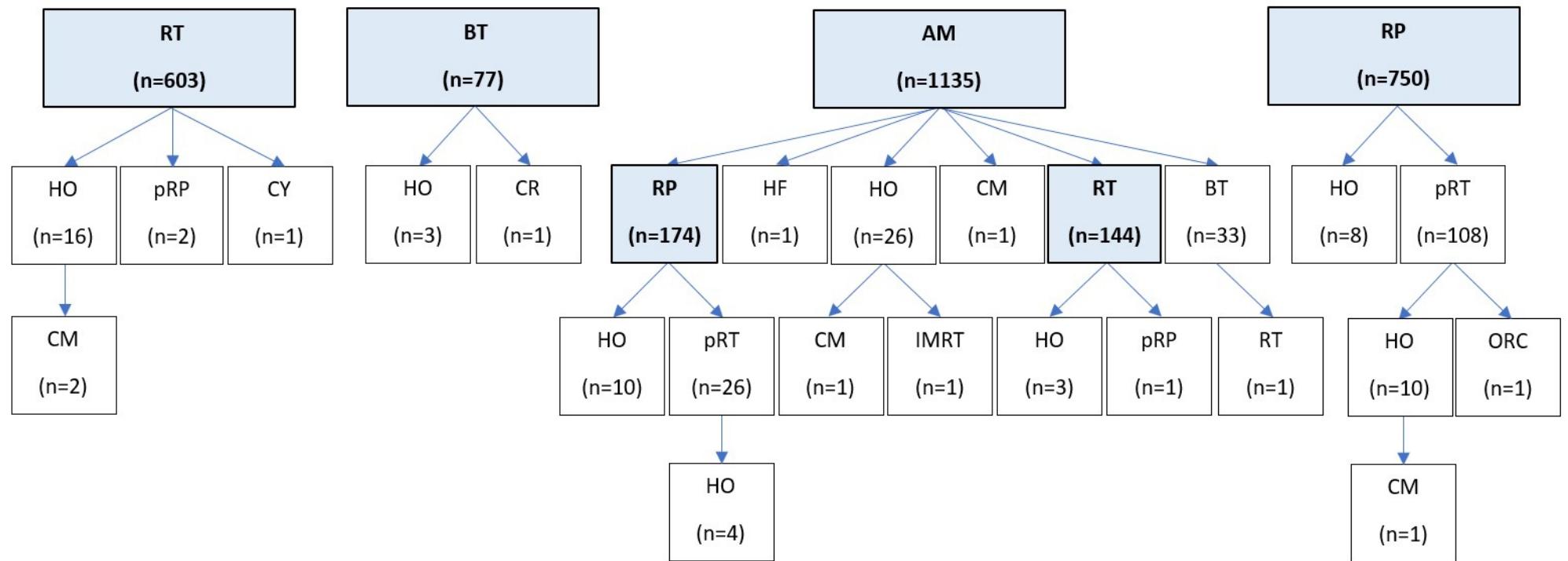


ProtecT Supplementary Online Content

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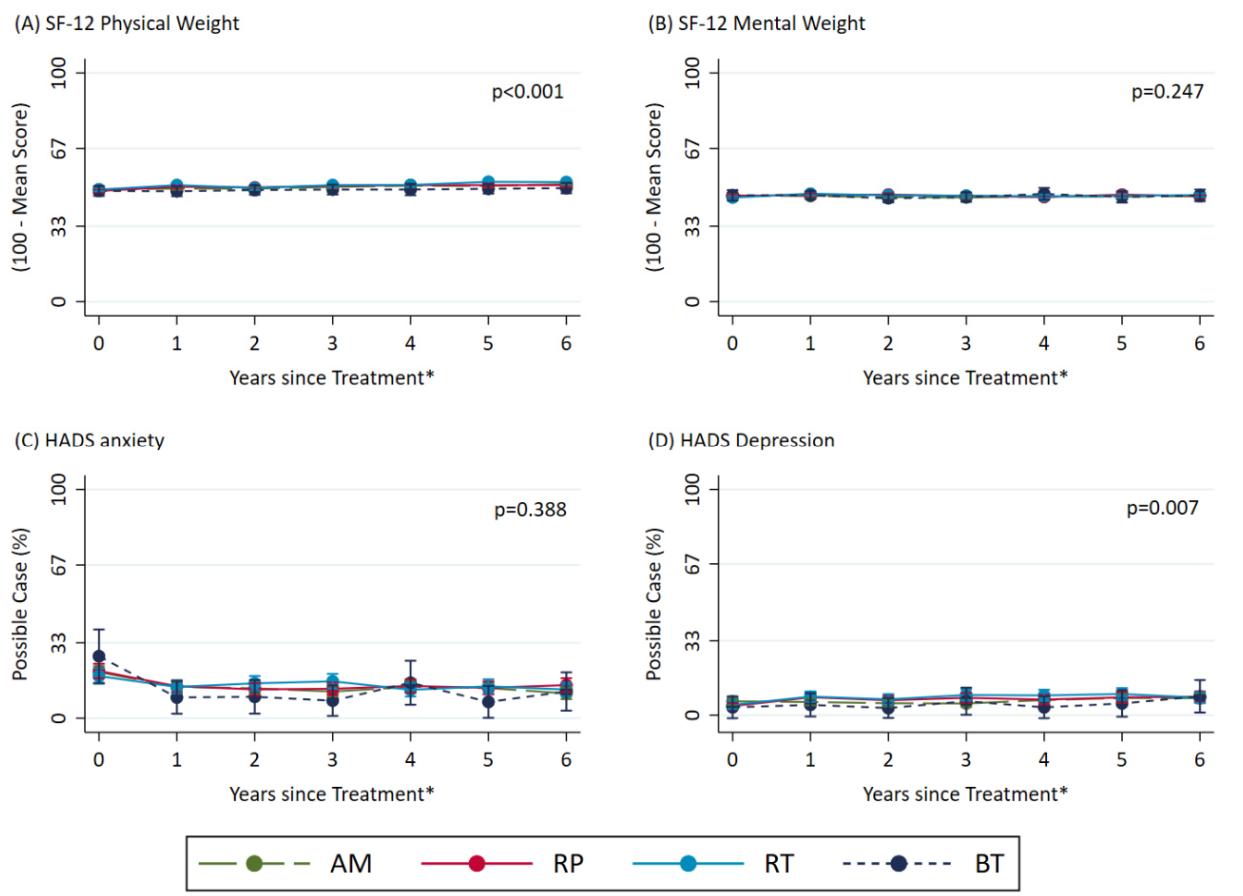
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Figure S1. Primary and secondary treatments for localized prostate cancer received over 6 years of follow up



Abbreviations: RT=radiation, BT=brachytherapy, RP=radical prostatectomy, AM=active monitoring, HO=hormones, pRT=post-surgery radiotherapy, pRP=post-radiotherapy surgery, CM=chemotherapy, HF=HIFU, IMRT=intensity-modulated radiation therapy, ORC=subcapsular orchidectomy + CPA, CY=cystoprostatectomy (for bladder cancer), CR=cryotherapy
Groups highlighted in blue analysed with others until they received a new treatment.

Figure S2. Adjusted physical and mental health and psychological outcomes after primary treatments for prostate cancer over 6 years



Abbreviations: AM, active monitoring, RP, radical prostatectomy, RT, radiation, BT brachytherapy.

*Time from treatment is the time between diagnosis and start of radical treatment or radical treatment after active monitoring and defined as questionnaires completed for e.g. year 2 as between 1 and 2 years after treatment. Higher scores or percentages indicate worse symptoms with SF-12 symptoms reversed.

