 3.1] | 0.99 | 3.3 | [1.0, 10.7] | 0.043 |
| 5 years | 3 (1%) | 3 (0%) | 2 (1%) | 3 (4%) | 0.004 | 0.5 | [0.1, 1.5] | 0.19 | 0.8 | [0.2, 2.8] | 0.68 | 2.3 | [0.5, 9.8] | 0.27 |
| 10 years | 2 (1%) | 4 (1%) | 2 (1%) | 1 (2%) | 0.57 | 0.4 | [0.1, 3.9] | 0.46 | 0.9 | [0.1, 9.5] | 0.93 | 3.8 | [0.3, 49.6] | 0.31 |
| **Frequent urination (individual item)** | | | Frequency (%) | | | | | | | | Adjusted odds ratio | | | |
| Baseline | 73 (20%) | 207 (20%) | 75 (21%) | 13 (14%) | 0.47 | | | | | | | | | |
| 6 months | 62 (17%) | 165 (17%) | 58 (17%) | 28 (30%) | 0.014 | 1.0 | [0.7, 1.4] | 0.96 | 0.7 | [0.4, 1.0] | 0.041 | 2.0 | [1.1, 3.6] | 0.024 |
| 1 year | 59 (17%) | 130 (13%) | 43 (13%) | 17 (19%) | 0.14 | 0.9 | [0.7, 1.3] | 0.66 | 0.6 | [0.4, 0.9] | 0.017 | 1.7 | [1.0, 2.8] | 0.036 |
| 3 years | 51 (17%) | 108 (12%) | 39 (13%) | 9 (12%) | 0.24 | 0.8 | [0.6, 1.1] | 0.11 | 0.6 | [0.4, 0.9] | 0.014 | 1.1 | [0.6, 2.0] | 0.87 |
| 5 years | 44 (16%) | 117 (14%) | 34 (13%) | 11 (15%) | 0.74 | 0.7 | [0.5, 1.0] | 0.07 | 0.5 | [0.3, 0.9] | 0.01 | 0.8 | [0.4, 1.8] | 0.65 |
| 10 years | 32 (17%) | 96 (14%) | 15 (9%) | 5 (12%) | 0.14 | 0.9 | [0.5, 1.5] | 0.59 | 0.4 | [0.2, 0.9] | 0.031 | 0.9 | [0.3, 3.4] | 0.92 |

Abbreviations: EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (5-7 points) for the urinary irritation function.

eTable 10: Unadjusted and adjusted bowel function outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. active surveillance) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Active surveillance | Radical prostatectomy | EBRT | Brachytherapy | | Radical prostatectomy | | | EBRT | | | Brachytherapy | | |
| | Median score (Quartiles) or frequency (%) | | | | p value | Effect | 95% CI | p value | Effect | 95% CI | p value | Effect | 95% CI | p value |
| **Bowel function domain score** | Median (Quartiles) [n] | | | | | Adjusted mean difference | | | | | | | | |
| Baseline | 100 (92, 100) [364] | 100 (96, 100) [1021] | 100 (92, 100) [351] | 100 (96, 100) [95] | 0.001 | | | | | | | | | |
| 6 months | 100 (95, 100) [362] | 100 (96, 100) [975] | 96 (88, 100) [345] | 96 (88, 100) [92] | <0.001 | -0.4 | [-1.6, 0.7] | 0.47 | -4.0[b] | [-5.8, -2.2] | <0.001 | -5.6[b] | [-8.4, -2.7] | <0.001 |
| 1 year | 100 (92, 100) [342] | 100 (96, 100) [964] | 96 (83, 100) [339] | 96 (83, 100) [91] | <0.001 | -0.3 | [-1.3, 0.7] | 0.61 | -3.7 | [-5.3, -2.1] | <0.001 | -5.1[b] | [-7.6, -2.5] | <0.001 |
| 3 years | 100 (92, 100) [308] | 100 (96, 100) [887] | 96 (88, 100) [294] | 100 (88, 100) [78] | <0.001 | 0.3 | [-0.8, 1.4] | 0.56 | -2.8 | [-4.4, -1.1] | <0.001 | -3.3 | [-5.5, -1.0] | 0.005 |
| 5 years | 100 (92, 100) [275] | 100 (96, 100) [837] | 100 (88, 100) [266] | 100 (88, 100) [72] | <0.001 | 0.6 | [-0.6, 1.9] | 0.31 | -2.2 | [-4.1, -0.4] | 0.019 | -2.2 | [-4.6, 0.2] | 0.07 |
| 10 years | 100 (92, 100) [184] | 100 (92, 100) [688] | 100 (88, 100) [168] | 100 (88, 100) [45] | 0.003 | 0.8 | [-1.3, 2.8] | 0.46 | -2.0 | [-5.1, 1.2] | 0.22 | -1.6 | [-4.8, 1.6] | 0.33 |
| **Bowel function bother (individual item)** | Frequency (%) | | | | | Adjusted odds ratio | | | | | | | | |
| Baseline | 17 (5%) | 37 (4%) | 9 (3%) | 4 (4%) | 0.50 | | | | | | | | | |
| 6 months | 11 (3%) | 34 (3%) | 25 (7%) | 7 (8%) | 0.006 | 2.0 | [1.0, 3.9] | 0.038 | 2.9 | [1.4, 5.7] | 0.002 | 3.1 | [1.2, 8.0] | 0.021 |
| 1 year | 13 (4%) | 31 (3%) | 23 (7%) | 5 (6%) | 0.032 | 1.7 | [1.0, 3.1] | 0.058 | 2.4 | [1.3, 4.4] | 0.005 | 2.6 | [1.2, 5.9] | 0.02 |
| 3 years | 14 (5%) | 23 (3%) | 14 (5%) | 3 (4%) | 0.19 | 1.0 | [0.6, 1.8] | 0.89 | 1.3 | [0.7, 2.5] | 0.45 | 1.4 | [0.5, 3.8] | 0.47 |
| 5 years | 10 (4%) | 22 (3%) | 11 (4%) | 4 (6%) | 0.38 | 0.7 | [0.4, 1.4] | 0.33 | 1.0 | [0.5, 2.1] | 1.00 | 0.9 | [0.3, 3.1] | 0.92 |
| 10 years | 14 (7%) | 19 (3%) | 14 (8%) | 1 (2%) | 0.002 | 0.5 | [0.2, 1.2] | 0.14 | 1.4 | [0.5, 3.6] | 0.54 | 0.5 | [0.1, 5.6] | 0.61 |
| **Bloody stools (individual item)** | Frequency (%) | | | | | | | | | | | | | |
| Baseline | 4 (1%) | 5 (0%) | 3 (1%) | 0 (0%) | 0.502 | | | | | | | | | |
| 6 months | 3 (1%) | 8 (1%) | 3 (1%) | 0 (0%) | 0.854 | | | | | | | | | |
| 1 year | 4 (1%) | 9 (1%) | 5 (1%) | 1 (1%) | 0.874 | | | | | | | | | |
| 3 years | 1 (0%) | 3 (0%) | 7 (2%) | 1 (1%) | 0.004 | Adjusted analysis not done due to small number of events | | | | | | | | |
| 5 years | 0 (0%) | 1 (0%) | 2 (1%) | 0 (0%) | 0.184 | | | | | | | | | |
| 10 years | 0 (0%) | 1 (0%) | 3 (2%) | 0 (0%) | 0.012 | | | | | | | | | |
| **Bowel urgency (individual item)** | Frequency (%) | | | | | Adjusted odds ratio | | | | | | | | |
| Baseline | 14 (4%) | 46 (5%) | 10 (3%) | 5 (5%) | 0.53 | | | | | | | | | |
| 6 months | 17 (5%) | 26 (3%) | 22 (6%) | 9 (10%) | <0.001 | 0.9 | [0.5, 1.8] | 0.85 | 1.8 | [0.9, 3.6] | 0.11 | 2.8 | [1.1, 7.3] | 0.037 |
| 1 year | 13 (4%) | 30 (3%) | 23 (7%) | 9 (10%) | 0.001 | 0.9 | [0.5, 1.5] | 0.59 | 1.8 | [0.9, 3.3] | 0.073 | 2.6 | [1.1, 5.8] | 0.025 |
| 3 years | 16 (5%) | 24 (3%) | 23 (8%) | 4 (5%) | 0.002 | 0.6 | [0.4, 1.1] | 0.11 | 1.7 | [0.9, 3.1] | 0.093 | 1.8 | [0.8, 4.0] | 0.16 |
| 5 years | 13 (5%) | 23 (3%) | 18 (7%) | 6 (8%) | 0.007 | 0.6 | [0.3, 1.1] | 0.076 | 1.6 | [0.8, 3.1] | 0.18 | 1.2 | [0.5, 3.0] | 0.69 |
| 10 years | 12 (6%) | 33 (5%) | 15 (9%) | 1 (2%) | 0.14 | 0.9 | [0.4, 2.0] | 0.71 | 1.2 | [0.4, 3.4] | 0.72 | 0.4 | [0.1, 1.9] | 0.25 |
| **Increased frequency of bowel movements (individual item)** | Frequency (%) | | | | | | | | | | | | | |
| Baseline | 15 (4%) | 31 (3%) | 9 (3%) | 2 (2%) | 0.592 | | | | | | | | | |
| 6 months | 6 (2%) | 18 (2%) | 18 (5%) | 5 (5%) | 0.002 | | | | | | | | | |
| 1 year | 9 (3%) | 21 (2%) | 20 (6%) | 3 (3%) | 0.007 | | | | | | | | | |
| 3 years | 12 (4%) | 17 (2%) | 17 (6%) | 3 (4%) | 0.008 | | | | | | | | | |
| 5 years | 12 (4%) | 13 (2%) | 7 (3%) | 3 (4%) | 0.043 | | | | | | | | | |
| 10 years | 5 (3%) | 12 (2%) | 8 (5%) | 0 (0%) | 0.08 | | | | | | | | | |
| **Fecal incontinence (individual item)** | Frequency (%) | | | | | | | | | | | | | |
| Baseline | 7 (2%) | 19 (2%) | 3 (1%) | 4 (4%) | 0.175 | | | | | | | | | |
| 6 months | 8 (2%) | 9 (1%) | 13 (4%) | 6 (7%) | <0.001 | | | | | | | | | |
| 1 year | 7 (2%) | 10 (1%) | 14 (4%) | 5 (6%) | <0.001 | | | | | | | | | |
| 3 years | 8 (3%) | 10 (1%) | 7 (2%) | 3 (4%) | 0.111 | | | | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 years | 7 (3%) | 7 (1%) | 9 (3%) | 1 (1%) | 0.022 | |
| 10 years | 5 (3%) | 6 (1%) | 9 (5%) | 0 (0%) | <0.001 | |
| **Abdominal, pelvic, or rectal pain (individual item)** | | | Frequency (%) | | | Adjusted odds ratio |
| Baseline | 10 (3%) | 39 (4%) | 9 (3%) | 2 (2%) | 0.523 | |
| 6 months | 4 (1%) | 21 (2%) | 11 (3%) | 0 (0%) | 0.114 | |
| 1 year | 5 (1%) | 26 (3%) | 6 (2%) | 2 (2%) | 0.534 | |
| 3 years | 3 (1%) | 11 (1%) | 5 (2%) | 0 (0%) | 0.638 | |
| 5 years | 0 (0%) | 10 (1%) | 4 (1%) | 0 (0%) | 0.202 | |
| 10 years | 2 (1%) | 6 (1%) | 2 (1%) | 0 (0%) | 0.891 | |

