Supplementary Table and Figures

Clinical estimation of alpha/beta values for prostate cancer from isoeffective phase III randomized trials with moderately hypofractionated radiotherapy, *Datta NR et al*

Supplementary Table I: Radiotherapy treatment details in the seven trials

Author	Radiotherapy technique*	Treatment portals			
		Seminal vesicles in CTV (% patients)		Lymph node	CTV expansion for PTV[#]
		No	Full / base		
PROFIT [4]	3D-CRT/ IMRT	91.6	8.4	No	+10 mm; +7 mm posteriorly
Arcangeli et al [5]	3D-CRT	0	100	No	+10 mm ; +6 mm posteriorly
RTOG 0415 [6]	3D-CRT/ IMRT (79.1%)	100	0	No	+4-10 mm
CHHiP [7]	IMRT	0	100	No	+5-10 mm for sequential PTVs during RT at various doses
HYPRO [8]	3D-CRT/ IMRT (95%)	19.7	80.3	No	+3-10 mm, boost to the seminal vesicles: +3-5 mm, +0 mm posteriorly
Pollack et al [9]	IMRT	0	100	Yes (31.7%)	CRT: +8 mm; +5 mm posteriorly HRT: +7 mm; +3 mm posteriorly
Kuban et al [10]	IMRT[Δ]	0[Δ]	100	No[Δ]	+10-15 mm, +4-8 mm posteriorly[Δ]

*% patients on IMRT indicated wherever available; [#]Posterior margin stated separately if mentioned; [Δ]based on [29]; 3D-CRT: three dimensional conformal radiation therapy; IMRT: intensity-modulated radiotherapy; CTV: clinical target volume; PTV: planning target volume;

Supplementary Table II: Effect measures of odds ratio, risk ratio and risk difference between hypofractionated (HRT) and conventional radiation therapy (CRT) for (a) biochemical failure (b) biochemical and /or clinical failure (c) overall mortality and (d) prostate cancer specific mortality.

Endpoint	Effect measure	Point estimate	95% CI		p value
			Lower	Upper	
Biochemical failure	Odds ratio	0.832	0.686	1.011	ns
	Risk ratio	0.858	0.729	1.009	ns
	Risk difference	-0.020	-0.040	0.001	ns
Biochemical and /or clinical failure	Odds ratio	0.949	0.794	1.134	ns
	Risk ratio	0.956	0.822	1.112	ns
	Risk difference	-0.006	-0.025	0.014	ns
Overall mortality	Odds ratio	0.911	0.786	1.057	ns
	Risk ratio	0.920	0.806	1.049	ns
	Risk difference	-0.008	-0.021	0.005	ns
Prostate cancer specific mortality	Odds ratio	0.849	0.527	1.368	ns
	Risk ratio	0.853	0.537	1.354	ns
	Risk difference	-0.002	-0.007	0.004	ns

ns: not significant

Supplementary Table III

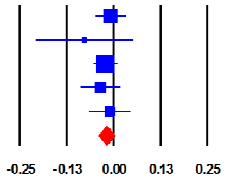
Stepwise multivariate regression including the PROFIT trial [4] for the computed α/β values (dependent variable) for trials between conventional fractionated and hypofractionated radiotherapy.

Model	Unstandardized coefficients		95% CI		Significance
	B	SE	Lower bound	Upper bound	
Constant	3.25	1.25	0.19	6.31	0.04
% low risk patients	0.08	0.03	0.00	0.17	0.05

Model $R^2 = 0.51$; Adjusted $R^2 = 0.43$; ANOVA, F = 6.30, df = 7; p = 0.05.