Figure S3. Patient-reported urinary, bowel and sexual symptoms after radical treatment for localised prostate cancer, either initially, or after a period of active monitoring over 4 years

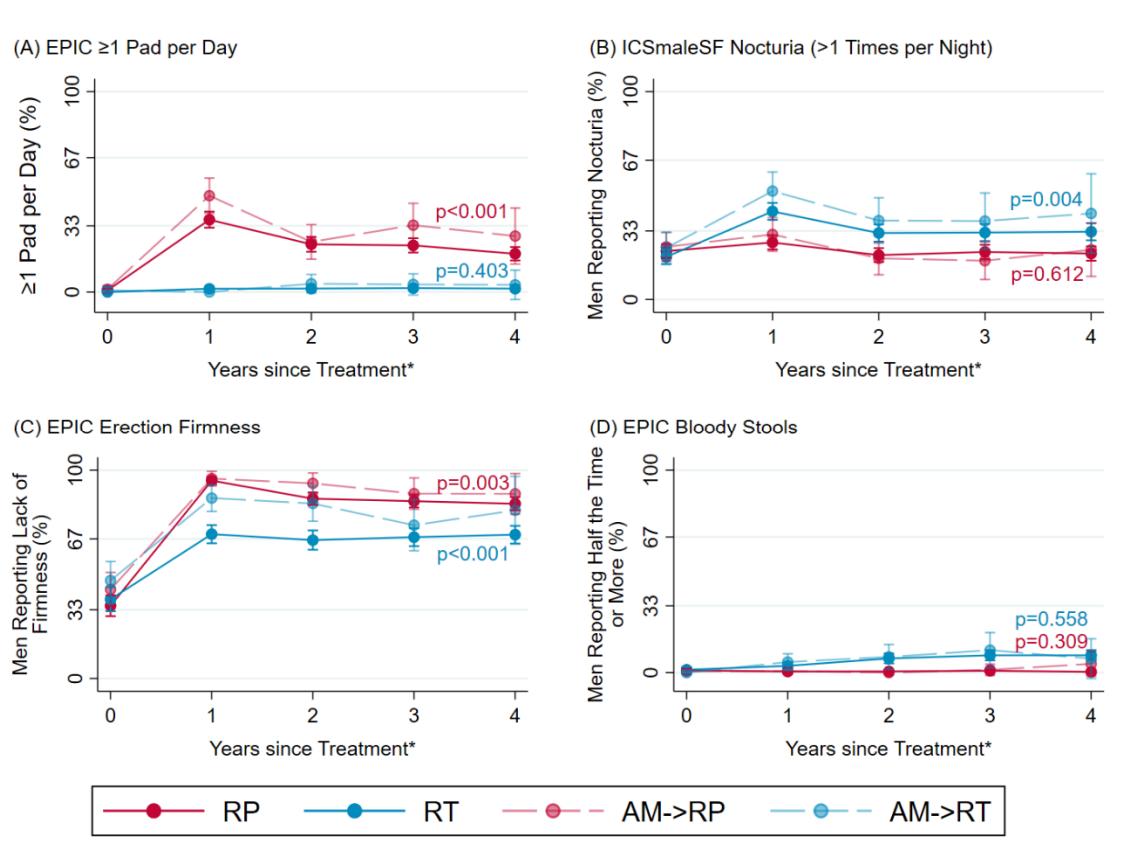
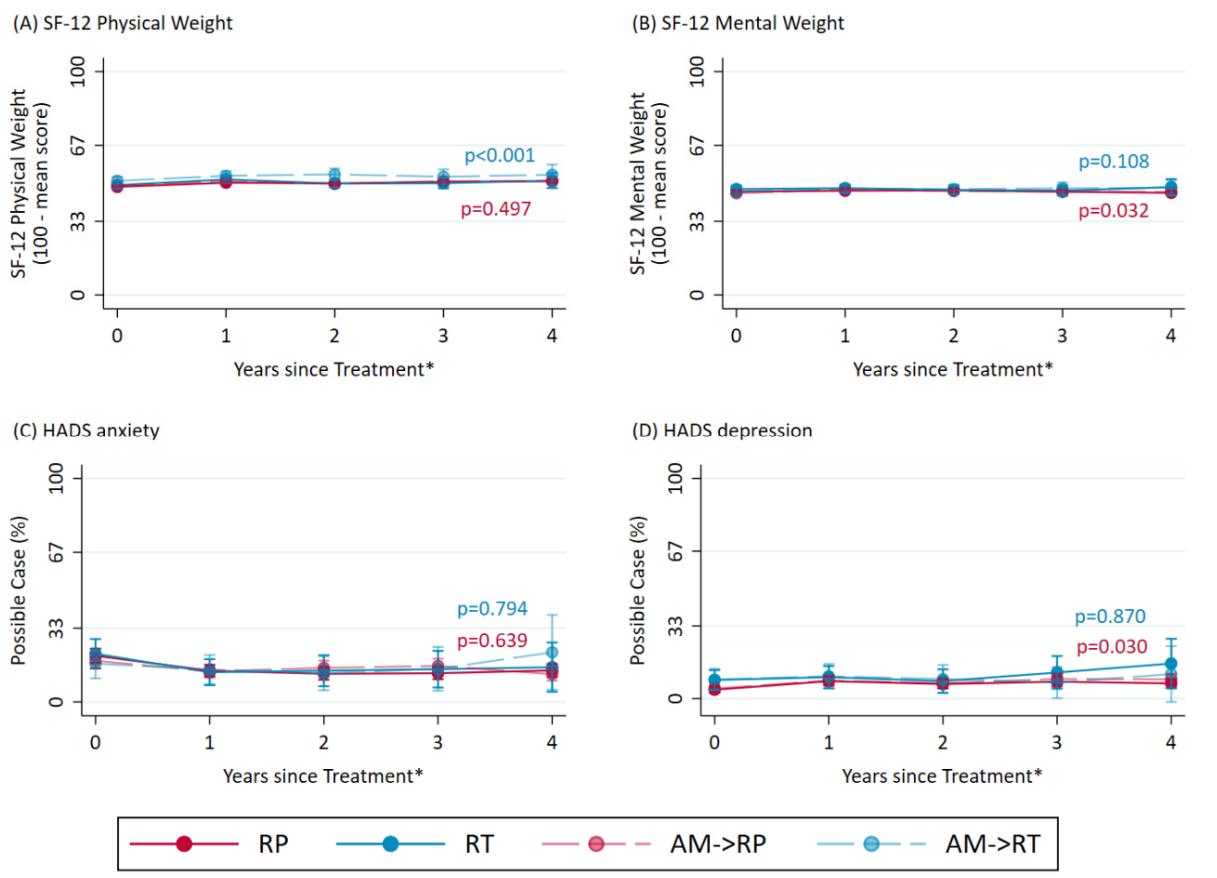


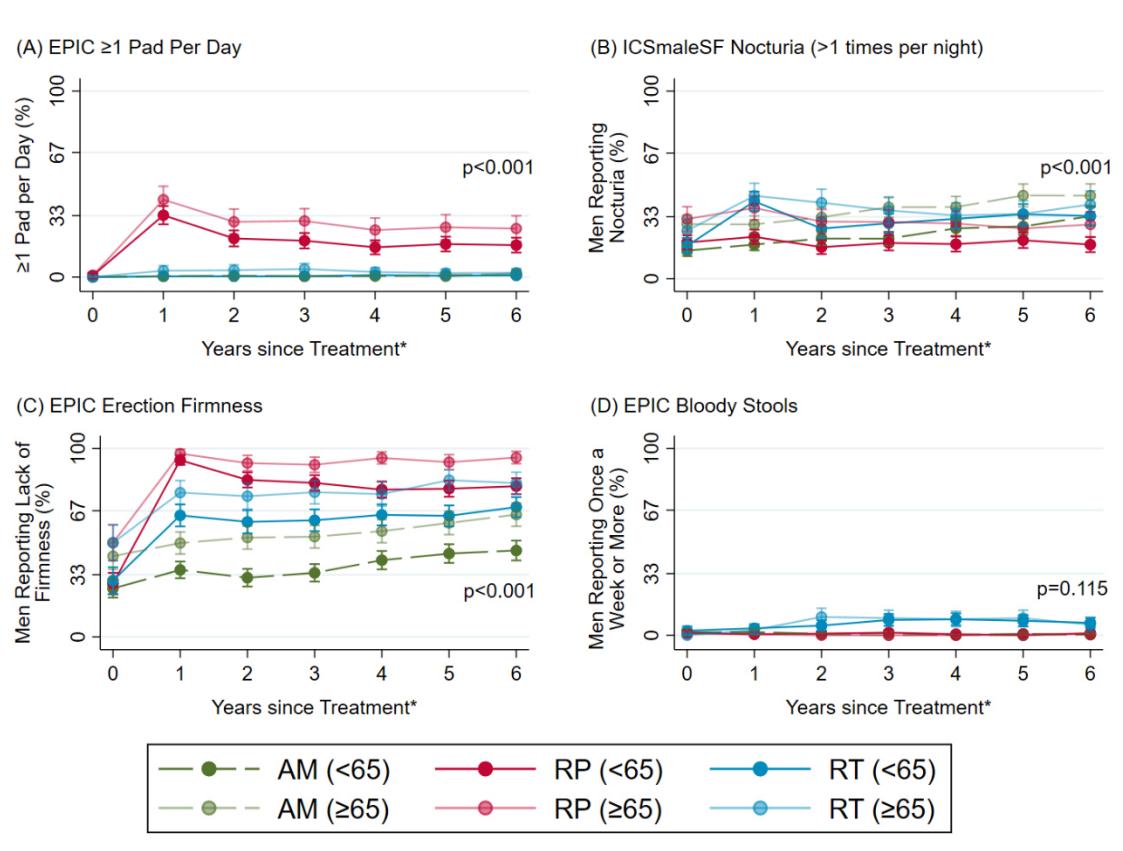
Figure S4. Adjusted quality of life outcomes after receiving radical treatment after primary active monitoring over 4 years