Abbreviations: EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (4-6 points) for the bowel function.

eTable 11: Unadjusted and adjusted hormonal function outcomes of men with favorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. active surveillance) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Active surveillance | Radical prostatectomy | EBRT | Brachytherapy | | Radical prostatectomy | | | EBRT | | | Brachytherapy | | |
| | Median score (Quartiles) or frequency (%) | | | | p value | Effect | 95% CI | p value | Effect | 95% CI | p value | Effect | 95% CI | p value |
| **Hormonal function domain score** | Median (Quartiles) [n] | | | | | Adjusted mean difference | | | | | | | | |
| Baseline | 95 (85, 100) [363] | 95 (85, 100) [1003] | 95 (80, 100) [341] | 100 (81, 100) [93] | 0.004 | | | | | | | | | |
| 6 months | 95 (85, 100) [357] | 95 (85, 100) [964] | 90 (75, 100) [333] | 95 (80, 100) [95] | <0.001 | -1.3 | [-2.6, 0.0] | 0.045 | -3.2 | [-4.9, -1.5] | <0.001 | -1.6 | [-3.8, 0.6] | 0.16 |
| 1 year | 95 (85, 100) [338] | 95 (85, 100) [956] | 90 (78, 100) [327] | 95 (80, 100) [91] | <0.001 | -1.1 | [-2.3, 0.0] | 0.056 | -2.5 | [-4.0, -1.0] | 0.001 | -1.0 | [-2.9, 0.9] | 0.28 |
| 3 years | 95 (85, 100) [305] | 95 (85, 100) [880] | 95 (85, 100) [285] | 95 (90, 100) [77] | 0.11 | -0.4 | [-1.7, 0.8] | 0.52 | -0.1 | [-1.6, 1.5] | 0.95 | 0.6 | [-1.4, 2.7] | 0.56 |
| 5 years | 95 (85, 100) [273] | 95 (85, 100) [832] | 95 (80, 100) [257] | 100 (85, 100) [69] | 0.11 | 0.1 | [-1.3, 1.5] | 0.92 | 1.3 | [-0.5, 3.1] | 0.16 | 1.0 | [-1.3, 3.3] | 0.41 |
| 10 years | 100 (90, 100) [180] | 100 (90, 100) [679] | 95 (89, 100) [163] | 100 (90, 100) [45] | 0.22 | 0.7 | [-1.4, 2.8] | 0.52 | 1.6 | [-1.3, 4.5] | 0.27 | -1.5 | [-5.5, 2.4] | 0.45 |
| **Hot flashes (individual item)** | Frequency (%). | | | | | | | | | | | | | |
| Baseline | 5 (1%) | 21 (2%) | 15 (4%) | 3 (3%) | 0.050 | | | | | | | | | |
| 6 months | 1 (0%) | 21 (2%) | 37 (11%) | 3 (3%) | <0.001 | | | | | | | | | |
| 1 year | 1 (0%) | 24 (3%) | 15 (5%) | 3 (3%) | 0.005 | | | | | | | | | |
| 3 years | 2 (1%) | 18 (2%) | 8 (3%) | 1 (1%) | 0.252 | | | | | | | | | |
| 5 years | 0 (0%) | 12 (1%) | 6 (2%) | 1 (1%) | 0.125 | | | | | | | | | |
| 10 years | 1 (1%) | 11 (2%) | 3 (2%) | 0 (0%) | 0.570 | | | | | | | | | |
| **Breast tenderness and enlargement (individual item)** | | | | | | | | | | | | | | |
| Baseline | 3 (1%) | 4 (0%) | 4 (1%) | 1 (1%) | 0.429 | | | | | | | | | |
| 6 months | 1 (0%) | 4 (0%) | 8 (2%) | 0 (0%) | 0.001 | | | | | | | | | |
| 1 year | 3 (1%) | 7 (1%) | 10 (3%) | 0 (0%) | 0.004 | | | | | | | | | |
| 3 years | 4 (1%) | 9 (1%) | 4 (1%) | 1 (1%) | 0.942 | | | | | | | | | |
| 5 years | 0 (0%) | 3 (0%) | 4 (2%) | 0 (0%) | 0.048 | | | | | | | | | |
| 10 years | 1 (1%) | 4 (1%) | 0 (0%) | 0 (0%) | 0.759 | | | | | | | | | |
| **Feeling depressed (individual item)** | | | | | | | | | | | | | | |
| Baseline | 19 (5%) | 75 (7%) | 31 (9%) | 5 (5%) | 0.237 | | | | | | | | | |
| 6 months | 17 (5%) | 78 (8%) | 28 (8%) | 8 (9%) | 0.189 | | | | | | | | | |
| 1 year | 19 (6%) | 79 (8%) | 32 (10%) | 6 (7%) | 0.254 | | | | | | | | | |
| 3 years | 15 (5%) | 56 (6%) | 20 (7%) | 4 (5%) | 0.710 | | | | | | | | | |
| 5 years | 11 (4%) | 41 (5%) | 15 (6%) | 5 (7%) | 0.656 | | | | | | | | | |
| 10 years | 6 (3%) | 18 (3%) | 6 (4%) | 1 (2%) | 0.879 | | | | | | | | | |
| **Lack of energy (individual item)** | | | | | | | | | | | | | | |
| Baseline | 40 (11%) | 86 (9%) | 49 (14%) | 14 (15%) | 0.010 | | | | | | | | | |
| 6 months | 42 (12%) | 89 (9%) | 60 (18%) | 13 (14%) | <0.001 | | | | | | | | | |
| 1 year | 43 (13%) | 103 (11%) | 58 (18%) | 15 (17%) | 0.011 | | | | | | | | | |
| 3 years | 28 (9%) | 81 (9%) | 34 (12%) | 9 (12%) | 0.563 | | | | | | | | | |
| 5 years | 23 (8%) | 67 (8%) | 33 (13%) | 7 (10%) | 0.136 | | | | | | | | | |
| 10 years | 16 (9%) | 40 (6%) | 19 (11%) | 2 (4%) | 0.060 | | | | | | | | | |
| **Change in body weight (individual item)** | | | | | | | | | | | | | | |
| Baseline | 18 (5%) | 55 (5%) | 26 (7%) | 8 (9%) | 0.300 | | | | | | | | | |
| 6 months | 21 (6%) | 60 (6%) | 30 (9%) | 5 (5%) | 0.278 | | | | | | | | | |
| 1 year | 17 (5%) | 63 (7%) | 27 (8%) | 6 (7%) | 0.441 | | | | | | | | | |
| 3 years | 15 (5%) | 55 (6%) | 16 (5%) | 1 (1%) | 0.300 | | | | | | | | | |
| 5 years | 18 (7%) | 60 (7%) | 18 (7%) | 4 (6%) | 0.964 | | | | | | | | | |
| 10 years | 10 (5%) | 32 (5%) | 8 (5%) | 1 (2%) | 0.832 | | | | | | | | | |

Abbreviations: EBRT, external beam radiotherapy.
[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.
[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (4-6 points) for the hormonal function.

eTable 12: Unadjusted general health-related quality of life outcomes for men with favorable and unfavorable-prognosis prostate cancer.