(a) Risk difference: Biochemical failure (HRT vs. CRT)

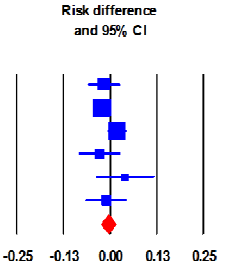
Trial Group / Author	Statistics for each study						Biochem. fail / Total		Relative weight
	Risk difference	Standard error	Lower limit	Upper limit	Z-Value	p-Value	HRT	CRT	
PROFIT [4]	-0.008	0.021	-0.049	0.034	-0.361	0.718	97 / 608	100 / 598	25.66
Arcangeli [5]	-0.077	0.067	-0.209	0.054	-1.153	0.249	18 / 83	25 / 85	2.59
RTOG 0415 [6]	-0.021	0.017	-0.054	0.011	-1.289	0.198	39 / 550	50 / 542	42.42
HYPRO [8]	-0.035	0.028	-0.089	0.020	-1.251	0.211	70 / 407	82 / 397	15.25
Kuban [10]	-0.010	0.029	-0.068	0.047	-0.341	0.733	4 / 102	5 / 102	14.08
Overall	-0.020	0.011	-0.041	0.001	-1.824	0.068	228 / 1750	262 / 1724	



Test for Heterogenity : $I^2 = 0.00$, p : ns

(b) Risk difference: Biochemical and/or clinical failure (HRT vs. CRT)

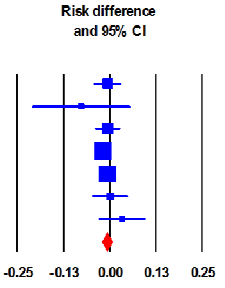
Trial group / Author	Statistics for each study						BCF / Total		Relative weight
	Risk difference	Standard error	Lower limit	Upper limit	Z-Value	p-Value	HRT	CRT	
PROFIT [4]	-0.016	0.022	-0.060	0.028	-0.729	0.466	109 / 608	117 / 598	14.88
CHHiP 60 Gy[7]	-0.022	0.013	-0.047	0.002	-1.775	0.076	88 / 1074	111 / 1065	31.07
CHHiP 57 Gy[7]	0.018	0.014	-0.009	0.045	1.339	0.181	132 / 1077	111 / 1065	28.42
HYPRO [8]	-0.028	0.029	-0.084	0.029	-0.961	0.337	80 / 407	89 / 397	10.05
Pollack [9]	0.041	0.040	-0.039	0.120	1.003	0.316	25 / 151	19 / 152	5.53
Kuban [10]	-0.010	0.029	-0.066	0.047	-0.341	0.733	4 / 102	5 / 102	10.05
Overall	-0.006	0.010	-0.025	0.014	-0.569	0.569	438 / 3419	452 / 3379	



Test for Heterogenity : $I^2 = 0.00$, p : ns

(c) Risk difference: Overall mortality (HRT vs. CRT)

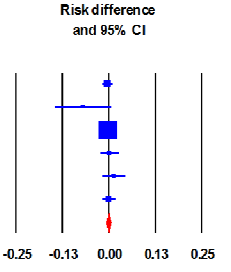
Author (et al) / Study	Statistics for each study						Deaths / Total		Relative weight
	Risk difference	Standard error	Lower limit	Upper limit	Z-Value	p-Value	HRT	CRT	
PROFIT [4]	-0.005	0.019	-0.043	0.032	-0.283	0.777	76 / 608	78 / 598	11.65
Arcangeli [5]	-0.077	0.068	-0.210	0.056	-1.132	0.258	19 / 83	26 / 85	0.93
RTOG 0415 [6]	-0.005	0.017	-0.039	0.029	-0.287	0.774	49 / 550	51 / 542	14.13
CHHiP (60 Gy) [7]	-0.018	0.012	-0.041	0.004	-1.596	0.110	73 / 1074	92 / 1065	32.35
CHHiP (57 Gy) [7]	-0.006	0.012	-0.029	0.018	-0.469	0.639	87 / 1077	92 / 1065	30.10
HYPRO [8]	0.001	0.025	-0.048	0.051	0.050	0.960	61 / 407	59 / 397	6.82
Pollack [9]	0.034	0.033	-0.030	0.098	1.027	0.304	16 / 151	11 / 152	4.03
Overall	-0.008	0.007	-0.021	0.005	-1.259	0.208	381 / 3950	409 / 3904	