Abbreviations: AM, active monitoring, RP, radical prostatectomy, RT, radiation, BT brachytherapy.

*Time from treatment is the time between diagnosis and start of radical treatment or radical treatment after active monitoring and defined as questionnaires completed for e.g. year 2 as between 1 and 2 years after treatment. Higher scores or percentages indicate worse symptoms with SF-12 symptoms reversed. P-value based on likelihood ratio test in blue (radiation) or red (radical prostatectomy) comparing symptoms between those men starting treatment within a year of diagnosis with those delaying it until at least a year after diagnosis after receiving active monitoring.

Figure S5. Patient-reported urinary, bowel and sexual symptoms by age groups by primary localised prostate cancer treatments over 6 years



Abbreviations: AM, active monitoring; RP, radical prostatectomy; RT, EBRT; BT LDR brachytherapy. *Time from treatment between diagnosis and start of radical treatment. Includes those who have completed a questionnaire within the previous year, e.g. "2 Years from Treatment" refers to the period between 1 year after treatment and 2 years after treatment. Higher scores or percentages indicate more severe symptoms. Points are estimated means from models with error bars representing 95% CIs. P values are from a likelihood ratio test comparing a mixed effects regression model with an interaction (age*treatment) versus one without it.

Table S1. Response rates for exemplar PROMs in the treatment received analysis

Assessment period	Completion rates: Completed ^a /expected ^b (%)		
	ICIQ score ^b	EPIC sexual function score ^c	HADS anxiety
Baseline	1807/2304 (78%)	970/1283 (76%)	2075/2560 (81%)
0-1 years	2158/2374 (91%)	1506/1658 (91%)	2274/2512 (91%)
1-2 years	1860/2372 (78%)	1424/1868 (76%)	1927/2410 (80%)
2-3 years	1820/2289 (80%)	1575/2002 (79%)	1871/2290 (82%)
3-4 years	1724/2175 (79%)	1595/2056 (78%)	1766/2175 (81%)
4-5 years	1671/2056 (81%)	1611/2059 (78%)	1708/2056 (83%)
5-6 years	1588/1955 (81%)	1566/2039 (77%)	1609/1955 (82%)

^aQuestionnaires completed within the time frame, excluding time points censored after second treatments and unexpected, ^bExpected counts were calculated if the questionnaire was introduced before the assessment period (excluding time points censored after second treatments, after death or after 15th November 2015), ^cICIQ introduced 1st October 2001, EPIC introduced 1st March 2005.

Table S2. Adjusted urinary symptoms corresponding to Figure 1 and subscales

Assessment period	AM		RP		RT		BT		P value ^a	
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N		
ICIQ questionnaire										
ICIQ Incontinence Score (0-21) – corresponding to Figure 1A										
Baseline	1.10 (2.27)	784	1.28 (2.32)	561	1.16 (2.08)	461	1.31 (2.62)	51	<0.001	
0-1 years	1.28 (2.36)	960	5.33 (4.59)	674	1.59 (2.52)	545	1.84 (2.86)	62		
1-2 years	1.38 (2.28)	813	4.46 (4.19)	572	1.71 (2.53)	477	1.73 (2.89)	63		
2-3 years	1.51 (2.44)	768	4.52 (4.13)	555	1.72 (2.62)	495	2.20 (3.33)	61		
3-4 years	1.65 (2.48)	691	4.32 (3.95)	542	1.91 (2.78)	482	1.90 (2.92)	58		
4-5 years	1.64 (2.56)	657	4.30 (3.90)	525	1.79 (2.69)	475	2.34 (3.63)	58		
5-6 years	1.72 (2.60)	588	4.41 (3.99)	514	1.82 (2.56)	471	2.17 (3.26)	58		
Incontinent (ICIQ score >0)										
Baseline	200 (26%)	784	168 (30%)	561	139 (30%)	461	14 (27%)	51	<0.001	
0-1 years	284 (30%)	960	556 (82%)	674	196 (36%)	545	22 (35%)	62		
1-2 years	277 (34%)	813	432 (76%)	572	186 (39%)	477	22 (35%)	63		
2-3 years	277 (36%)	768	426 (77%)	554	189 (38%)	495	26 (43%)	61		
3-4 years	266 (38%)	691	415 (77%)	542	208 (43%)	482	25 (43%)	58		
4-5 years	250 (38%)	657	405 (77%)	525	195 (41%)	475	25 (43%)	58		
5-6 years	226 (38%)	588	403 (78%)	514	205 (44%)	471	26 (45%)	58		
ICIQ incontinence Problem (4+) – corresponding to Figure 1C										
Baseline	14 (2%)	790	12 (2%)	566	9 (2%)	466	3 (6%)	52	<0.001	
0-1 years	21 (2%)	973	118 (17%)	680	13 (2%)	554	4 (6%)	64		
1-2 years	13 (2%)	824	76 (13%)	577	18 (4%)	483	3 (5%)	63		
2-3 years	14 (2%)	774	75 (13%)	562	16 (3%)	497	3 (5%)	62		
3-4 years	22 (3%)	701	60 (11%)	549	16 (3%)	483	2 (3%)	58		
4-5 years	21 (3%)	660	63 (12%)	530	21 (4%)	479	3 (5%)	60		
5-6 years	24 (4%)	592	66 (13%)	517	16 (3%)	474	4 (7%)	58		
ICS male questionnaire										
Voiding score (0-20) – corresponding to Figure 1E										
Baseline	3.24 (2.99)	888	3.43 (3.24)	634	3.16 (2.92)	507	3.17 (3.82)	59	<0.001	
0-1 years	3.44 (3.14)	998	2.52 (2.89)	686	3.67 (3.41)	562	5.55 (3.89)	67		
1-2 years	3.68 (3.22)	847	2.29 (2.79)	591	3.14 (3.01)	488	4.31 (3.50)	64		
2-3 years	3.95 (3.36)	797	2.58 (2.89)	576	3.29 (3.05)	508	3.79 (3.58)	66		
3-4 years	4.08 (3.41)	720	2.43 (2.62)	557	3.27 (2.97)	492	3.55 (2.97)	60		
4-5 years	4.32 (3.46)	678	2.54 (2.74)	543	3.52 (3.17)	488	3.68 (3.19)	60		
5-6 years	4.43 (3.54)	606	2.64 (2.63)	524	3.43 (2.92)	482	3.73 (3.17)	59		
Incontinence score (0-24)										
Baseline	1.71 (1.80)	887	1.85 (1.87)	634	1.76 (1.82)	506	1.83 (2.22)	59	<0.001	
0-1 years	1.68 (1.84)	995	4.60 (3.68)	681	2.12 (2.05)	561	2.16 (1.78)	67		
1-2 years	1.80 (1.94)	844	4.19 (3.52)	582	2.07 (2.01)	489	2.00 (1.93)	64		
2-3 years	1.96 (2.05)	791	4.35 (3.49)	568	2.17 (2.13)	503	2.24 (2.37)	63		
3-4 years	2.02 (2.09)	710	4.07 (3.27)	552	2.21 (2.21)	490	1.82 (1.72)	60		
4-5 years	2.11 (2.07)	676	4.23 (3.28)	536	2.18 (2.15)	483	2.32 (2.16)	59		
5-6 years	2.14 (2.16)	605	4.08 (3.15)	525	2.24 (2.18)	478	2.30 (2.16)	60		
ICSmale QoL ("somewhat/a lot" of impact) – corresponding to Figure 1F										
Baseline	29 (3%)	897	19 (3%)	636	13 (3%)	511	3 (5%)	59	<0.001	
0-1 years	20 (2%)	1003	91 (13%)	689	31 (6%)	563	9 (13%)	67		
1-2 years	25 (3%)	842	58 (10%)	590	15 (3%)	488	5 (8%)	64		
2-3 years	32 (4%)	791	63 (11%)	574	18 (4%)	504	5 (8%)	64		
3-4 years	31 (4%)	714	45 (8%)	559	20 (4%)	495	3 (5%)	60		
4-5 years	35 (5%)	674	44 (8%)	541	24 (5%)	487	5 (8%)	60		
5-6 years	32 (5%)	606	44 (8%)	528	22 (5%)	478	5 (8%)	60		
Daytime frequency (more frequent than once every three hours)										
Baseline	265 (30%)	888	229 (36%)	631	162 (32%)	502	12 (20%)	59	=0.293	
0-1 years	312 (31%)	1000	280 (41%)	685	202 (36%)	556	29 (44%)	66		
1-2 years	255 (30%)	840	194 (33%)	586	154 (31%)	489	18 (29%)	63		
2-3 years	247 (31%)	790	193 (34%)	572	165 (33%)	503	21 (33%)	64		
3-4 years	224 (31%)	713	185 (34%)	550	162 (33%)	494	22 (37%)	60		
4-5 years	212 (32%)	670	190 (36%)	534	152 (31%)	483	19 (32%)	60		
5-6 years	194 (32%)	601	173 (33%)	519	159 (33%)	479	14 (24%)	59		
Nocturia (>1 times per night) – corresponding to Figure 1G										
Baseline	183 (20%)	894	147 (23%)	631	104 (21%)	507	9 (15%)	59	<0.001	