| | Favorable- prognosis prostate cancer | | | | | Unfavorable-prognosis prostate caner | | |
|---|---|---|---|---|---|---|---|---|
| | Active surveillance | Radical prostatectomy | EBRT | Brachytherapy | p value | EBRT | Radical prostatectomy | p value |
| **Health-related quality of life outcomes through first 5 years, median (Quartiles)[a] [n]** | | | | | | | | |
| **Physical functioning** | | | | | | | | |
| Baseline | 95 (80, 100) [354] | 100 (85, 100) [1006] | 90 (70, 100) [346] | 95 (80, 100) [92] | <0.001 | 85 (59, 100) [196] | 95 (80, 100) [354] | <0.001 |
| 6 months | 95 (75, 100) [361] | 95 (85, 100) [979] | 89 (69, 95) [346] | 95 (80, 100) [95] | <0.001 | 78 (45, 91) [196] | 90 (78, 100) [342] | <0.001 |
| 1 year | 95 (85, 100) [344] | 100 (90, 100) [969] | 90 (75, 100) [340] | 95 (80, 100) [93] | <0.001 | 85 (55, 95) [189] | 95 (80, 100) [336] | <0.001 |
| 3 years | 95 (80, 100) [306] | 95 (85, 100) [889] | 85 (65, 95) [296] | 90 (75, 100) [78] | <0.001 | 80 (50, 95) [165] | 92 (78, 100) [310] | <0.001 |
| 5 years | 90 (80, 100) [277] | 95 (85, 100) [840] | 85 (64, 95) [270] | 90 (75, 100) [72] | <0.001 | 80 (40, 95) [141] | 90 (75, 100) [287] | <0.001 |
| **Emotional well-being** | | | | | | | | |
| Baseline | 84 (72, 92) [362] | 84 (68, 92) [1018] | 84 (72, 92) [351] | 84 (75, 94) [94] | 0.31 | 84 (68, 92) [202] | 84 (64, 92) [357] | 0.11 |
| 6 months | 88 (76, 92) [363] | 88 (76, 92) [981] | 84 (68, 92) [346] | 88 (77, 92) [94] | 0.25 | 88 (72, 92) [195] | 84 (76, 92) [341] | 0.94 |
| 1 year | 88 (72, 92) [342] | 88 (76, 92) [960] | 88 (72, 92) [339] | 92 (76, 96) [93] | 0.53 | 84 (68, 92) [188] | 84 (72, 92) [338] | 0.24 |
| 3 years | 88 (76, 92) [307] | 88 (76, 92) [888] | 88 (72, 92) [295] | 92 (76, 96) [77] | 0.56 | 84 (72, 92) [163] | 84 (72, 92) [310] | 0.83 |
| 5 years | 88 (76, 92) [278] | 88 (76, 92) [840] | 88 (76, 92) [269] | 88 (74, 96) [72] | 0.64 | 84 (68, 92) [141] | 85 (72, 92) [287] | 0.31 |
| **Energy and fatigue** | | | | | | | | |
| Baseline | 75 (60, 85) [363] | 80 (60, 87) [1018] | 70 (55, 85) [351] | 75 (55, 88) [95] | 0.001 | 75 (55, 85) [202] | 75 (55, 85) [358] | 0.20 |
| 6 months | 75 (60, 85) [363] | 75 (60, 85) [980] | 70 (50, 80) [346] | 75 (55, 85) [94] | <0.001 | 65 (50, 80) [195] | 75 (60, 80) [341] | 0.001 |
| 1 year | 75 (60, 85) [343] | 80 (60, 85) [960] | 70 (50, 80) [339] | 75 (55, 90) [93] | <0.001 | 65 (50, 76) [188] | 75 (60, 85) [338] | <0.001 |
| 3 years | 75 (60, 85) [307] | 75 (60, 85) [888] | 70 (55, 80) [295] | 75 (55, 85) [77] | 0.033 | 65 (55, 80) [163] | 70 (60, 85) [310] | 0.007 |
| 5 years | 75 (55, 85) [278] | 75 (60, 85) [840] | 70 (55, 80) [269] | 70 (60, 85) [72] | 0.003 | 65 (50, 80) [141] | 70 (55, 80) [287] | 0.18 |
| **Health-related quality of life outcomes at year 10, median (Quartiles)[b] [n]** | | | | | | | | |
| **Physical Health** | 57 (49, 60) [157] | 58 (51, 62) [620] | 56 (45, 60) [151] | 59 (54, 61) [40] | 0.002 | 53 (39, 59) [62] | 56 (48, 61) [190] | 0.048 |
| **Mental Health** | 13 (8, 21) [157] | 12 (7, 19) [620] | 13 (8, 23) [151] | 10 (7, 18) [40] | 0.039 | 17 (9, 27) [62] | 14 (8, 22) [190] | 0.15 |

Abbreviations: ADT, androgen deprivation therapy; EBRT, external beam radiotherapy.

[a] Medical Outcomes Short-Form Health Survey 36 (SF-36) domain scores (score range 0 to100), higher scores indicate better function or less disability were used through year 5.

[b] Medical Outcomes Short-Form Health Survey 12 (SF-12) domain scores (score range 0 to100), higher scores indicate better function or less disability were used at year 10.

eTable 13: Adjusted general health-related quality of life outcomes for men with favorable and unfavorable prognosis prostate cancer at year 10.[a]

| | Favorable prognosis prostate cancer (reference active surveillance) | | | | | | | | | Unfavorable prognosis prostate cancer (reference radical prostatectomy) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Radical prostatectomy | 95% CI | p value | EBRT | 95% CI | p value | Brachytherapy | 95% CI | p value | EBRT with ADT | 95% CI | p value |
| Physical Health | 0.5 | [-0.9, 1.9] | 0.51 | -0.7 | [-2.6, 1.2] | 0.49 | 0.1 | [-2.5, 2.7] | 0.94 | 0.0 | [-3.4, 3.3] | 0.99 |
| Mental Health | -1.0 | [-2.5, 0.6] | 0.22 | 0.5 | [-1.5, 2.6] | 0.61 | 0.0 | [-3.0, 2.9] | 0.99 | -1.2 | [-4.6, 2.3] | 0.51 |

Abbreviations: ADT, androgen deprivation therapy; CI, confidence interval; EBRT, external beam radiotherapy.

[a]Adjusted mean difference of Medical Outcomes Short-Form Health Survey 12 (SF-12) domain scores, higher scores indicate better function or less disability were used at year 10.

eTable 14: Baseline characteristics of men with favorable-prognosis prostate cancer enrolled in the CEASAR study by treatment received including men who were untreated on active surveillance according.

| | | Favorable risk prognosis | | | | |
|---|---|---|---|---|---|---|
| | | Untreated active surveillance | Radical prostatectomy | EBRT | Brachytherapy | p value |
| | | (n=269) | (n=1043) | (n=359) | (n=96) | |
| **Age at diagnosis, median (Quartiles) [n], year** | | 95 (80, 100) [250] | 100 (85, 100) [1006] | 90 (70, 100) [346] | 95 (80, 100) [92] | <0.001 |
| **Race/ethnicity, n (%)** | Non-Hispanic White | 200 (75%) | 768 (74%) | 260 (72%) | 81 (84%) | |
| | Non-Hispanic Black | 39 (15%) | 136 (13%) | 62 (17%) | 10 (10%) | |
| | Hispanic | 16 (6%) | 92 (9%) | 21 (6%) | 2 (2%) | |
| | Asian | 7 (3%) | 33 (3%) | 12 (3%) | 0 (0%) | 0.042 |
| | Other | 6 (2%) | 12 (1%) | 4 (1%) | 3 (3%) | |
| **Marital status, n (%)** | Not married | 55 (19%) | 177 (17%) | 95 (27%) | 22 (23%) | <0.001 |
| | Married | 228 (81%) | 871 (83%) | 262 (73%) | 74 (77%) | |
| **Education, n (%)** | Less than high school | 23 (9%) | 84 (9%) | 49 (14%) | 6 (6%) | 0.033 |
| | High school graduate | 50 (20%) | 204 (21%) | 76 (22%) | 24 (25%) | |
| | Some college | 48 (19%) | 223 (23%) | 75 (22%) | 30 (32%) | |
| | College graduate | 64 (25%) | 222 (23%) | 74 (21%) | 15 (16%) | |
| | Graduate/professional school | 70 (27%) | 247 (25%) | 72 (21%) | 20 (21%) | |
| **Comorbidity score, n (%)** | 0-2 | 64 (25%) | 350 (36%) | 66 (19%) | 32 (34%) | <0.001 |
| | 3-4 | 105 (41%) | 419 (43%) | 148 (43%) | 29 (31%) | |
| | 5 or more | 88 (34%) | 214 (22%) | 133 (38%) | 34 (36%) | |
| **Employment, n (%)** | Full time | 81 (30%) | 606 (59%) | 93 (26%) | 30 (32%) | <0.001 |
| | Part time | 29 (11%) | 71 (7%) | 28 (8%) | 8 (9%) | |
| | Retired | 146 (55%) | 307 (30%) | 208 (58%) | 54 (57%) | |
| | Unemployed | 11 (4%) | 51 (5%) | 27 (8%) | 2 (2%) | |
| **Risk Groups, n (%)** | Low risk | 216 (80%) | 600 (58%) | 169 (47%) | 72 (75%) | <0.001 |
| | Favorable Intermediate risk | 53 (20%) | 443 (42%) | 190 (53%) | 24 (25%) | |
| **Receipt of ADT in year one, n (%)** | Yes | 0 (0%) | 11 (1%) | 98 (27%) | 10 (10%) | <0.001 |
| | No | 240 (89%) | 1025 (98%) | 257 (72%) | 85 (89%) | |
| | Missing | 29 (11%) | 7 (1%) | 4 (1%) | 1 (1%) | |
| **PSA at diagnosis, median (Quartiles) [n], year** | | 5 (4, 7) [269] | 5 (4, 7) [1043] | 6 (4, 8) [359] | 5 (4, 7) [96] | <0.001 |
| **Clinical tumor stage n (%)** | T1 | 224 (85%) | 864 (83%) | 294 (82%) | 82 (85%) | 0.73 |
| | T2 | 40 (15%) | 177 (17%) | 65 (18%) | 14 (15%) | |
| **Biopsy grade group, n (%)** | 1 | 239 (89%) | 662 (63%) | 186 (52%) | 77 (80%) | <0.001 |
| | 2 | 30 (11%) | 381 (37%) | 173 (48%) | 19 (20%) | |
| **Positive cores at biopsy, median (Quartiles) [n]** | | 1 (1, 2) [204] | 3 (1, 5) [818] | 2 (1, 5) [311] | 2 (1, 3) [88] | <0.001 |
| **Study site n (%)** | Utah | 43 (16%) | 93 (9%) | 6 (2%) | 14 (15%) | <0.001 |
| | Atlanta | 38 (14%) | 130 (12%) | 31 (9%) | 22 (23%) | |
| | Los Angeles | 93 (35%) | 336 (32%) | 94 (26%) | 18 (19%) | |
| | Louisiana | 70 (26%) | 287 (28%) | 119 (33%) | 34 (35%) | |
| | New Jersey | 25 (9%) | 197 (19%) | 109 (30%) | 8 (8%) | |
| **EPIC 26 baseline scores, median (Quartiles)[b] [n]** | Sexual function | 75 (42, 85) [248] | 80 (43, 95) [994] | 60 (27, 82) [339] | 72 (38, 85) [94] | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Urinary incontinence | 100 (79, 100) [251] | 100 (79, 100) [1005] | 100 (79, 100) [341] | 100 (92, 100) [93] | 0.17 |
| | Urinary irritation | 88 (75, 94) [255] | 88 (75, 100) [1004] | 88 (75, 94) [340] | 94 (75, 100) [93] | 0.064 |
| | Bowel function | 100 (93, 100) [258] | 100 (96, 100) [1021] | 100 (92, 100) [351] | 100 (96, 100) [95] | <0.001 |
| | Hormonal function | 95 (85, 100) [257] | 95 (85, 100) [1003] | 95 (80, 100) [341] | 100 (81, 100) [93] | 0.004 |
| **SF-36 baseline scores, median (Quartiles)[c] [n]** | Physical functioning | 95 (80, 100) [250] | 100 (85, 100) [1006] | 90 (70, 100) [346] | 95 (80, 100) [92] | <0.001 |
| | Emotional well-being | 84 (72, 92) [256] | 84 (68, 92) [1018] | 84 (72, 92) [351] | 84 (75, 94) [94] | 0.36 |
| | Energy and fatigue | 75 (60, 85) [257] | 80 (60, 87) [1018] | 70 (55, 85) [351] | 75 (55, 88) [95] | <0.001 |
| | General health scale | 80 (60, 80) [269] | 80 (60, 80) [1040] | 60 (60, 80) [357] | 80 (60, 80) [96] | <0.001 |
| **Social support scale, median (Quartiles)[d] [n]** | | 95 (70, 100) [267] | 95 (70, 100) [1038] | 95 (75, 100) [358] | 95 (60, 100) [95] | 0.64 |
| **Depression scale, median (Quartiles)[e] [n]** | | 15 (4, 26) [256] | 15 (4, 30) [1014] | 11 (4, 30) [351] | 15 (4, 33) [92] | 0.81 |
| **Participatory decision-making Quartiles, median (QUARTILES)[f] [n]** | | 85 (68, 93) [255] | 86 (71, 93) [1032] | 79 (64, 93) [355] | 86 (75, 93) [93] | 0.014 |