Test for Heterogenity : $I^2 = 0.00$, p : ns

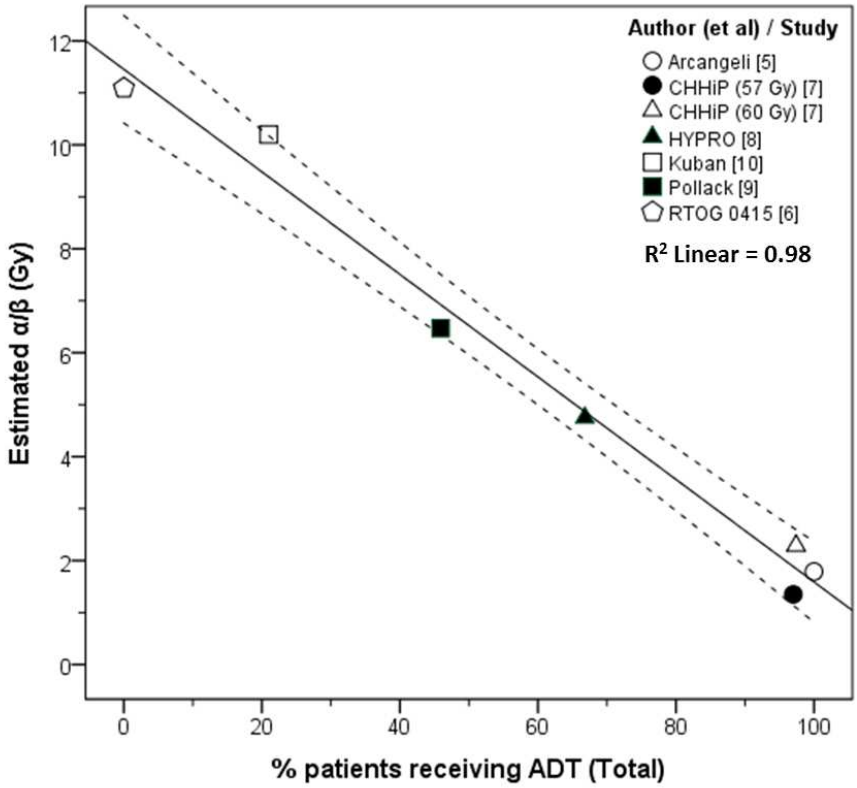
(d) Risk difference: Prostate cancer specific mortality (HRT vs. CRT)

Author (et al) / Study	Statistics for each study						Pr. Ca death / Total		Relative weight
	Risk difference	Standard error	Lower limit	Upper limit	Z-Value	p-Value	HRT	CRT	
PROFIT [4]	-0.004	0.008	-0.019	0.011	-0.469	0.639	10 / 608	12 / 598	12.30
Arcangeli [5]	-0.070	0.039	-0.146	0.007	-1.781	0.075	3 / 83	9 / 85	0.48
RTOG 0415 [6]	-0.002	0.003	-0.008	0.004	-0.589	0.556	1 / 550	2 / 542	72.59
HYPRO [8]	0.002	0.014	-0.025	0.028	0.113	0.910	16 / 407	15 / 397	3.97
Pollack [9]	0.013	0.016	-0.018	0.045	0.833	0.405	4 / 151	2 / 152	2.86
Kuban [10]	0.000	0.010	-0.019	0.019	0.000	1.000	0 / 102	0 / 102	7.80
	-0.002	0.003	-0.007	0.004	-0.627	0.531	34 / 1901	40 / 1876	