0-1 years	223 (22%)	998	188 (27%)	685	239 (42%)	564	29 (43%)	67	
1-2 years	219 (26%)	844	126 (21%)	590	156 (32%)	488	19 (30%)	64	
2-3 years	221 (28%)	790	131 (23%)	573	161 (32%)	500	20 (32%)	63	
3-4 years	224 (31%)	715	123 (22%)	556	162 (33%)	497	16 (28%)	58	
4-5 years	230 (34%)	672	121 (22%)	538	166 (34%)	482	18 (30%)	60	
5-6 years	227 (38%)	601	114 (22%)	525	171 (36%)	479	15 (25%)	59	
EPIC questionnaire									
≥1 Pad per day – corresponding to Figure 1B									<0.001
Baseline	0 (0%)	520	3 (1%)	362	0 (0%)	277	0 (0%)	39	
0-1 years	3 (0%)	756	197 (36%)	546	7 (2%)	442	1 (2%)	46	
1-2 years	4 (1%)	660	123 (24%)	517	7 (2%)	414	2 (4%)	45	
2-3 years	3 (0%)	691	126 (23%)	542	9 (2%)	466	2 (4%)	54	
3-4 years	4 (1%)	655	102 (19%)	535	8 (2%)	478	3 (5%)	56	
4-5 years	5 (1%)	646	109 (21%)	529	6 (1%)	485	3 (5%)	57	
5-6 years	8 (1%)	595	101 (20%)	505	7 (1%)	475	2 (3%)	59	
Urinary summary score (0-100, reversed^b) – corresponding to Figure 1D									<0.001
Baseline	6.62 (8.52)	520	7.38 (9.21)	362	7.06 (8.69)	276	8.19 (10.23)	39	
0-1 years	6.99 (8.40)	756	15.70 (14.58)	546	9.49 (10.85)	443	14.72 (12.52)	46	
1-2 years	6.97 (8.27)	659	12.25 (12.64)	516	7.90 (8.85)	413	13.57 (13.84)	45	
2-3 years	7.78 (9.00)	693	12.47 (12.34)	541	8.47 (10.06)	459	12.56 (14.16)	54	
3-4 years	8.28 (9.56)	654	11.27 (11.43)	536	8.20 (9.48)	477	9.48 (11.41)	56	
4-5 years	8.25 (9.31)	644	11.48 (11.50)	529	8.23 (9.47)	483	10.72 (13.29)	56	
5-6 years	8.96 (9.80)	594	11.11 (11.10)	508	8.23 (8.95)	475	9.45 (11.19)	59	
Urinary function score (0-100, reversed^b)									<0.001
Baseline	4.16 (7.41)	520	4.58 (8.61)	363	4.74 (7.60)	278	3.75 (7.01)	39	
0-1 years	4.92 (7.86)	758	18.55 (16.09)	549	6.29 (8.70)	442	9.90 (10.19)	46	
1-2 years	4.56 (7.16)	660	14.28 (13.83)	518	6.09 (8.23)	414	9.91 (11.33)	45	
2-3 years	5.23 (7.68)	693	14.68 (13.85)	542	5.89 (8.51)	465	9.58 (11.61)	54	
3-4 years	5.59 (8.05)	656	13.29 (12.82)	538	6.19 (8.70)	478	8.01 (10.90)	56	
4-5 years	5.69 (8.41)	647	13.65 (13.08)	531	5.88 (8.08)	484	7.81 (11.21)	57	
5-6 years	6.09 (8.60)	595	13.35 (13.10)	510	5.95 (7.67)	475	7.94 (9.74)	59	
Urinary bother score (0-100, reversed^b)									=0.001
Baseline	8.38 (11.11)	520	9.38 (11.72)	364	8.67 (11.19)	275	11.36 (13.61)	39	
0-1 years	8.50 (10.53)	753	13.62 (15.30)	546	11.84 (14.02)	443	18.17 (16.73)	46	
1-2 years	8.70 (10.74)	657	10.78 (13.86)	513	9.20 (11.06)	410	16.19 (17.17)	45	
2-3 years	9.64 (11.70)	694	10.85 (13.23)	542	10.15 (12.59)	458	14.68 (18.07)	54	
3-4 years	10.17 (12.31)	653	9.79 (12.17)	532	9.63 (11.87)	476	10.52 (13.91)	56	
4-5 years	10.06 (11.71)	645	9.92 (12.22)	527	9.87 (12.19)	481	12.69 (16.26)	56	
5-6 years	11.03 (12.60)	592	9.46 (11.45)	507	9.90 (11.51)	476	10.53 (13.70)	59	
Urinary incontinence score (0-100, reversed^b)									<0.001
Baseline	5.95 (10.76)	513	6.38 (10.86)	358	6.86 (11.02)	273	5.49 (10.50)	39	
0-1 years	7.18 (11.33)	750	28.50 (24.93)	533	8.55 (11.94)	438	10.61 (13.75)	46	
1-2 years	7.04 (11.02)	649	21.89 (21.62)	502	9.51 (12.59)	408	9.61 (13.79)	45	
2-3 years	7.86 (11.43)	681	22.96 (22.14)	529	9.02 (12.32)	451	11.22 (16.99)	53	
3-4 years	8.25 (11.94)	638	20.69 (20.19)	527	9.44 (12.72)	474	11.58 (15.86)	56	
4-5 years	8.42 (12.31)	636	21.29 (20.95)	521	8.77 (11.88)	472	12.50 (18.10)	56	
5-6 years	9.03 (12.29)	587	20.80 (20.45)	500	9.25 (12.06)	464	10.56 (14.82)	59	
Urinary irritative score (0-100, reversed^b)									<0.001
Baseline	6.66 (8.60)	520	7.42 (9.45)	362	6.79 (8.52)	276	8.61 (10.35)	39	
0-1 years	6.45 (8.07)	756	7.78 (10.13)	546	9.11 (11.49)	442	16.07 (14.65)	46	
1-2 years	6.50 (8.22)	659	6.14 (8.93)	517	6.49 (8.01)	413	14.68 (15.18)	45	
2-3 years	7.19 (8.76)	693	5.99 (8.15)	541	7.56 (9.57)	460	12.37 (15.10)	54	
3-4 years	7.74 (9.37)	654	5.20 (7.39)	536	6.93 (8.61)	477	7.46 (9.57)	56	
4-5 years	7.59 (8.75)	645	5.50 (7.23)	530	7.29 (9.13)	484	8.93 (11.00)	56	
5-6 years	8.24 (9.54)	594	5.20 (6.94)	508	7.07 (8.32)	475	8.17 (10.34)	59	