Abbreviations: ADT, androgen deprivation therapy; CaPSURE, Cancer of the Prostate Strategic Urologic Research Endeavor; EBRT, external beam radiotherapy; PSA, prostate-specific antigen.

[a] Total Illness Burden Index score measures the severity of comorbidities (score range 0-23), higher values indicate worse comorbid illnesses.

[b] Expanded Prostate Cancer Index Composite (EPIC) scores (score range 0-100), higher scores indicate better function.

[c] Medical Outcomes Short-Form Health Survey 36 (SF-36) domain scores (score range 0 to100), higher scores indicate better function or less disability.

[d] The social support scale is a modified domain score created using five questions from the Medical Outcomes Study Social Support Scale (score range 0-100), higher scores indicating greater support.

[e] Epidemiologic Studies Depression Scale was used to derive the depression score (scores were scaled to 100), higher scores indicating more severe depressive symptoms.

[f] Seven items were scored to determine participatory decision-making **(**score range 0 to 100), higher scores indicating increased patient control, responsibility, and choice.

eTable 15: Unadjusted and adjusted functional outcomes of favorable-prognosis patients compared to untreated men on active surveillance on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | | | Adjusted analysis (ref. untreated active surveillance) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Untreated active surveillance | Radical prostatectomy | EBRT | Brachytherapy | | Radical prostatectomy | | EBRT | | | Brachytherapy | | |
| | Median score (Quartiles) [n] or frequency (%) | | | | p value | Adjusted mean difference or odds ratio | p value | Adjusted mean difference or odds ratio | p value | | Adjusted mean difference or odds ratio | | p value |
| **Sexual function** | | | | | | | | | | | | | |
| Sexual function domain score | | | | | | Mean adjusted difference [95% CI] | | | | | | | |
| Baseline | 75 (42, 85) [248] | 80 (43, 95) [994] | 60 (27, 82) [339] | 72 (38, 85) [94] | <0.001 | | | | | | | | |
| 6 months | 70 (37, 85) [245] | 25 (7, 58) [953] | 47 (10, 75) [327] | 55 (18, 80) [92] | <0.001 | -36.3[b] | [-39.6, -32.9] | <0.001 | -10.8[b] | [-14.8, -6.9] | <0.001 | -12.1[b] | [-17.2, -7.0] | <0.001 |
| 1 year | 73 (38, 85) [225] | 35 (10, 68) [955] | 43 (12, 73) [325] | 53 (17, 75) [90] | <0.001 | -32.7[b] | [-35.8, -29.7] | <0.001 | -9.9 | [-13.5, -6.3] | <0.001 | -10.6[b] | [-15.2, -6.0] | <0.001 |
| 3 years | 65 (23, 85) [195] | 38 (12, 75) [876] | 43 (10, 75) [280] | 58 (19, 80) [75] | <0.001 | -20.4[b] | [-23.8, -17.0] | <0.001 | -6.6 | [-10.6, -2.5] | 0.001 | -5.7 | [-11.3, -0.1] | 0.048 |
| 5 years | 57 (31, 85) [168] | 43 (12, 78) [825] | 33 (7, 68) [251] | 51 (22, 75) [68] | <0.001 | -13.8[b] | [-17.7, -9.9] | <0.001 | -4.9 | [-9.5, -0.3] | 0.038 | -4.3 | [-10.8, 2.3] | 0.20 |
| 10 years | 54 (17, 85) [94] | 38 (10, 73) [673] | 25 (7, 64) [160] | 38 (15, 82) [42] | 0.002 | -12.3[b] | [-18.8, -5.8] | <0.001 | -5.1 | [-13.0, 2.7] | 0.2 | -9.8 | [-20.8, 1.1] | 0.079 |
| Moderate to big problems with sexual function | | | | | | Adjusted odds ratio [95% CI] | | | | | | | |
| Baseline | 59 (24%) | 253 (25%) | 104 (31%) | 21 (23%) | 0.15 | | | | | | | | |
| 6 months | 47 (19%) | 541 (56%) | 118 (35%) | 28 (30%) | <0.001 | 7.6 | [5.3, 10.7] | <0.001 | 2.1 | [1.4, 3.1] | <0.001 | 1.9 | [1.1, 3.3] | 0.027 |
| 1 year | 45 (20%) | 480 (50%) | 115 (35%) | 26 (28%) | <0.001 | 6.2 | [4.5, 8.4] | <0.001 | 1.9 | [1.3, 2.7] | <0.001 | 1.7 | [1.1, 2.9] | 0.025 |
| 3 years | 50 (26%) | 394 (45%) | 89 (31%) | 23 (31%) | <0.001 | 3.1 | [2.3, 4.2] | <0.001 | 1.4 | [1.0, 2.0] | 0.063 | 1.3 | [0.8, 2.3] | 0.27 |
| 5 years | 38 (22%) | 326 (39%) | 94 (37%) | 18 (26%) | <0.001 | 2.2 | [1.6, 3.1] | <0.001 | 1.3 | [0.9, 2.0] | 0.197 | 1.2 | [0.6, 2.2] | 0.60 |
| 10 years | 18 (19%) | 230 (34%) | 55 (34%) | 8 (19%) | 0.004 | 2.4 | [1.2, 4.9] | 0.013 | 1.9 | [0.8, 4.2] | 0.128 | 1.2 | [0.4, 4.1] | 0.76 |
| Erection insufficient for penetration | | | | | | Adjusted odds ratio [95% CI] | | | | | | | |
| Baseline | 102 (41%) | 379 (38%) | 186 (54%) | 44 (47%) | <0.001 | | | | | | | | |
| 6 months | 105 (42%) | 747 (78%) | 222 (66%) | 54 (57%) | <0.001 | 13.6 | [9.6, 19.2] | <0.001 | 2.5 | [1.8, 3.7] | <0.001 | 2.2 | [1.3, 3.7] | 0.003 |
| 1 year | 96 (42%) | 671 (71%) | 218 (66%) | 50 (56%) | <0.001 | 10.4 | [7.6, 14.2] | <0.001 | 2.4 | [1.7, 3.3] | <0.001 | 2.0 | [1.3, 3.2] | 0.003 |
| 3 years | 93 (47%) | 589 (67%) | 189 (66%) | 41 (55%) | <0.001 | 4.1 | [3.0, 5.7] | <0.001 | 1.8 | [1.2, 2.6] | 0.002 | 1.5 | [0.9, 2.5] | 0.14 |
| 5 years | 94 (55%) | 536 (65%) | 188 (73%) | 44 (63%) | 0.002 | 2.5 | [1.8, 3.6] | <0.001 | 1.5 | [1.0, 2.3] | 0.054 | 1.4 | [0.8, 2.5] | 0.29 |
| 10 years | 51 (54%) | 472 (69%) | 118 (74%) | 29 (69%) | 0.008 | 2.3 | [1.3, 4.1] | 0.003 | 1.3 | [0.6, 2.5] | 0.523 | 2.2 | [0.9, 5.7] | 0.1 |
| **Urinary function** | | | | | | | | | | | | | |
| Urinary incontinence domain score | | | | | | Mean adjusted difference [95% CI] | | | | | | | |
| Baseline | 100 (79, 100) [251] | 100 (79, 100) [1005] | 100 (79, 100) [341] | 100 (92, 100) [93] | 0.17 | | | | | | | | |
