Table 1: Clinical trial demographics

Reference	Country	Years of study	Patient and/or clinician reported toxicity (P/C)	Toxicity or PRO reporting tool	Design	Trial name	Multi-center study	Internat-ional (more than one country)	N= overall study	N= toxicity follow up	Timing of toxicity follow up (median years)	Primary end point	Treatment arms	RT dose	Difference in primary outcome	Significant clinician toxicity reporting between treatment arms	Significant PRO reported toxicity/QOL between treatment arms
Al-Mamgani, et al. (2008, 2011)	Netherlands	1997-2003	C & P	SF-36 RTOG	Phase III	Dutch randomized dose-escalation trial (CKTO 96-10)	Yes	No	669	300	1.5	QoL	3D CRT Conventional v high dose	68 or 78 Gy both 2Gy/#	No	No	Yes decrease in role and physical functioning in the higher dose arm.
Arcangeli, et al. (2011) and (2010)	Italy	2003-2007	C	RTOG + extra items LENT-SOMA	Phase III	RCT	No	No	168	168	2.6/2.9	Toxicity	3D CRT Conventional v Hypo-RT	80 Gy in 2Gy/# vs 62 Gy in 3.1Gy/#	No	No	N/A
Armstrong et al (2011) and Daly et al (2012)	Ireland	1997-2008	C	RTOG + LENT-SOMA: own ED item (Daly)	Phase III	ICORG 97-01	No	No	276	248	7.1	Freedom from biochemical relapse	NAD (8 months) + 3D CRT RT v NAD (4 months) +3D CRT RT	70Gy in 2Gy/#	No	No	No
Barnett, et al (2011). Dearnaley (2007), Syndikus (2010) Gulliford, (2010)	UK	1998-2007	C & P	RTOG LENT-SOMA RMH UCLA-PCI; FACT G/P (Syndikus)	Phase III	MRC RT01 ISRCTN 47772397	Yes	Yes	843	788 and 306 at final 5 year time point. 388 answered PROs	2 and up to 5 years 4.2 (PRO)	Toxicity (factors leading to late toxicity)	Conventional v high dose 3D CRT Conformal 64Gy V 74Gy with NAS	64 Gy vs 74 Gy both in 2Gy/# PRO Analysis on Conventional 30-70Gy	Yes	Yes, high dose led to significant increased late GI and GU	Yes
Beckendorf, et al (2011) Pommier (2007)	France	1999-2008	C & P	RTOG LENT-SOMA EORTC QLQC-30 +PR25	Phase III	Getug 06 trial	Yes	No	306	280	5	Freedom from biochemical relapse	3D CRT Conventional v high dose	70 Gy vs 80 Gy both in 2Gy/#	Yes	Yes significant increase in bladder toxicity	No difference in QOL scores
Crook, et al. (2010)	Canada	2004-2008	C	LENT-SOMA IPSS	Phase III	RCT	No	No	316	300	0.33	Toxicity (prostate oedema)	Meloxican (same day) + BT v Meloxican (one week before) + BT	All patients received 145Gy iodine-125 BT	No	No	No
Dearnaley, et al. (2012)	UK	2002-2006	C	LENT-SOMA RMH	Phase III	CHHiP RCT	Yes	No	457	404	4.2	Toxicity at 24months	IMRT Conventional V Hypo-RT (2 doses)	Conventional: 74Gy in 2Gy/# vs 60 Gy in 3Gy/#, or 57 Gy in 3Gy/#	Yes (non-inferiority trial)	No difference in acute/late toxicity	N/A
Hirano, et al. (2010)	Japan	2003-2006	C	RTOG CTCAE-V 2.0	Phase III	RCT	No	No	41	39	2.2	Freedom from biochemical relapse and toxicity	3D-CRT +LHRH agonist +EMP v 3D-CRT +LHRH agonist	70Gy in 2Gy /#	Yes for Intermediate or high risk	N/A	N/A
Hoskin, et al. (2012; 2013)	UK	1997-2005	C & P	Dische scales; FACT G & P (Hoskin 2013)	Phase III	RCT	No	No	218	216	10.5	Freedom from biochemical relapse	3D CRT -RT v -RT + BT boost	55Gy in 2.75Gy/# vs ERBT + HDR: 35.75Gy in 2.75Gy/# plus HDR BT boost	Yes	No	Yes decrease in ED for BT+ arm