Abbreviations: AM=Active Monitoring, RP=Radical Prostatectomy, RT=Radiotherapy, BT=Brachytherapy, ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received as a covariate. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis.

^bScores were reversed so that higher scores indicate worse symptoms

Table S3. Adjusted sexual symptoms corresponding to Figure 2 and subscales

Assessment period	AM		RP		RT		BT		P value ^a
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	
EPIC questionnaire									
Men reporting lack of firmness – corresponding to Figure 2A									<0.001
Baseline	164 (32%)	507	123 (35%)	352	105 (38%)	276	14 (37%)	38	
0-1 years	302 (41%)	735	514 (95%)	541	300 (69%)	433	23 (51%)	45	
1-2 years	255 (40%)	637	435 (86%)	504	267 (66%)	402	27 (61%)	44	
2-3 years	279 (42%)	670	452 (85%)	531	308 (68%)	454	29 (54%)	54	
3-4 years	302 (47%)	646	448 (84%)	534	319 (69%)	462	34 (60%)	57	
4-5 years	319 (50%)	632	438 (83%)	527	336 (71%)	470	34 (58%)	59	
5-6 years	310 (53%)	580	435 (85%)	512	346 (74%)	470	30 (52%)	58	
Men reporting problem (moderate/big) with erectile dysfunction – corresponding to Figure 2B									<0.001
Baseline	70 (14%)	501	61 (17%)	353	55 (20%)	277	4 (11%)	38	
0-1 years	143 (20%)	725	378 (70%)	540	186 (44%)	422	10 (22%)	46	
1-2 years	123 (19%)	638	310 (62%)	504	149 (38%)	396	19 (42%)	45	
2-3 years	143 (22%)	659	274 (52%)	528	184 (41%)	448	17 (33%)	52	
3-4 years	147 (23%)	639	284 (53%)	532	176 (38%)	460	18 (31%)	58	
4-5 years	152 (24%)	628	259 (50%)	523	186 (40%)	470	13 (22%)	59	
5-6 years	146 (26%)	572	252 (50%)	509	181 (39%)	459	17 (29%)	59	
Sexual summary score (0-100, reversed^b)									<0.001
Baseline	36.79 (20.91)	496	38.75 (23.32)	347	40.64 (25.32)	273	36.68 (19.80)	37	
0-1 years	40.86 (23.70)	717	76.12 (18.92)	533	62.17 (27.62)	424	49.00 (23.46)	45	
1-2 years	41.27 (23.86)	630	69.42 (21.71)	499	57.91 (25.49)	390	55.09 (24.27)	45	
2-3 years	42.67 (24.19)	650	68.87 (22.24)	519	59.56 (25.46)	444	53.30 (26.01)	52	
3-4 years	45.12 (24.66)	632	67.65 (23.06)	527	58.96 (25.61)	454	52.40 (25.56)	56	
4-5 years	45.90 (24.48)	618	67.66 (23.47)	518	60.62 (24.59)	465	50.92 (23.91)	59	
5-6 years	47.06 (24.17)	565	68.23 (22.88)	507	60.51 (24.93)	452	50.24 (23.85)	58	
Sexual function score (0-100, reversed^b) – corresponding to Figure 2C									<0.001
Baseline	44.07 (21.11)	498	45.70 (22.85)	348	48.26 (25.08)	273	43.17 (20.55)	37	
0-1 years	48.29 (23.95)	722	82.44 (17.74)	534	69.25 (27.21)	425	56.49 (24.98)	45	
1-2 years	48.61 (23.91)	628	75.77 (21.49)	501	64.38 (25.19)	392	60.42 (23.34)	45	
2-3 years	49.75 (24.23)	657	76.17 (21.84)	526	66.88 (25.17)	450	60.37 (25.61)	54	
3-4 years	52.46 (24.41)	641	75.41 (23.06)	531	66.44 (25.47)	459	60.02 (26.90)	57	
4-5 years	53.00 (24.42)	626	76.07 (23.26)	518	67.72 (24.46)	471	58.92 (24.71)	59	
5-6 years	55.33 (24.79)	578	77.01 (22.79)	505	68.69 (25.34)	461	58.01 (26.00)	58	
Sexual bother score (0-100, reversed^b) – corresponding to Figure 2D									<0.001
Baseline	20.10 (26.47)	496	23.07 (29.66)	347	24.14 (31.86)	270	21.55 (23.91)	38	
0-1 years	24.74 (29.69)	716	61.94 (32.29)	534	46.50 (37.78)	422	32.74 (29.67)	46	
1-2 years	25.18 (29.66)	634	55.29 (32.99)	500	43.57 (34.78)	390	41.57 (31.25)	43	
2-3 years	27.39 (30.69)	655	52.31 (34.90)	520	43.91 (35.33)	441	39.42 (33.66)	52	
3-4 years	28.91 (31.85)	634	50.43 (34.71)	527	42.52 (35.06)	456	34.54 (31.25)	57	
4-5 years	29.70 (31.14)	623	49.11 (35.83)	518	44.17 (35.38)	464	33.16 (30.14)	59	
5-6 years	29.55 (31.57)	569	49.04 (35.14)	503	42.51 (35.66)	454	32.20 (29.95)	59	
Men reporting impact (moderate/big) of sexual dysfunction on quality of life – corresponding to Figure 2E									<0.001
Baseline	69 (14%)	500	57 (16%)	351	46 (17%)	274	4 (11%)	38	
0-1 years	134 (19%)	721	341 (64%)	537	179 (42%)	426	10 (22%)	46	
1-2 years	117 (18%)	639	271 (54%)	502	155 (39%)	398	17 (39%)	44	
2-3 years	125 (19%)	657	249 (48%)	523	169 (38%)	447	16 (31%)	52	
3-4 years	133 (21%)	638	238 (45%)	531	165 (36%)	459	14 (25%)	57	
4-5 years	141 (22%)	627	242 (46%)	524	168 (36%)	469	12 (20%)	59	
5-6 years	124 (22%)	572	217 (43%)	509	168 (37%)	460	15 (25%)	59	

Abbreviations: AM=Active Monitoring, RP=Radical Prostatectomy, RT=Radiotherapy, BT=Brachytherapy, ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received as a covariate. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis.