| 6 months | 100 (79, 100) [255] | 67 (46, 94) [972] | 100 (79, 100) [346] | 93 (73, 100) [92] | <0.001 | -24.3[b] | [-27.0, -21.5] | <0.001 | 1.1 | [-1.7, 3.9] | 0.437 | -6.6[b] | [-10.7, -2.5] | 0.002 |
| 1 year | 100 (81, 100) [235] | 79 (52, 100) [926] | 100 (79, 100) [327] | 94 (79, 100) [88] | <0.001 | -22.6[b] | [-25.1, -20.1] | <0.001 | 1.2 | [-1.2, 3.7] | 0.326 | -5.9 | [-9.6, -2.2] | 0.002 |
| 3 years | 100 (79, 100) [205] | 79 (54, 100) [875] | 100 (79, 100) [289] | 100 (79, 100) [77] | <0.001 | -17.1[b] | [-19.7, -14.5] | <0.001 | 1.9 | [-0.7, 4.6] | 0.155 | -3.4 | [-7.6, 0.9] | 0.12 |
| 5 years | 94 (76, 100) [182] | 77 (54, 100) [829] | 100 (79, 100) [262] | 97 (79, 100) [72] | <0.001 | -14.7[b] | [-17.5, -11.9] | <0.001 | 2.8 | [-0.2, 5.8] | 0.064 | -1.9 | [-6.4, 2.6] | 0.41 |
| 10 years | 92 (75, 100) [95] | 79 (52, 100) [681] | 100 (79, 100) [166] | 100 (84, 100) [44] | <0.001 | -16.8[b] | [-21.1, -12.5] | <0.001 | 5.7 | [0.9, 10.4] | 0.02 | -1.1 | [-7.1, 4.9] | 0.72 |
| Urinary irritation domain score | | | | | | Mean adjusted difference [95% CI] | | | | | | | |
| Baseline | 88 (75, 94) [255] | 88 (75, 100) [1004] | 88 (75, 94) [340] | 94 (75, 100) [93] | 0.064 | | | | | | | | |
| 6 months | 88 (81, 100) [249] | 94 (81, 100) [960] | 88 (81, 97) [343] | 81 (62, 88) [92] | <0.001 | 2.1 | [0.4, 3.9] | 0.015 | 0.0 | [-2.1, 2.1] | 0.996 | -10.0[b] | [-14, -6.1] | <0.001 |
| 1 year | 88 (81, 100) [237] | 94 (88, 100) [952] | 88 (81, 94) [336] | 88 (75, 94) [89] | <0.001 | 2.5 | [1.0, 4.1] | 0.001 | 0.4 | [-1.5, 2.3] | 0.667 | -8.0[b] | [-11.3, -4.7] | <0.001 |
| 3 years | 88 (81, 100) [206] | 94 (88, 100) [875] | 88 (81, 100) [287] | 94 (88, 94) [75] | <0.001 | 4.0 | [2.4, 5.5] | <0.001 | 2.0 | [0.1, 3.9] | 0.037 | -0.9 | [-3.7, 1.9] | 0.53 |
| 5 years | 88 (75, 100) [180] | 94 (88, 100) [824] | 94 (81, 100) [262] | 94 (81, 100) [71] | <0.001 | 4.9 | [3.1, 6.6] | <0.001 | 3.4 | [1.3, 5.5] | 0.001 | 2.8 | [-0.3, 5.9] | 0.08 |
| 10 years | 88 (75, 94) [92] | 94 (88, 100) [665] | 94 (86, 100) [164] | 94 (88, 100) [41] | <0.001 | 5.7[b] | [2.6, 8.8] | <0.001 | 6.5[b] | [2.9, 10.2] | <0.001 | 2.9 | [-1.9, 7.7] | 0.24 |
| Moderate to big problem with urinary function | | | | | | Adjusted odds ratio [95% CI] | | | | | | | |
| Baseline | 32 (13%) | 137 (14%) | 45 (13%) | 11 (12%) | 0.93 | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 months | 26 (10%) | 159 (16%) | 37 (11%) | 20 (22%) | 0.003 | 2.0 | [1.3, 3.0] | 0.001 | 0.7 | [0.4, 1.2] | 0.266 | 1.8 | [0.9, 3.4] | 0.086 |
| 1 year | 27 (11%) | 111 (12%) | 26 (8%) | 8 (9%) | 0.24 | 1.9 | [1.3, 2.9] | <0.001 | 0.8 | [0.5, 1.3] | 0.35 | 1.6 | [0.9, 2.9] | 0.085 |
| 3 years | 18 (9%) | 98 (11%) | 27 (9%) | 7 (9%) | 0.65 | 1.8 | [1.2, 2.9] | 0.009 | 1.0 | [0.6, 1.7] | 0.951 | 1.2 | [0.6, 2.5] | 0.59 |
| 5 years | 13 (7%) | 98 (12%) | 23 (9%) | 7 (10%) | 0.21 | 1.8 | [1.1, 2.9] | 0.019 | 0.9 | [0.5, 1.7] | 0.775 | 1.0 | [0.4, 2.2] | 0.93 |
| 10 years | 9 (9%) | 87 (13%) | 8 (5%) | 2 (4%) | 0.011 | 2.0 | [0.9, 4.5] | 0.102 | 0.4 | [0.1, 1.2] | 0.09 | 0.6 | [0.1, 3.0] | 0.54 |
| Urinary leakage | | | | | | | | | | Adjusted odds ratio [95% CI] | | | | |
| Baseline | 13 (5%) | 65 (6%) | 16 (5%) | 3 (3%) | 0.40 | | | | | | | | | |
| 6 months | 10 (4%) | 178 (18%) | 14 (4%) | 10 (11%) | <0.001 | 6.3 | [3.3, 12.1] | <0.001 | 0.7 | [0.3, 1.7] | 0.438 | 2.1 | [0.8, 5.2] | 0.13 |
| 1 year | 14 (6%) | 133 (14%) | 14 (4%) | 2 (2%) | <0.001 | 5.9 | [3.3, 10.3] | <0.001 | 0.8 | [0.4, 1.6] | 0.495 | 1.8 | [0.8, 3.9] | 0.18 |
| 3 years | 9 (4%) | 120 (14%) | 11 (4%) | 2 (3%) | <0.001 | 4.4 | [2.5, 7.9] | <0.001 | 1.0 | [0.5, 2.0] | 0.928 | 0.9 | [0.3, 3.3] | 0.93 |
| 5 years | 8 (4%) | 112 (13%) | 16 (6%) | 3 (4%) | <0.001 | 3.8 | [2.1, 7.1] | <0.001 | 1.0 | [0.4, 2.1] | 0.907 | 0.5 | [0.1, 2.3] | 0.40 |
| 10 years | 5 (5%) | 96 (14%) | 6 (4%) | 0 (0%) | <0.001 | 3.7 | [1.2, 11.1] | 0.021 | 0.5 | [0.1, 2.1] | 0.335 | 0.1 | [0.0, 0.8] | 0.022 |
| Burning on urination | | | | | | | | | | Adjusted odds ratio [95% CI] | | | | |
| Baseline | 9 (4%) | 37 (4%) | 17 (5%) | 3 (3%) | 0.72 | | | | | | | | | |
| 6 months | 4 (2%) | 13 (1%) | 12 (3%) | 8 (9%) | <0.001 | 1.0 | [0.3, 3.3] | 0.988 | 2.2 | [0.6, 7.5] | 0.223 | 11.2 | [3.2, 39.2] | <0.001 |
| 1 year | 3 (1%) | 10 (1%) | 10 (3%) | 10 (11%) | <0.001 | 0.9 | [0.3, 2.6] | 0.908 | 1.9 | [0.7, 5.5] | 0.217 | 9.1 | [3.3, 25.2] | <0.001 |
| 3 years | 2 (1%) | 11 (1%) | 7 (2%) | 1 (1%) | 0.49 | 0.7 | [0.2, 3.0] | 0.662 | 1.3 | [0.3, 5.6] | 0.722 | 4.4 | [1.0, 18.9] | 0.05 |
| 5 years | 2 (1%) | 3 (0%) | 2 (1%) | 3 (4%) | 0.004 | 0.6 | [0.1, 3.1] | 0.531 | 1.0 | [0.2, 5.4] | 0.978 | 3.1 | [0.5, 18.7] | 0.22 |
| 10 years | 1 (1%) | 4 (1%) | 2 (1%) | 1 (2%) | 0.58 | 0.4 | [0.0, 5.0] | 0.479 | 0.8 | [0.1, 12.3] | 0.898 | 3.6 | [0.2, 60.2] | 0.37 |
| Frequent urination | | | | | | | | | | Adjusted odds ratio [95% CI] | | | | |
| Baseline | 52 (20%) | 207 (20%) | 75 (21%) | 13 (14%) | 0.47 | | | | | | | | | |
| 6 months | 46 (18%) | 165 (17%) | 58 (17%) | 28 (30%) | 0.015 | 1.0 | [0.7, 1.4] | 0.897 | 0.6 | [0.4, 1.0] | 0.041 | 1.9 | [1.0, 3.5] | 0.038 |
| 1 year | 44 (18%) | 130 (13%) | 43 (13%) | 17 (19%) | 0.12 | 0.9 | [0.7, 1.3] | 0.665 | 0.6 | [0.4, 0.9] | 0.017 | 1.7 | [1.0, 2.8] | 0.056 |