Jones, et al. (2011)	USA and Canada	1994-2010	C & P	RTOG + own ED item LENT-SOMA SAQ	Phase III	RCT	Yes	Yes	2028	1979	9.1	Overall survival	3D CRT RT v 3D CRT RT+ADT	66Gy in 1.8Gy/#	Yes, in intermediate risk	No	No
Michalski, et al. (2013)	USA and Canada	2002-2012	C	RTOG+ CTCAE v 2.0	Phase III	RTOG 0126 Prostate Cancer trial	Yes	Yes	1532	748	3.5 (IMRT) 4.6(3D-CRT)	Overall survival	Conventional v high dose RT delivered using 3D CRT or IMRT	70.2Gy or 79.2Gy both in 1.8Gy/#	preliminary toxicity results only	Decrease in toxicity for IMRT	N/A
Pollack, A., G. Walker, et al. (2013)	USA	2002-2011	C & P	RTOG LENT-SOMA IPSS	Phase III	RCT	Yes	No	307	303	5.7	Toxicity	IMRT conventional v high dose	76Gy in 2.0Gy/# vs Hypo-RT 70.2Gy in 2.7Gy /#	No	No	N/A
Warde, et al. (2011)	Canada & UK	1995-2005	C & P	RTOG + NCICCTU-CTC EORTC QLQC-30 +PR25 FACT G & P	Phase III	MRC UK PR07 trial	Yes	Yes	1205	1205	6 years	Overall survival	ADT v ADT + 3D CRT conventional RT	65-69 Gy to prostate and seminal vesicles, 45 Gy to pelvic nodes	Yes	No	Yes EORTCQLQC showed small increase in GU toxicity at 6 months
Yeoh, et al. (2011) Yeoh 2006	Australia	1996-2009	C	LENT-SOMA (adapted)	Phase III	RCT	No	No	2217	217	7.5	Freedom from biochemical relapse	3D CRT conventional v hypo-RT	64 Gy in 2Gy/# vs 55 Gy in 2.75Gy/#	Yes	No	N/A
Zietman, et al. (2005,2008,2010), Nguyen et al (2010)	USA	1996-2008	C&P	RTOG; Own QoL/PRO from MOS-SP &SF-36 (Nguyen)	Phase III	PROG/ACR 95-09	Yes	No	393	393 with PROs in subgroup of 50	8.9	Local failure (including biochemical relapse)	3D CRT followed by proton boost to two dose levels	50.4Gy in 1.8Gy/ # with a proton boost dose of either 19.8 Gy (conventional) or 28.8 Gy (high dose)	Yes	No	No

Key 1: RCT - Randomised controlled trial; RT- Radiotherapy; 3D CRT- 3 dimensional conformal radiotherapy; BT- Brachytherapy; BTb-brachytherapy boost; # - fraction; Gy- Gray units, ADT- Androgen deprivation therapy; IMRT- Intensity modulated RT; 3D-CRT – 3 dimensional conformal RT; LHRH: luteinising hormone releasing hormone; EBRT: external beam RT; GU-genitourinary; GI-gastrointestinal; EMP- Estramustine phosphate; HDR- high dose rate; ED: Erectile dysfunction; RTOG- Radiation Therapy Oncology group; NAS- neoadjuvant androgen suppression; NAD-neoadjuvant androgen deprivation; PS- performance status; NCI-CCTU-CTC-National cancer institute of Canada clinical trials group expanded common toxicity criteria; IPSS-International prostate symptom score; CTCAE-Common toxicity criteria for adverse events; LENT-SOMA-Late effects of normal tissue –subjective objective management analytic; University of California, Los Angeles Prostate Cancer Index (ULCA-PCI); SAQ-; sexual adjustment questionnaire FACT G & P-Functional assessment of cancer therapy (general & prostate); EORTC QLQC-30- European organisation for research & treatment of cancer, quality of life questionnaire; RMH- Royal Marsden hospital scale; MOS Sexual Problems (MS-SP); Short Form (36) Health Survey (SF-36).