^bScores were reversed so that higher scores indicate worse symptoms

Table S4. Adjusted bowel symptoms corresponding to Figure 3 and subscales

Assessment period	AM		RP		RT		BT		P value ^a
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	
EPIC questionnaire									
Bowel summary score									<0.001
Baseline	6.22 (7.75)	517	6.82 (8.34)	362	5.39 (6.93)	276	7.60 (10.59)	39	
0-1 years	5.87 (8.37)	755	5.59 (7.39)	546	11.42 (13.91)	445	10.63 (10.85)	45	
1-2 years	5.86 (8.27)	657	5.30 (7.36)	516	10.99 (12.07)	415	10.41 (11.31)	45	
2-3 years	6.20 (9.47)	683	5.18 (6.92)	544	9.78 (11.21)	464	8.63 (11.51)	53	
3-4 years	6.23 (9.49)	657	5.00 (7.10)	536	9.02 (11.19)	475	7.79 (10.01)	58	
4-5 years	6.13 (8.97)	647	5.15 (7.43)	535	8.91 (9.93)	481	7.41 (12.04)	60	
5-6 years	6.23 (9.40)	591	5.08 (6.78)	520	9.10 (10.70)	475	8.33 (11.06)	60	
Bowel function score – corresponding to Figure 3A									<0.001
Baseline	7.66 (8.42)	517	8.50 (8.71)	364	7.25 (7.79)	279	7.42 (9.60)	39	
0-1 years	6.85 (8.50)	758	7.13 (8.17)	548	11.23 (12.43)	446	9.84 (9.79)	45	
1-2 years	6.94 (8.24)	657	6.77 (7.68)	518	10.54 (10.00)	415	9.38 (9.82)	45	
2-3 years	7.18 (9.38)	685	6.54 (7.27)	543	9.83 (10.01)	465	8.96 (10.07)	53	
3-4 years	7.00 (8.80)	660	6.28 (7.54)	538	9.38 (9.99)	477	8.56 (8.51)	58	
4-5 years	7.14 (9.23)	651	6.62 (7.66)	537	9.20 (9.14)	481	7.62 (11.38)	60	
5-6 years	7.37 (9.07)	591	6.44 (7.21)	522	9.50 (9.87)	477	8.63 (9.67)	60	
Bowel bother score – corresponding to Figure 3B									<0.001
Baseline	4.87 (9.50)	519	5.09 (10.15)	363	3.56 (7.73)	276	7.78 (13.56)	39	
0-1 years	4.87 (9.84)	756	4.03 (8.35)	547	11.58 (17.09)	445	11.43 (13.65)	45	
1-2 years	4.78 (9.93)	659	3.81 (8.69)	518	11.42 (16.27)	416	11.43 (15.03)	45	
2-3 years	5.25 (11.06)	691	3.83 (8.44)	546	9.73 (14.30)	466	8.57 (15.08)	55	
3-4 years	5.42 (11.57)	662	3.72 (8.26)	538	8.68 (14.10)	479	7.02 (13.43)	58	
4-5 years	5.07 (10.17)	653	3.69 (8.81)	537	8.65 (13.10)	488	7.20 (13.82)	60	
5-6 years	5.09 (11.18)	599	3.74 (8.27)	521	8.55 (13.47)	482	8.04 (14.77)	60	
Loose stools – corresponding to Figure 3C									<0.001
Baseline	87 (17%)	517	62 (17%)	364	42 (15%)	280	7 (18%)	39	
0-1 years	111 (15%)	759	59 (11%)	549	106 (24%)	446	5 (11%)	45	
1-2 years	78 (12%)	657	65 (13%)	518	78 (19%)	414	6 (13%)	46	
2-3 years	89 (13%)	688	60 (11%)	543	75 (16%)	466	8 (15%)	53	
3-4 years	78 (12%)	659	54 (10%)	539	75 (16%)	478	8 (14%)	58	
4-5 years	89 (14%)	653	55 (10%)	541	83 (17%)	482	5 (8%)	60	
5-6 years	77 (13%)	598	55 (10%)	526	76 (16%)	478	8 (13%)	60	
Faecal incontinence – corresponding to Figure 3D									<0.001
Baseline	17 (3%)	518	10 (3%)	365	5 (2%)	280	0 (0%)	39	
0-1 years	23 (3%)	759	5 (1%)	549	57 (13%)	446	8 (18%)	45	
1-2 years	21 (3%)	656	11 (2%)	518	46 (11%)	414	2 (4%)	46	
2-3 years	32 (5%)	688	8 (1%)	545	36 (8%)	466	4 (8%)	53	
3-4 years	23 (3%)	660	12 (2%)	538	43 (9%)	475	2 (3%)	58	
4-5 years	27 (4%)	652	10 (2%)	540	31 (6%)	483	2 (3%)	60	
5-6 years	26 (4%)	597	16 (3%)	524	46 (10%)	477	5 (8%)	60	
Bloody stools – corresponding to Figure 3E									<0.001
Baseline	7 (1%)	516	4 (1%)	364	4 (1%)	279	0 (0%)	39	
0-1 years	12 (2%)	758	3 (1%)	550	15 (3%)	446	1 (2%)	45	
1-2 years	4 (1%)	658	3 (1%)	519	29 (7%)	414	3 (7%)	46	
2-3 years	5 (1%)	687	5 (1%)	543	40 (9%)	466	2 (4%)	53	
3-4 years	1 (0%)	659	2 (0%)	539	41 (9%)	478	1 (2%)	58	
4-5 years	3 (0%)	652	1 (0%)	540	40 (8%)	482	2 (3%)	60	
5-6 years	2 (0%)	597	5 (1%)	526	30 (6%)	477	2 (3%)	60	
Bowel habits – corresponding to Figure 3F									<0.001
Baseline	12 (2%)	520	9 (2%)	363	4 (1%)	277	1 (3%)	39	
0-1 years	14 (2%)	758	13 (2%)	548	32 (7%)	445	3 (7%)	45	
1-2 years	10 (2%)	661	7 (1%)	521	31 (7%)	416	5 (11%)	45	
2-3 years	11 (2%)	693	8 (1%)	548	21 (5%)	466	2 (4%)	55	
3-4 years	18 (3%)	666	10 (2%)	538	16 (3%)	480	4 (7%)	58	
4-5 years	13 (2%)	653	12 (2%)	539	18 (4%)	488	3 (5%)	60	
5-6 years	16 (3%)	603	7 (1%)	523	16 (3%)	483	3 (5%)	60	

Abbreviations: AM=Active Monitoring, RP=Radical Prostatectomy, RT=Radiotherapy, BT=Brachytherapy, ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received as a covariate. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis.

Table S5. Adjusted symptoms from immediate radical treatments or after active monitoring corresponding to Figure S3

Assessment period	RP		AM -> RP		P value ^a	RT		AM -> RT		P value ^b
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N		n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	
EPIC: ≥1 Pad per day					=0.001					=0.911
Baseline	3 (1%)	362	2 (1%)	149		0 (0%)	277	1 (1%)	121	
0-1 years	197 (36%)	546	62 (48%)	129		7 (2%)	442	0 (0%)	113	
1-2 years	123 (24%)	517	25 (25%)	100		7 (2%)	414	3 (4%)	73	
2-3 years	126 (23%)	542	25 (33%)	75		9 (2%)	466	2 (4%)	53	
3-4 years	102 (19%)	535	12 (28%)	43		8 (2%)	478	1 (4%)	28	
ICS male: Nocturia (>1 times per night)					=0.277					=0.087
Baseline	147 (23%)	631	39 (25%)	154		104 (21%)	507	32 (25%)	129	
0-1 years	188 (27%)	685	41 (31%)	131		239 (42%)	564	61 (52%)	117	
1-2 years	126 (21%)	590	20 (20%)	101		156 (32%)	488	30 (38%)	79	
2-3 years	131 (23%)	573	14 (19%)	75		161 (32%)	500	20 (38%)	53	
3-4 years	123 (22%)	556	11 (24%)	46		162 (33%)	497	12 (41%)	29	
EPIC: Men reporting lack of firmness					=0.033					=0.002
Baseline	123 (35%)	352	62 (43%)	145		105 (38%)	276	56 (47%)	119	
0-1 years	514 (95%)	541	119 (96%)	124		300 (69%)	433	97 (87%)	112	
1-2 years	435 (86%)	504	89 (94%)	95		267 (66%)	402	63 (84%)	75	
2-3 years	452 (85%)	531	63 (89%)	71		308 (68%)	454	39 (74%)	53	
3-4 years	448 (84%)	534	39 (89%)	44		319 (69%)	462	21 (81%)	26	
EPIC: Bloody stools					=0.478					=0.907
Baseline	4 (1%)	364	1 (1%)	149		4 (1%)	279	0 (0%)	119	
0-1 years	3 (1%)	550	1 (1%)	131		15 (3%)	446	6 (5%)	115	
1-2 years	3 (1%)	519	0 (0%)	99		29 (7%)	414	6 (8%)	77	
2-3 years	5 (1%)	543	1 (1%)	72		40 (9%)	466	6 (11%)	54	
3-4 years	2 (0%)	539	2 (4%)	46		41 (9%)	478	2 (7%)	29	

Abbreviation: RP=Radical Prostatectomy, RT=Radiotherapy, AM->RP and AM->RT refer to those who commenced with active monitoring for at least one year before switching to radical prostatectomy or radiotherapy, respectively. ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received (RP vs. AM->RP) as a covariate. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis. ^bP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received (RT vs. AM->RT) as a covariate with other covariates, described above.