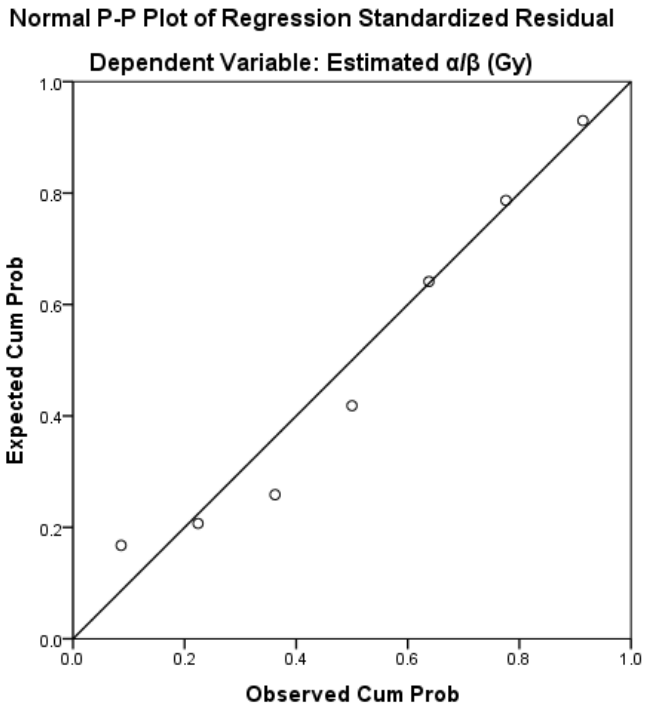


Test for Heterogenity : $I^2 = 0.00$, p : ns

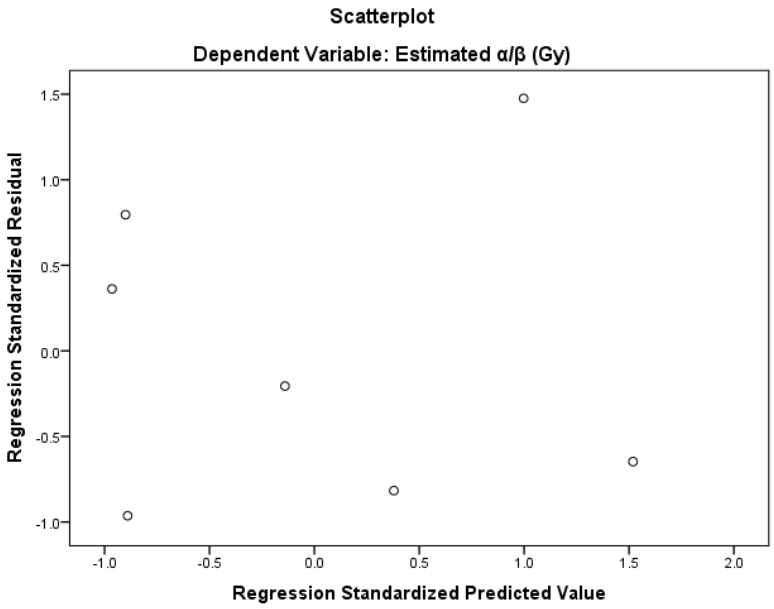
Supplementary Figures 1 a-d: Risk difference between hypofractionated (HRT) and conventional radiation therapy (CRT) for (a) biochemical failure (b) biochemical and /or clinical failure (c) overall mortality and (d) prostate cancer specific mortality.



Supplementary Figure 2. Percentage of patients who received androgen deprivation therapy (ADT) excluding the PROFIT study [4] vs. the estimated α/β for each of the seven isoeffective treatment arms. The linear regression line (in solid) and the 95% confidence intervals (in broken lines) are depicted in the scatterplot.



Supplementary Figure 3a. Normal probability plot of regression standardized residual. Estimated α/β values were considered as dependent variable with all trials except the PROFIT study [4].



Supplementary Figure 3b: Scatter plot between standardized predicted and residual values with all trials except the PROFIT study [4].