Table 2: Comparison between clinician and patient-reported toxicity measures using QUANTEC reporting recommendations

	RCT PUBLICATIONS REPORTING ON TOXICITY WITH PATIENT REPORTING		RCT PUBLICATIONS REPORTING ON TOXICITY WITH CLINICIAN REPORTING	
TOTAL NUMBER OF RCT PUBLICATIONS INCLUDED N=21*	N=10		N=11	
COCHRANE RISK OF BIAS				
Overall number of RCTs with a overall low risk of bias assessed	21			
FREQUENCY OF TOXICITY INSTRUMENT USED				
Acute reporting	IPSS (baseline only)	1	RTOG	9
	SAQ(baseline only)	1	RTOG (Extended)	2
			CTCAE V 02	1
			LENT-SOMA (Adapted)	1
			IPSS clinician reported	1
			NC CCTG CTC	1
			Own EF question	2
Late reporting	FACT G & FACT-P	3	LENT SOMA	9
	EORTC QLQC-30 +PR25	2	LENT SOMA (Adapted)	1
	UCLA-PCI	3	IPSS (clinician reported)	1
	SAQ	1	RMH	4
	SF-36	1	RTOG	6
	QOL measure (own developed)	1	CTCAE Version 02 CTCAE Version 03	1 2
	Own ED score	2	EF (own scale)	2
			Dische scales	2
Total number of instruments used	9		14 (including adapted measures)	
REPORTING OF TOXICITY				
Baseline symptom reporting	Yes	9	Yes	21
	No	1	No	0
Acute symptom reporting	Yes	0	Yes	14
	No	10	No	7
Are all grades of toxicity reported (from mild to severe symptoms)?	Yes, all grades	3	Yes, all grades (including >grade 2)	18
	No, more severe grades only (grade 3+)	0	No, more severe grades only (grade 3+)	2

	No, presence or absence of symptom	7	No, presence or absence of symptom	1
Most frequent type of toxicity reported	Bowel	4	Bowel	14
	Urinary	1	Urinary	15
	Sexual	2	Sexual	2
	QOL	7	QOL	0
	Skin	0	Skin	0
	Haematological	0	Haematological	1
Are various symptoms referable to a single organ grouped together (e.g. urinary frequency and incontinence grouped as 'bladder symptoms')?	Yes (grouped symptoms)	6	Yes (grouped symptoms)	16
	No (individual symptoms	4	No (individual symptoms	5
	Both		Both	
	Unclear		Unclear	

Key: FACT G_P: Functional assessment of Cancer therapy General/Prostate; EORTC_QLQC_30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; ULCA-PCI: University of California, Los Angeles Prostate Cancer Index; SAQ: Sexual adjustment questionnaire; SF-36: short-form health survey; ED: erectile dysfunction; QOL: quality of Life; RTOG: Radiotherapy Oncology Group; LENT-SOMA: Late Effects Normal Tissue Task Force -Subjective, Objective, Management, Analytic scales; IPSS: International Prostate Symptom Score; RMH: Royal Marsden Hospital scale; CTCAE; Common Terminology Criteria for Adverse Events; EF: Erectile function

Table 3: Overview of RCTs PRO quality of reporting

		TOTAL: n = 10
TITLE AND ABSTRACT		
The PRO should be identified in the abstract as a primary or secondary outcome	Yes	5 (50%)
(If PRO or QOL mentioned in the title/abstract this is sufficient for 'Yes')	Yes	1 (10%)
INTRODUCTION, BACKGROUND AND OBJECTIVES		
Including background and rationale for PRO assessment	Yes	6 (60%)
The PRO hypothesis should be stated and relevant domains identified, if applicable	Yes	6 (60%)
METHODS		
Participants: Not PRO-specific, unless the PROs were used in eligibility or stratification	Yes	10 (100%)
Outcomes: Evidence of PRO instrument validity and reliability should be provided or cited if available	Yes	9 (90%)
Outcomes: States methods of data collection	Not stated	0 (0%)
Outcomes: States who completed the assessment	Patients	10 (100%)
Sample size: Number of participants included in analysis required for PRO results	Yes	10 (100%)
RANDOMIZATION		
Statistical methods: Statistical approaches for dealing with missing data are explicitly stated	Yes	2 (20%)

RESULTS and ANALYSIS		
Participant flow: The number of PRO outcome data at baseline and at subsequent time points should be made transparent	Yes	8 (80%)
Baseline data: Including baseline PRO data when collected	Yes	9 (90%)
Outcomes and estimations: For each primary and secondary outcome, results for each group - for multidimensional PRO results from each domain and time point	Yes	10 (100%)
Outcomes and estimations: The estimated effect size, and it's precision	Effect size not stated	0 (0%)
DISCUSSION		
Limitations: PRO-specific limitations	Yes	3 (30%)
Limitations: Implications for generalizability and implications for clinical practice	Yes	9 (90%)
Interpretation: PRO data should be interpreted in relation to clinical outcomes including survival data, where relevant	Yes	9 (90%)