| 3 years | 35 (17%) | 108 (12%) | 39 (13%) | 9 (12%) | 0.37 | 0.8 | [0.6, 1.1] | 0.222 | 0.6 | [0.4, 0.9] | 0.02 | 1.0 | [0.5, 2.0] | 0.89 |
| 5 years | 28 (15%) | 117 (14%) | 34 (13%) | 11 (15%) | 0.86 | 0.8 | [0.5, 1.2] | 0.253 | 0.6 | [0.3, 0.9] | 0.025 | 0.9 | [0.4, 1.9] | 0.76 |
| 10 years | 14 (14%) | 96 (14%) | 15 (9%) | 5 (12%) | 0.36 | 1.1 | [0.5, 2.5] | 0.724 | 0.5 | [0.2, 1.4] | 0.179 | 1.2 | [0.3, 4.9] | 0.76 |
| **Bowel function** | | | | | | | | | | | | | | |
| Bowel function domain score | | | | | | | | | | Mean adjusted difference [95% CI] | | | | |
| Baseline | 100 (93, 100) [258] | 100 (96, 100) [1021] | 100 (92, 100) [351] | 100 (96, 100) [95] | <0.001 | | | | | | | | | |
| 6 months | 100 (95, 100) [257] | 100 (96, 100) [975] | 96 (88, 100) [345] | 96 (88, 100) [92] | <0.001 | -0.1 | [-1.5, 1.2] | 0.848 | -3.7 | [-5.6, -1.8] | <0.001 | -5.3[b] | [-8.3, -2.4] | <0.001 |
| 1 year | 100 (92, 100) [244] | 100 (96, 100) [964] | 96 (83, 100) [339] | 96 (83, 100) [91] | <0.001 | -0.1 | [-1.2, 1.1] | 0.904 | -3.5 | [-5.2, -1.8] | <0.001 | -4.9[b] | [-7.5, -2.3] | <0.001 |
| 3 years | 100 (92, 100) [211] | 100 (96, 100) [887] | 96 (88, 100) [294] | 100 (88, 100) [78] | <0.001 | 0.2 | [-1.1, 1.4] | 0.803 | -2.9 | [-4.7, -1.1] | 0.001 | -3.5 | [-5.8, -1.1] | 0.004 |
| 5 years | 100 (92, 100) [181] | 100 (96, 100) [837] | 100 (88, 100) [266] | 100 (88, 100) [72] | <0.001 | 0.3 | [-1.2, 1.9] | 0.654 | -2.5 | [-4.5, -0.5] | 0.015 | -2.6 | [-5.1, -0.1] | 0.045 |
| 10 years | 100 (92, 100) [98] | 100 (92, 100) [688] | 100 (88, 100) [168] | 100 (88, 100) [45] | 0.004 | 0.7 | [-2.2, 3.5] | 0.649 | -2.0 | [-5.7, 1.7] | 0.28 | -1.8 | [-5.6, 2.0] | 0.35 |
| Moderate to big problem with bowel function | | | | | | | | | | Adjusted odds ratio [95% CI] | | | | |
| Baseline | 14 (5%) | 37 (4%) | 9 (3%) | 4 (4%) | 0.32 | | | | | | | | | |
| 6 months | 11 (4%) | 34 (3%) | 25 (7%) | 7 (8%) | 0.017 | 1.4 | [0.7, 2.8] | 0.306 | 2.3 | [1.1, 4.5] | 0.02 | 2.6 | [1.0, 6.6] | 0.042 |
| 1 year | 12 (5%) | 31 (3%) | 23 (7%) | 5 (6%) | 0.035 | 1.3 | [0.7, 2.3] | 0.441 | 1.9 | [1.0, 3.5] | 0.037 | 2.2 | [1.0, 4.9] | 0.048 |
| 3 years | 10 (5%) | 23 (3%) | 14 (5%) | 3 (4%) | 0.20 | 0.8 | [0.4, 1.4] | 0.448 | 1.0 | [0.5, 2.1] | 0.899 | 1.2 | [0.5, 3.3] | 0.69 |
| 5 years | 10 (6%) | 22 (3%) | 11 (4%) | 4 (6%) | 0.15 | 0.6 | [0.3, 1.1] | 0.106 | 0.8 | [0.4, 1.8] | 0.609 | 0.8 | [0.2, 2.7] | 0.73 |
| 10 years | 8 (8%) | 19 (3%) | 14 (8%) | 1 (2%) | 0.002 | 0.4 | [0.1, 1.2] | 0.106 | 1.1 | [0.4, 3.6] | 0.843 | 0.5 | [0.0, 4.9] | 0.53 |
| Bloody stools | | | | | | | | | | | | | | |
| Baseline | 4 (2%) | 5 (0%) | 3 (1%) | 0 (0%) | 0.25 | | | | | | | | | |
| 6 months | 2 (1%) | 8 (1%) | 3 (1%) | 0 (0%) | 0.85 | | | | | | | | | |
| 1 year | 4 (2%) | 9 (1%) | 5 (1%) | 1 (1%) | 0.75 | Adjusted analysis not done due to small number of events | | | | | | | | |
| 3 years | 0 (0%) | 3 (0%) | 7 (2%) | 1 (1%) | 0.002 | | | | | | | | | |
| 5 years | 0 (0%) | 1 (0%) | 2 (1%) | 0 (0%) | 0.23 | | | | | | | | | |
| 10 years | 0 (0%) | 1 (0%) | 3 (2%) | 0 (0%) | 0.021 | | | | | | | | | |
| Bowel urgency | | | | | | | | | | Adjusted odds ratio [95% CI] | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Baseline | 13 (5%) | 46 (5%) | 10 (3%) | 5 (5%) | 0.48 | | | | | | | | | |
| 6 months | 15 (6%) | 26 (3%) | 22 (6%) | 9 (10%) | <0.001 | 0.8 | [0.4, 1.5] | 0.433 | 1.5 | [0.7, 3.2] | 0.261 | 2.4 | [0.9, 6.3] | 0.065 |
| 1 year | 11 (5%) | 30 (3%) | 23 (7%) | 9 (10%) | 0.002 | 0.7 | [0.4, 1.3] | 0.26 | 1.5 | [0.8, 2.9] | 0.193 | 2.3 | [1.0, 5.0] | 0.047 |
| 3 years | 13 (6%) | 24 (3%) | 23 (8%) | 4 (5%) | 0.001 | 0.6 | [0.3, 1.0] | 0.056 | 1.5 | [0.8, 2.9] | 0.196 | 1.6 | [0.7, 3.7] | 0.26 |
| 5 years | 10 (5%) | 23 (3%) | 18 (7%) | 6 (8%) | 0.005 | 0.5 | [0.3, 1.0] | 0.044 | 1.4 | [0.7, 2.8] | 0.347 | 1.1 | [0.4, 2.7] | 0.89 |
| 10 years | 8 (8%) | 33 (5%) | 15 (9%) | 1 (2%) | 0.096 | 0.6 | [0.2, 1.7] | 0.335 | 0.9 | [0.3, 2.8] | 0.871 | 0.3 | [0.1, 1.6] | 0.16 |
| **Hormonal function** | | | | | | | | | | | | | | |
| Hormonal domain score | | | | | | Mean adjusted difference [95% CI] | | | | | | | | |
| Baseline | 95 (85, 100) [257] | 95 (85, 100) [1003] | 95 (80, 100) [341] | 100 (81, 100) [93] | 0.004 | | | | | | | | | |
| 6 months | 95 (85, 100) [252] | 95 (85, 100) [964] | 90 (75, 100) [333] | 95 (80, 100) [95] | <0.001 | -1.2 | [-2.7, 0.4] | 0.135 | -3.2 | [-5, -1.3] | <0.001 | -1.5 | [-3.8, 0.9] | 0.22 |
| 1 year | 95 (85, 100) [241] | 95 (85, 100) [956] | 90 (78, 100) [327] | 95 (80, 100) [91] | <0.001 | -1.1 | [-2.4, 0.3] | 0.122 | -2.5 | [-4.2, -0.9] | 0.002 | -1.0 | [-3.1, 1.0] | 0.31 |
| 3 years | 95 (88, 100) [208] | 95 (85, 100) [880] | 95 (85, 100) [285] | 95 (90, 100) [77] | 0.074 | -0.7 | [-2.2, 0.7] | 0.331 | -0.4 | [-2.1, 1.3] | 0.63 | 0.3 | [-1.9, 2.4] | 0.81 |
| 5 years | 95 (85, 100) [180] | 95 (85, 100) [832] | 95 (80, 100) [257] | 100 (85, 100) [69] | 0.15 | -0.6 | [-2.3, 1.1] | 0.481 | 0.6 | [-1.4, 2.5] | 0.577 | 0.3 | [-2.2, 2.7] | 0.83 |
| 10 years | 100 (90, 100) [98] | 100 (90, 100) [679] | 95 (89, 100) [163] | 100 (90, 100) [45] | 0.18 | -0.8 | [-3.0, 1.4] | 0.463 | 0.0 | [-2.9, 3.0] | 0.986 | -3.1 | [-7.1, 0.9] | 0.13 |