Table S6. Adjusted quality of life items by treatment received corresponding to Figure S4

Assessment period	AM		RP		RT		BT		P value ^a
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	
12-Item Short Form Survey (SF-12)									
Physical weight									=0.012
Baseline	49.14 (8.32)	794	48.40 (7.50)	574	49.00 (7.68)	448	48.40 (8.19)	59	
0-1 years	49.44 (8.36)	915	50.26 (8.75)	629	50.98 (9.39)	526	48.28 (8.42)	63	
1-2 years	49.42 (8.44)	790	49.97 (8.52)	555	49.74 (8.35)	448	48.81 (7.65)	57	
2-3 years	50.21 (8.93)	739	50.66 (9.04)	538	50.98 (9.47)	466	49.03 (8.61)	63	
3-4 years	50.72 (9.24)	660	50.97 (9.21)	528	51.05 (9.45)	461	49.06 (9.02)	53	
4-5 years	50.64 (9.04)	633	50.93 (9.57)	500	52.41 (10.28)	451	49.36 (7.79)	56	
5-6 years	51.41 (9.31)	555	50.98 (9.63)	471	52.31 (9.79)	449	49.66 (8.51)	57	
Mental weight									=0.250
Baseline	46.46 (8.12)	794	46.29 (7.72)	574	45.54 (6.59)	448	46.53 (8.72)	59	
0-1 years	46.20 (7.74)	915	46.69 (8.89)	629	47.22 (8.91)	526	46.53 (6.53)	63	
1-2 years	45.77 (7.57)	790	46.82 (9.11)	555	46.52 (8.34)	448	45.22 (6.93)	57	
2-3 years	45.60 (7.68)	739	46.25 (8.44)	538	46.32 (8.18)	466	45.71 (8.15)	63	
3-4 years	45.97 (7.94)	660	45.75 (7.95)	528	46.13 (7.94)	461	47.11 (9.47)	53	
4-5 years	45.94 (7.99)	633	46.81 (8.67)	500	46.25 (8.34)	451	45.82 (9.27)	56	
5-6 years	46.16 (8.38)	555	46.18 (8.18)	471	46.63 (8.32)	449	46.45 (9.53)	57	
Hospital Anxiety and Depression Scale (HADS)									
Anxiety cases (score ≥8)									=0.768
Baseline	179 (20%)	888	129 (21%)	624	93 (18%)	504	16 (27%)	59	
0-1 years	137 (14%)	995	95 (14%)	679	77 (14%)	563	6 (9%)	66	
1-2 years	109 (13%)	836	74 (13%)	586	74 (15%)	485	6 (9%)	64	
2-3 years	92 (12%)	786	74 (13%)	574	81 (16%)	502	5 (8%)	65	
3-4 years	98 (14%)	715	78 (14%)	553	61 (12%)	490	9 (16%)	58	
4-5 years	89 (13%)	674	71 (13%)	535	68 (14%)	488	4 (7%)	56	
5-6 years	65 (11%)	598	75 (14%)	518	60 (13%)	477	7 (12%)	60	
Depression cases (score ≥8)									=0.027
Baseline	54 (6%)	880	25 (4%)	622	23 (5%)	505	2 (3%)	58	
0-1 years	58 (6%)	994	54 (8%)	684	46 (8%)	561	3 (5%)	66	
1-2 years	44 (5%)	833	39 (7%)	590	34 (7%)	486	2 (3%)	64	
2-3 years	41 (5%)	793	44 (8%)	575	45 (9%)	505	4 (6%)	65	
3-4 years	48 (7%)	718	38 (7%)	552	43 (9%)	492	2 (3%)	58	
4-5 years	51 (8%)	672	42 (8%)	535	46 (9%)	491	3 (5%)	58	
5-6 years	45 (8%)	597	42 (8%)	515	37 (8%)	479	5 (8%)	60	

Abbreviation: AM=Active Monitoring, RP=Radical Prostatectomy, RT=Radiotherapy, BT=Brachytherapy, ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received as a covariate, adjusting for the measure at baseline. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis.

Table S7. Adjusted quality of life of radical treatments after active monitoring and immediate: radical treatment corresponding to Figure S5

Assessment period	AM		AM -> RP		P value	RT		AM -> RT		P value
	n (%) / Mean (SD)	N	n (%) / Mean (SD)	N		n (%) / Mean (SD)	N	n (%) / Mean (SD)	N	
12-Item Short Form Survey (SF-12)										
Physical weight					=0.554					=0.020
Baseline	48.40 (7.50)	574	49.18 (8.48)	147		49.00 (7.68)	448	51.14 (9.29)	113	
0-1 years	50.26 (8.75)	629	51.78 (9.51)	129		50.98 (9.39)	526	53.37 (10.53)	110	
1-2 years	49.97 (8.52)	555	49.89 (9.03)	100		49.74 (8.35)	448	53.97 (11.03)	68	
2-3 years	50.66 (9.04)	538	50.06 (9.78)	72		50.98 (9.47)	466	52.93 (11.55)	49	
3-4 years	50.97 (9.21)	528	51.26 (10.83)	42		51.05 (9.45)	461	53.82 (11.44)	27	
Mental weight					=0.224					=0.487
Baseline	46.29 (7.72)	574	47.40 (9.31)	147		45.54 (6.59)	448	46.33 (8.36)	113	
0-1 years	46.69 (8.89)	629	47.81 (9.75)	129		47.22 (8.91)	526	47.68 (10.03)	110	
1-2 years	46.82 (9.11)	555	47.05 (9.48)	100		46.52 (8.34)	448	47.42 (8.37)	68	
2-3 years	46.25 (8.44)	538	46.73 (9.80)	72		46.32 (8.18)	466	47.79 (9.00)	49	
3-4 years	45.75 (7.95)	528	48.28 (11.71)	42		46.13 (7.94)	461	48.01 (8.27)	27	
Hospital Anxiety and Depression Scale (HADS)										
Anxiety cases (score ≥8)					=0.630					=0.574
Baseline	129 (21%)	624	33 (22%)	153		93 (18%)	504	22 (17%)	128	
0-1 years	95 (14%)	679	18 (13%)	135		77 (14%)	563	17 (15%)	117	
1-2 years	74 (13%)	586	14 (14%)	100		74 (15%)	485	10 (13%)	78	
2-3 years	74 (13%)	574	11 (15%)	75		81 (16%)	502	8 (15%)	54	
3-4 years	78 (14%)	553	7 (16%)	45		61 (12%)	490	6 (22%)	27	
Depression cases (score ≥8)					=0.084					>0.999
Baseline	25 (4%)	622	13 (8%)	154		23 (5%)	505	11 (9%)	128	
0-1 years	54 (8%)	684	13 (10%)	134		46 (8%)	561	12 (10%)	118	
1-2 years	39 (7%)	590	8 (8%)	101		34 (7%)	486	7 (9%)	79	
2-3 years	44 (8%)	575	9 (12%)	76		45 (9%)	505	4 (7%)	55	
3-4 years	38 (7%)	552	7 (16%)	44		43 (9%)	492	3 (11%)	27	

Abbreviation: RP=Radical Prostatectomy, RT=Radiotherapy, AM->RP and AM->RT refer to those who commenced with active monitoring for at least one year before switching to radical prostatectomy or radiotherapy, respectively. ^aP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received (RP vs. AM->RP) as a covariate. Other covariates included a treatment cohort indicator (randomised/preference) and propensity scores. Baseline measures were not included, or adjusted for, based on this being an 'as treated' analysis. ^bP value from a likelihood ratio test comparing a mixed effects model, with and without treatment received (RT vs. AM->RT) as a covariate. Other covariates included the baseline measure of the symptom, a treatment cohort indicator (randomised/preference) and propensity scores.

