CPAG Summary Report for Clinical Panel – Policy 1631: Hypofractionated external beam radiotherapy in the treatment of localised prostate cancer

The Benefits of the Proposition			
No	*Outcome measures*	*Grade of evidence*	*Summary from evidence review*
1.	Survival	Not measured	
2.	Progression free survival	There is a survival benefit [A]	After radiotherapy treatment, the level of prostate-specific antigen (PSA) in the blood provides a reasonable indicator of who will go on to develop clinically relevant recurrent prostate cancer. Generally, patients who undergo prostate cancer radiotherapy should have low PSA levels after treatment (under 2.0 ng/mL). Biochemical Failure Free Survival after radiotherapy treatment for prostate cancer means patients' PSA levels do not rise more than 2 ng/mL from nadir PSA (the lowest level recorded at any time after treatment). The CHHiP trial (Dearnaley et al, 2016) reported that after a median follow-up of 62 months the proportion of patients who were biochemical/clinical failure free at 5 years was: • 74 Gy 88.3% (95% confidence interval 86.0-90.2); • 60 Gy 90.6% (95% confidence interval 88.5-92.3); • 57 Gy 85.9% (95% confidence interval 83.4-88.0). The above results provide an estimate of the true value of the proportion of individuals who were biochemical failure free at 5 years in each treatment group. The true population value is contained within the 95% confidence interval range that has been provided. It shows that the

			proportion of individuals treated with hypofractionated radiotherapy (HFRT) were similar in comparison to the conventional fractionated radiotherapy (CFRT) group. The critical hazard ratio (HR) is a statistical method used to compare survival rates between groups and assess if there is non-inferiority (i.e. HFRT is no worse than CFRT). A treatment is assessed as non-inferior if the HR was below 1.208 and the 90% confidence interval did not contain this value. The results from the CHHiP trial (Dearnaley et al 2016) compared the biochemical/clinical failure free survival rates between the groups and reported the corresponding HRs - 60 Gy was shown to be non-inferior to 74 Gy (HR 0.84, 90% confidence interval 0.68-1.03, p=0.0018). Non-inferiority could not be claimed for 57 Gy (HR 1.20, 90% confidence interval 0.99-1.46, p=0.48). There was no heterogeneity of effect for different prostate cancer risk groups (i.e. the effect size was the same). The CHHiP trial (Dearnaley et al, 2016) is the largest and most generalizable study to NHS practice comparing HFRT with CFRT for the treatment of prostate cancer. It is a well-conducted, high quality, randomised controlled trial testing the hypothesis that HFRT is non-inferior for outcomes compared with CFRT.
3.	Mobility	Not measured	
4.	Self-care	Not measured	
5.	Usual activities	Not measured	
6.	Pain	Not measured	

7.	Anxiety / Depression	Not measured	
8.	Replacement of more toxic treatment	Not measured	
9.	Dependency on care giver / supporting independence	Not measured	
10.	Safety	Adverse events identified [A]	Radiotherapy, when being used to treat prostate cancer, may cause unwanted bowel (gastrointestinal) and bladder (genitourinary) symptoms. Safety outcomes in the CHHiP study were measured using the Radiation Therapy Oncology Group toxicity grading. This scores bowel and bladder symptoms from 0 (no symptoms) to 5 (causing death). Short term results reported bowel and bladder symptoms peaked sooner with HFRT schedules (4 - 5 weeks) than CFRT (7 - 8 weeks). There was a higher proportion of grade 2 peak gastrointestinal toxicity in both HFRT groups (CFRT 25%: HFRT 38%; P < 0.0001). By 18 weeks both bowel and bladder toxicity was similar for CFRT/HFRT. There were no differences in long-term side-effects between CFRT and HFRT groups in either the proportion or cumulative incidence of patients reporting grade 2 gastrointestinal/genitourinary toxicity at 5 years (cumulative incidence: 74 Gy: 13.7%/9.1%; 60 Gy: 11.9%/11.7%; 57 Gy: 11.3%/6.6%). There was a slightly higher rate of grade 2 gastrointestinal/genitourinary side-effects in the 60 Gy group compared with 57 Gy at 2 and 5 years. Patient reported outcomes suggest an overall low incidence of gastrointestinal

			and genitourinary symptoms in all treatment groups. The CHHiP study confirmed that HFRT (60Gy/20 fractions schedule) is safe and effective when compared to CFRT. It is a study of high quality and generalizable to NHS practice.
11.	Delivery of intervention	Not measured	

Other health metrics determined by the evidence review			
No	Metric	Grade of evidence	Summary from evidence review
12	Quality of Life (QOL)	Grade A	A number of different qualitative instruments were used to assess this in the CHHiP study: - UCLA Prostate Cancer Index - Short form SF-36 - Functional Assessment of Cancer Therapy Prostate (FACT-P) - Expanded Prostate Cancer Index (EPIC) - Sf-12 QOL Overall this study demonstrated no clinically meaningful differences in QOL outcomes between the schedules. There is very limited data on QOL outcomes in other trials and this is likely to be generalizable.