Abbreviations: CI, confidence interval; EBRT, external beam radiotherapy

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the induvial items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to untreated active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance. A minimally important difference in domain scores is 10-12 points for the sexual function, 6-9 points for the urinary incontinence; 5-7 points for the urinary irritation, 4-6 points for the bowel function, and 4-6 points for the hormonal function.

eTable 16: Unadjusted and adjusted sexual function outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | Adjusted analysis | | |
|---|---|---|---|---|---|---|
| | **Radical prostatectomy** | **EBRT** | | **EBRT with ADT vs. radical prostatectomy** | | |
| | Median score (Quartiles) or frequency (%) | | p value | Effect | 95% CI | p value |
| **Sexual function domain score** | Median (Quartiles) [n] | | | | Adjusted mean difference | |
| Baseline | 65 (32, 85) [344] | 48 (12, 80) [189] | <0.001 | | | |
| 6 months | 15 (0, 38) [334] | 5 (0, 45) [180] | 0.021 | 5.1 | [0.0, 10.2] | 0.052 |
| 1 year | 17 (0, 47) [332] | 17 (0, 53) [182] | 0.54 | 5.3 | [0.4, 10.3] | 0.034 |
| 3 years | 20 (0, 53) [298] | 18 (0, 61) [156] | 0.79 | 6.1 | [0.4, 11.7] | 0.035 |
| 5 years | 12 (0, 55) [280] | 27 (0, 65) [128] | 0.28 | 5.6 | [-0.6, 11.8] | 0.074 |
| 10 years | 17 (0, 43) [206] | 13 (0, 51) [66] | 1.00 | 1.4 | [-8.3, 11.1] | 0.78 |
| **Sexual function bother (individual item)** | Frequency (%)] | | | | Adjusted odds ratio | |
| Baseline | 113 (33%) | 67 (34%) | 0.73 | | | |
| 6 months | 189 (56%) | 82 (44%) | 0.007 | 0.5 | [0.4, 0.8] | 0.007 |
| 1 year | 185 (56%) | 84 (47%) | 0.054 | 0.6 | [0.4, 0.9] | 0.008 |
| 3 years | 145 (48%) | 63 (40%) | 0.14 | 0.7 | [0.5, 1.1] | 0.11 |
| 5 years | 139 (49%) | 58 (44%) | 0.33 | 0.8 | [0.5, 1.3] | 0.39 |
| 10 years | 67 (32%) | 22 (32%) | 0.94 | 1.0 | [0.5, 2.3] | 0.91 |
| **Erection insufficient for intercourse (individual item)** | Frequency (%)] | | | | Adjusted odds ratio | |
| Baseline | 164 (47%) | 112 (58%) | 0.019 | | | |
| 6 months | 290 (87%) | 147 (80%) | 0.046 | 0.4 | [0.3, 0.8] | 0.004 |
| 1 year | 276 (83%) | 147 (80%) | 0.43 | 0.5 | [0.3, 0.8] | 0.005 |
| 3 years | 239 (79%) | 122 (78%) | 0.87 | 0.6 | [0.4, 1.1] | 0.095 |
| 5 years | 230 (81%) | 97 (75%) | 0.12 | 0.7 | [0.4, 1.3] | 0.22 |
| 10 years | 178 (86%) | 56 (81%) | 0.38 | 0.6 | [0.2, 1.5] | 0.25 |

Abbreviations: ADT, androgen deprivation therapy; EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (10-12 points) for the sexual function.

eTable 17: Unadjusted and adjusted urinary incontinence function outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | Adjusted analysis | | |
|---|---|---|---|---|---|---|
| | **Radical prostatectomy** | **EBRT** | | **EBRT with ADT vs. radical prostatectomy** | | |
| | Median score (Quartiles) or frequency (%) | | p value | Effect | 95% CI | p value |
| **Urinary incontinence function domain score** | Median (Quartiles) [n] | | | Adjusted mean difference | | |
| Baseline | 100 (79, 100) [347] | 100 (75, 100) [200] | 0.53 | | | |
| 6 months | 60 (40, 85) [341] | 88 (67, 100) [195] | <0.001 | 27.2[b] | [22.3, 32.2] | <0.001 |
| 1 year | 67 (46, 95) [328] | 92 (73, 100) [176] | <0.001 | 26.4[b] | [21.7, 31.2] | <0.001 |
| 3 years | 67 (46, 89) [304] | 92 (74, 100) [159] | <0.001 | 24.0[b] | [18.8, 29.1] | <0.001 |
| 5 years | 67 (46, 89) [280] | 92 (73, 100) [137] | <0.001 | 23.3[b] | [17.9, 28.8] | <0.001 |
| 10 years | 67 (40, 85) [207] | 92 (78, 100) [72] | <0.001 | 26.6[b] | [18.2, 35.0] | <0.001 |
| **Urinary leakage (individual item)** | Frequency (%)] | | | Adjusted odds ratio | | |
| Baseline | 35 (10%) | 7 (3%) | 0.006 | | | |
| 6 months | 75 (22%) | 16 (8%) | <0.001 | 0.1 | [0.1, 0.3] | <0.001 |
| 1 year | 68 (20%) | 15 (8%) | <0.001 | 0.1 | [0.1, 0.3] | <0.001 |
| 3 years | 54 (18%) | 11 (7%) | 0.001 | 0.2 | [0.1, 0.3] | <0.001 |
| 5 years | 47 (16%) | 10 (7%) | 0.008 | 0.2 | [0.1, 0.4] | <0.001 |
| 10 years | 51 (25%) | 8 (11%) | 0.014 | 0.2 | [0.1, 0.7] | 0.012 |

Abbreviations: ADT, Androgen deprivation therapy; EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (6-9 points) for the urinary incontinence.

eTable 18: Unadjusted and adjusted urinary irritation function outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | Adjusted analysis | | |
|---|---|---|---|---|---|---|
| | **Radical prostatectomy** | **EBRT** | | **EBRT with ADT vs. radical prostatectomy** | | |
| | Median score (Quartiles) or frequency (%) | | p value | Effect | 95% CI | p value |
| **Urinary irritation domain score** | Median (Quartiles) [n] | | | Adjusted mean difference | | |
| Baseline | 88 (69, 100) [345] | 88 (75, 94) [199] | 0.77 | | | |
| 6 months | 88 (81, 100) [338] | 88 (75, 94) [193] | <0.001 | -3.2 | [-5.7, -0.6] | 0.016 |
| 1 year | 94 (81, 100) [332] | 88 (75, 94) [183] | 0.007 | -2.4 | [-4.8, 0.0] | 0.052 |
| 3 years | 94 (81, 100) [307] | 88 (81, 100) [159] | 0.045 | 0.1 | [-2.7, 2.8] | 0.96 |
| 5 years | 88 (81, 100) [284] | 88 (81, 94) [138] | 0.11 | 0.5 | [-2.5, 3.5] | 0.76 |
| 10 years | 88 (75, 100) [205] | 88 (69, 100) [72] | 0.25 | -3.7 | [-8.5, 1.0] | 0.13 |
| **Urinary function bother (individual item).** | Frequency (%) | | | Adjusted odds ratio | | |
| Baseline | 64 (18%) | 23 (12%) | 0.038 | | | |
| 6 months | 72 (21%) | 34 (17%) | 0.27 | 0.4 | [0.2, 0.7] | 0.002 |
| 1 year | 55 (17%) | 24 (13%) | 0.27 | 0.4 | [0.2, 0.7] | <0.001 |
| 3 years | 53 (17%) | 18 (11%) | 0.076 | 0.3 | [0.2, 0.6] | <0.001 |
| 5 years | 52 (18%) | 18 (13%) | 0.17 | 0.3 | [0.2, 0.7] | 0.001 |
| 10 years | 44 (21%) | 16 (23%) | 0.81 | 0.8 | [0.4, 1.9] | 0.67 |
| **Burning on urination (individual item)** | Frequency (%) | | | Adjusted odds ratio | | |
| Baseline | 12 (3%) | 6 (3%) | 0.80 | | | |
| 6 months | 7 (2%) | 16 (8%) | <0.001 | 3.6 | [1.5, 8.6] | 0.004 |
| 1 year | 7 (2%) | 6 (3%) | 0.43 | 2.0 | [0.9, 4.8] | 0.11 |
| 3 years | 10 (3%) | 3 (2%) | 0.38 | 0.3 | [0.1, 1.4] | 0.13 |
| 5 years | 10 (3%) | 2 (1%) | 0.22 | 0.3 | [0.1, 1.3] | 0.11 |
| 10 years | 2 (1%) | 4 (5%) | 0.022 | 9.1 | [1.2, 71.9] | 0.036 |
| **Frequent urination (individual item)** | Frequency (%) | | | Adjusted odds ratio | | |
| Baseline | 89 (25%) | 48 (24%) | 0.75 | | | |
| 6 months | 79 (23%) | 43 (22%) | 0.77 | 0.8 | [0.5, 1.3] | 0.36 |
| 1 year | 71 (21%) | 35 (19%) | 0.52 | 0.7 | [0.5, 1.2] | 0.18 |
| 3 years | 49 (16%) | 26 (16%) | 0.99 | 0.6 | [0.3, 1.0] | 0.05 |
| 5 years | 54 (19%) | 20 (14%) | 0.21 | 0.6 | [0.3, 1.1] | 0.13 |
| 10 years | 48 (23%) | 24 (33%) | 0.090 | 1.7 | [0.8, 3.6] | 0.21 |

Abbreviations: ADT, Androgen deprivation therapy; EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (5-7 points) for the urinary irritation and obstructive function.