Table S8. Adjusted interaction between treatment and age group on symptoms corresponding to Figure S4

Assessment period	AM (<65)		AM (≥ 65)		RP (<65)		RP (≥ 65)		RT (<65)		RT (≥ 65)		P values	
	n (%) / Mean (SD)	N	Overall ^a	Pairwise ^b										
EPIC: ≥ 1 Pad per day														
Baseline	0 (0%)	318	0 (0%)	202	2 (1%)	251	1 (1%)	111	0 (0%)	164	0 (0%)	113		
0-1 years	2 (0%)	459	1 (0%)	297	120 (33%)	361	77 (42%)	185	1 (0%)	266	6 (3%)	176		
1-2 years	2 (1%)	389	2 (1%)	271	71 (21%)	342	52 (30%)	175	1 (0%)	251	6 (4%)	163		
2-3 years	2 (0%)	413	1 (0%)	278	69 (20%)	353	57 (30%)	189	1 (0%)	281	8 (4%)	185		
3-4 years	2 (1%)	388	2 (1%)	267	57 (16%)	357	45 (25%)	178	3 (1%)	294	5 (3%)	184		
4-5 years	4 (1%)	392	1 (0%)	254	64 (18%)	361	45 (27%)	168	2 (1%)	299	4 (2%)	186		
5-6 years	3 (1%)	352	5 (2%)	243	59 (17%)	344	42 (26%)	161	3 (1%)	301	4 (2%)	174		
ICS male: Nocturia (>1 times per night)														
Baseline	82 (15%)	547	101 (29%)	347	83 (19%)	430	64 (32%)	201	56 (18%)	320	48 (26%)	187		
0-1 years	111 (18%)	611	112 (29%)	387	102 (22%)	457	86 (38%)	228	144 (41%)	349	95 (44%)	215		RP vs. AM
1-2 years	108 (21%)	505	111 (33%)	339	66 (17%)	393	60 (30%)	197	81 (27%)	303	75 (41%)	185		P=0.612
2-3 years	102 (21%)	478	119 (38%)	312	72 (19%)	378	59 (30%)	195	90 (30%)	305	71 (36%)	195		RT vs. AM
3-4 years	116 (27%)	432	108 (38%)	283	68 (18%)	369	55 (29%)	187	98 (32%)	307	64 (34%)	190		P=0.003
4-5 years	115 (28%)	413	115 (44%)	259	75 (20%)	366	46 (27%)	172	102 (34%)	297	64 (35%)	185		RP vs. RT
5-6 years	119 (33%)	357	108 (44%)	244	64 (18%)	352	50 (29%)	173	101 (33%)	302	70 (40%)	177		P=0.019
EPIC: Men reporting lack of firmness														
Baseline	37 (12%)	308	33 (17%)	193	35 (14%)	242	26 (23%)	111	22 (13%)	163	33 (29%)	114		
0-1 years	81 (18%)	448	62 (22%)	277	257 (72%)	356	121 (66%)	184	106 (41%)	257	80 (48%)	165		
1-2 years	64 (17%)	380	59 (23%)	258	207 (62%)	333	103 (60%)	171	80 (33%)	242	69 (45%)	154		
2-3 years	83 (21%)	398	60 (23%)	261	173 (50%)	344	101 (55%)	184	91 (34%)	268	93 (52%)	180		
3-4 years	84 (22%)	389	63 (25%)	250	180 (51%)	351	104 (57%)	181	92 (33%)	283	84 (47%)	177		
4-5 years	82 (21%)	385	70 (29%)	243	169 (47%)	360	90 (55%)	163	97 (33%)	292	89 (50%)	178		
5-6 years	82 (24%)	345	64 (28%)	227	165 (48%)	345	87 (53%)	164	101 (34%)	293	80 (48%)	166		
EPIC: Bloody stools														
Baseline	5 (2%)	316	2 (1%)	200	3 (1%)	251	1 (1%)	113	4 (2%)	166	0 (0%)	113		
0-1 years	8 (2%)	460	4 (1%)	298	2 (1%)	362	1 (1%)	188	10 (4%)	269	5 (3%)	177		
1-2 years	3 (1%)	385	1 (0%)	273	3 (1%)	342	0 (0%)	177	13 (5%)	251	16 (10%)	163		
2-3 years	5 (1%)	413	0 (0%)	274	5 (1%)	352	0 (0%)	191	23 (8%)	281	17 (9%)	185		
3-4 years	1 (0%)	393	0 (0%)	266	2 (1%)	356	0 (0%)	183	25 (9%)	293	16 (9%)	185		
4-5 years	3 (1%)	395	0 (0%)	257	0 (0%)	367	1 (1%)	173	23 (8%)	297	17 (9%)	185		
5-6 years	1 (0%)	355	1 (0%)	242	4 (1%)	354	1 (1%)	172	20 (7%)	301	10 (6%)	176		

Abbreviation: AM=active monitoring, RP=radical prostatectomy, RT=radiotherapy only, ^aOverall p value for the likelihood ratio test of inclusion/exclusion of an interaction term between age (continuous) and treatment group, ^bWhere there was evidence of an interaction, pairwise comparisons were carried out to see where treatment effect was modified by age group

Table S9. Adjusted symptoms and quality five years after enrolment in the CEASAR cohort or diagnosis in the ProtecT trial

EPIC score/item	ProtecT (all)* Median (IQR) / %	CEASAR (low risk) Median (IQR) / %
Active monitoring/surveillance (n)*	1135 (EPIC c.570)	363
Urinary function		
Incontinence score	100 (86, 100)	92 (73, 100)
Leakage (%)	1%	7%
Irritative score	96 (89, 100)	88 (81, 100)
Frequency of problem (%)	4%	15%
Sexual function		
Sexual function score	50 (29, 67)	55 (22, 85)
Erection, lack of firmness	50%	57%
Bowel function		
Bowel function score	96 (89, 100)	100 (92, 100)
Bloody stools	<1%	0%
Radical prostatectomy (n)	Open 750 (EPIC c.520)	Robotic-Assisted 675
Urinary function		
Incontinence score	86 (67, 94)	79 (58, 100)
Leakage (%)	6%	10%
Irritative score	96 (93, 100)	94 (88, 100)
Frequency of problem (%)	6%	12%
Sexual function		
Sexual function score	31 (9, 53)	48 (15, 80)
Erection, lack of firmness	71%	61%
Bowel function		
Bowel function score	93 (86, 96)	100 (96, 100)
Bloody stools	<1%	0%
Radiotherapy (n)	EBRT¹ 603 (EPIC c.480)	IMRT² 261
Urinary function		
Incontinence score	100 (86, 100)	100 (79, 100)
Leakage (%)	1%	6%
Irritative score	96 (89, 100)	94 (81, 100)
Frequency of problem (%)	4%	13%
Sexual function		
Sexual function score	31 (9, 53)	28 (9, 69)
Erection, lack of firmness	71%	74%
Bowel function		
Bowel function score	93 (86, 96)	96 (88, 100)
Bloody stools	8%	0%
Low-dose-rate brachytherapy (n)	77 (EPIC c. 60)	87
Urinary function		
Incontinence score	97 (79, 100)	100 (81, 100)
Leakage (%)	5%	5%
Irritative score	93 (88, 100)	94 (84, 100)
Frequency of problem (%)	7%	14%
Sexual function		
Sexual function score	42 (21, 64)	53 (24, 78)
Erection, lack of firmness	58%	61%
Bowel function		
Bowel function score	96 (89, 100)	100 (88, 100)
Bloody stools	3%	0%

ProtecT used EPIC-50, CEASAR used EPIC-26, ¹External Beam Radiotherapy, ²IMRT; Intensity modulated radiation therapy low risk group patients, *ProtecT adjusted results censored at second treatment, unlike CEASAR unadjusted results in Table e5 (numbers of men unavailable for binary items).

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