eTable 19: Unadjusted and adjusted bowel function outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | Unadjusted analysis | | | Adjusted analysis | | |
|---|---|---|---|---|---|---|
| | Radical prostatectomy | EBRT | | EBRT with ADT vs. radical prostatectomy | | |
| | Median score (Quartiles) or frequency (%) | | p value | Effect | 95% CI | p value |
| **Bowel function domain score** | | | | | | |
| Baseline | 100 (88, 100) [354] | 100 (92, 100) [201] | 0.70 | | | |
| 6 months | 100 (92, 100) [342] | 92 (79, 100) [196] | <0.001 | -6.9[b] | [-9.6, -4.2] | <0.001 |
| 1 year | 100 (92, 100) [336] | 92 (79, 100) [189] | <0.001 | -6.1[b] | [-8.6, -3.7] | <0.001 |
| 3 years | 100 (92, 100) [309] | 96 (83, 100) [163] | <0.001 | -3.6 | [-6.2, -1.1] | 0.005 |
| 5 years | 100 (88, 100) [285] | 94 (83, 100) [140] | 0.007 | -2.8 | [-5.5, 0.0] | 0.049 |
| 10 years | 100 (92, 100) [210] | 96 (82, 100) [72] | 0.045 | -4.9[b] | [-9.2, -0.7] | 0.022 |
| **Bowel function bother (individual item)** | Frequency (%) | | | | | |
| Baseline | 16 (5%) | 11 (5%) | 0.65 | | | |
| 6 months | 21 (6%) | 20 (10%) | 0.086 | 2.1 | [0.9, 4.8] | 0.068 |
| 1 year | 15 (4%) | 19 (10%) | 0.013 | 1.9 | [0.9, 4.2] | 0.089 |
| 3 years | 13 (4%) | 13 (8%) | 0.088 | 1.5 | [0.6, 3.5] | 0.40 |
| 5 years | 18 (6%) | 9 (6%) | 0.94 | 1.4 | [0.6, 3.4] | 0.49 |
| 10 years | 6 (3%) | 5 (7%) | 0.13 | 2.1 | [0.5, 9.1] | 0.31 |
| **Bloody stools (individual item)** | Frequency (%) | | | | | |
| Baseline | 0 (0%) | 1 (0%) | 0.18 | | | |
| 6 months | 2 (1%) | 4 (2%) | 0.12 | | | |
| 1 year | 3 (1%) | 6 (3%) | 0.053 | | | |
| 3 years | 6 (2%) | 1 (1%) | 0.25 | Adjusted analysis not done due to small number of events | | |
| 5 years | 3 (1%) | 2 (1%) | 0.73 | | | |
| 10 years | 1 (0%) | 0 (0%) | 0.56 | | | |
| **Bowel urgency (individual item)** | Frequency (%) | | | | | |
| Baseline | 23 (6%) | 10 (5%) | 0.46 | | | |
| 6 months | 19 (6%) | 22 (11%) | 0.016 | 2.5 | [1.3, 5.1] | 0.009 |
| 1 year | 20 (6%) | 17 (9%) | 0.20 | 2.4 | [1.3, 4.5] | 0.008 |
| 3 years | 11 (4%) | 10 (6%) | 0.21 | 2.0 | [0.9, 4.3] | 0.08 |
| 5 years | 18 (6%) | 13 (9%) | 0.26 | 2.0 | [0.8, 4.7] | 0.12 |
| 10 years | 11 (5%) | 8 (11%) | 0.092 | 3.0 | [0.9, 10.0] | 0.067 |
| **Increased frequency of bowel movements (individual item)** | Frequency (%) | | | | | |
| Baseline | 14 (4%) | 8 (4%) | 0.979 | | | |
| 6 months | 14 (4%) | 20 (10%) | 0.005 | | | |
| 1 year | 14 (4%) | 15 (8%) | 0.073 | | | |
| 3 years | 12 (4%) | 8 (5%) | 0.580 | | | |
| 5 years | 15 (5%) | 10 (7%) | 0.434 | | | |
| 10 years | 5 (2%) | 5 (7%) | 0.071 | | | |
| **Fecal incontinence (individual item)** | Frequency (%) | | | | | |
| Baseline | 1 (0%) | 2 (1%) | 0.271 | | | |
| 6 months | 1 (0%) | 11 (6%) | <0.001 | | | |
| 1 year | 2 (1%) | 8 (4%) | 0.004 | | | |
| 3 years | 7 (2%) | 5 (3%) | 0.598 | | | |
| 5 years | 6 (2%) | 5 (4%) | 0.368 | | | |
| 10 years | 1 (1%) | 2 (3%) | 0.103 | | | |
| **Abdominal, pelvic, or rectal pain (individual item)** | Frequency (%)] | | | | | |

| | | | | |
|---|---|---|---|---|
| Baseline | 24 (7%) | 24 (3%) | 0.030 | |
| 6 months | 10 (3%) | 10 (2%) | 0.313 | |
| 1 year | 14 (4%) | 14 (3%) | 0.388 | |
| 3 years | 8 (3%) | 8 (1%) | 0.136 | |
| 5 years | 7 (3%) | 7 (1%) | 0.489 | |
| 10 years | 2 (1%) | 2 (1%) | 0.750 | |

Abbreviations: ADT, Androgen deprivation therapy; EBRT, external beam radiotherapy.

[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.

[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (4-6 points) for the bowel function.

eTable 20: Unadjusted and adjusted hormonal function outcomes of men with unfavorable-prognosis prostate cancer on the Expanded Prostate Cancer Index Composite (EPIC) domain scores and selected individual item responses by treatment and time point.[a]

| | **Unadjusted analysis** | | | Adjusted analysis | | |
|---|---|---|---|---|---|---|
| | **Radical prostatectomy** | **EBRT** | | **EBRT with ADT vs. radical prostatectomy** | | |
| | Median score (Quartiles) or frequency (%) | | p value | Effect | 95% CI | p value |
| **Hormonal function domain score** | Median (Quartiles) [n] | | | Adjusted mean difference | | |
| Baseline | 90 (80, 100) [350] | 90 (80, 95) [192] | 0.011 | | | |
| 6 months | 94 (80, 100) [335] | 81 (70, 95) [191] | <0.001 | -8.8[b] | [-11.7, -5.9] | <0.001 |
| 1 year | 90 (80, 100) [330] | 85 (70, 95) [186] | <0.001 | -7.5[b] | [-10.2, -4.9] | <0.001 |
| 3 years | 95 (80, 100) [303] | 90 (75, 95) [159] | 0.016 | -3.3 | [-6.1, -0.4] | 0.026 |
| 5 years | 90 (80, 100) [280] | 90 (80, 100) [137] | 0.26 | -1.7 | [-4.8, 1.3] | 0.27 |
| 10 years | 95 (85, 100) [210] | 90 (80, 100) [72] | 0.11 | -4.9[b] | [-9.5, -0.3] | 0.036 |
| **Hot flashes (individual item)** | Frequency (%) | | | | | |
| Baseline | 14 (4%) | 16 (8%) | 0.038 | | | |
| 6 months | 19 (6%) | 56 (29%) | <0.001 | | | |
| 1 year | 28 (9%) | 34 (18%) | 0.001 | | | |
| 3 years | 19 (6%) | 10 (6%) | 0.994 | | | |
| 5 years | 16 (6%) | 8 (6%) | 0.966 | | | |
| 10 years | 11 (5%) | 2 (3%) | 0.405 | | | |
| **Breast tenderness and enlargement (individual item)** | Frequency (%) | | | | | |
| Baseline | 3 (1%) | 0 (0%) | 0.202 | | | |
| 6 months | 1 (0%) | 1 (1%) | 0.689 | | | |
| 1 year | 2 (1%) | 6 (3%) | 0.020 | | | |
| 3 years | 7 (2%) | 5 (3%) | 0.562 | | | |
| 5 years | 5 (2%) | 2 (2%) | 0.818 | | | |
| 10 years | 1 (1%) | 2 (3%) | 0.101 | | | |
| **Feeling depressed (individual item)** | Frequency (%) | | | | | |
| Baseline | 31 (9%) | 15 (8%) | 0.683 | | | |
| 6 months | 27 (8%) | 15 (8%) | 0.947 | | | |
| 1 year | 31 (9%) | 21 (12%) | 0.461 | | | |
| 3 years | 22 (7%) | 12 (8%) | 0.927 | | | |
| 5 years | 29 (10%) | 15 (11%) | 0.863 | | | |
| 10 years | 10 (5%) | 7 (10%) | 0.122 | | | |
| **Lack of energy (individual item)** | Frequency (%) | | | | | |
| Baseline | 45 (13%) | 29 (15%) | 0.494 | | | |
| 6 months | 40 (12%) | 35 (18%) | 0.047 | | | |
| 1 year | 52 (16%) | 42 (22%) | 0.059 | | | |
| 3 years | 41 (14%) | 32 (20%) | 0.065 | | | |
| 5 years | 35 (12%) | 21 (15%) | 0.427 | | | |
| 10 years | 19 (9%) | 13 (18%) | 0.038 | | | |
| **Change in body weight (individual item) )** | Frequency (%) | | | | | |
| Baseline | 20 (6%) | 15 (8%) | 0.345 | | | |
| 6 months | 27 (8%) | 16 (8%) | 0.898 | | | |
| 1 year | 23 (7%) | 15 (8%) | 0.646 | | | |
| 3 years | 28 (9%) | 9 (6%) | 0.190 | | | |
| 5 years | 27 (10%) | 7 (5%) | 0.112 | | | |
| 10 years | 18 (9%) | 5 (7%) | 0.663 | | | |

Abbreviations: ADT, Androgen deprivation therapy; EBRT, external beam radiotherapy.
[a]Function domain scores are reported from the Expanded Prostate Cancer Index Composite-26 (score range 0 to 100), higher score indicates better function. Selected individual items are clinically important components of the domain that are scored on a Likert scale and dichotomized for group comparisons. The unadjusted number (%) of patients reporting a moderate or big problem for the individual items are shown. The adjusted mean point differences (effect size) between groups are shown using multivariable models for the domain scores at each time point relative to active surveillance. The adjusted odds ratio of men reporting a moderate or big problem for the individual items are shown relative to active surveillance.
[b]Denotes that the difference between groups exceeds the minimally important difference for clinical significance (4-6 points) for the hormonal function.

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