Table 18: Clinical evidence profile: Comparison 1. No whole breast radiotherapy versus whole breast radiotherapy

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RT-	RT+	Relative (95% CI)	Absolute	Quality	Importance
Overall survival - T stage: 1 (12 year follow-up)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	None	26/125 (20.8%)	21/138 (15.2%)	HR 1.59 (1.29 to 1.96)	79 more per 1000 (from 40 more to 124 more)	MODERATE	IMPORTANT
Overall survival - N stage: 0 (5 to 12 year follow-up)												
3	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	No serious imprecision	None	210/572 (36.7%)	200/582 (34.4%)	HR 1.29 (1.12 to 1.5)	75 more per 1000 (from 32 more to 125 more)	MODERATE	IMPORTANT
Overall survival - Margins: negative (5 to 12 year follow-up)												
3	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	No serious imprecision	None	210/572 (36.7%)	200/582 (34.4%)	HR 1.29 (1.12 to 1.5)	75 more per 1000 (from 32 more to 125 more)	MODERATE	IMPORTANT
Overall survival - Age: 65+ (5 to 10 year follow-up)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	184/447 (41.2%)	179/444 (40.3%)	HR 1.06 (0.87 to 1.3)	18 more per 1000 (from 41 fewer to 86 more)	HIGH	IMPORTANT
Overall survival - Adjuvant systemic therapy: none (20 year follow-up)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RT-	RT+	Relative (95% CI)	Absolute		
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[3]	None	106/197 (53.8%)	92/184 (50%)	HR 1.1 (0.85 to 1.42)	33 more per 1000 (from 55 fewer to 126 more)	MODERATE	IMPORTANT
Local recurrence - T stage: 1 (10 to 12 year follow-up)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[3]	None	91/682 (13.3%)	38/696 (5.5%)	HR 2.7 (1.84 to 3.97)	86 more per 1000 (from 44 more to 145 more)	MODERATE	CRITICAL
Local recurrence - N stage: 0 (5 to 12 year follow-up)												
4	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[3]	None	149/1669 (8.9%)	49/1671 (2.9%)	HR 3.22 (2.31 to 4.49)	62 more per 1000 (from 37 more to 96 more)	MODERATE	CRITICAL
Local recurrence - Margins: negative (5 to 12 year follow-up)												
4	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[3]	None	149/1669 (8.9%)	49/1671 (2.9%)	HR 3.22 (2.31 to 4.49)	62 more per 1000 (from 37 more to 96 more)	MODERATE	CRITICAL
Local recurrence - Age: 65+ (5 to 10 year follow-up)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	58/987 (5.9%)	11/975 (1.1%)	HR 5.35 (2.78 to 10.29)	48 more per 1000 (from 20 more to 99 more)	LOW	CRITICAL
Treatment-related morbidity – fractures (cause unspecified; all patients N stage 0, 65+, negative margins; 5 year follow-up)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RT-	RT+	Relative (95% CI)	Absolute		
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[4]	None	10/86 (11.6%)	9/85 (10.6%)	RR 1.10 (0.47 to 2.57)	11 more per 1000 (from 56 fewer to 166 more)	LOW	CRITICAL
Treatment-related morbidity - congestive cardiac failure (all patients N stage 0, 65+, negative margins; 5 year follow-up)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[8]	None	3/86 (3.5%)	3/85 (3.5%)	RR 0.99 (0.21 to 4.76)	0 fewer per 1000 (from 28 fewer to 133 more)	MODERATE	CRITICAL
Treatment-related morbidity - myocardial infarction (all patients N stage 0, 65+, negative margins; 5 year follow-up)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[4]	None	5/86 (5.8%)	6/85 (7.1%)	RR 0.82 (0.26 to 2.6)	13 fewer per 1000 (from 52 fewer to 113 more)	LOW	CRITICAL
Treatment-related morbidity - secondary cancer (cause unspecified; all patients N stage 0, 65+, negative margins; 5 year follow-up)												
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	35/754 (4.6%)	26/743 (3.5%)	RR 2.53 (0.24 to 26.51)	-	LOW	CRITICAL
Treatment-related morbidity - score 10+ on HADS depression scale (all patients N stage 0, 65+, negative margins; 5 year follow-up)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**RT-**	**RT+**	**Relative (95% CI)**	**Absolute**		
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[4]	None	3/101 (3%)	1/105 (1%)	RR 3.12 (0.33 to 29.49)	20 more per 1000 (from 6 fewer to 271 more)	LOW	CRITICAL
Treatment-related morbidity - score 10+ on HADS anxiety scale (all patients N stage 0, 65+, negative margins; 5 year follow-up)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[4]	None	12/101 (11.9%)	9/105 (8.6%)	RR 1.39 (0.61 to 3.15)	33 more per 1000 (from 33 fewer to 184 more)	LOW	CRITICAL
HRQoL - EQ5D scale (all patients N stage 0, 65+, negative margins; 5 year follow-up) (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[5]	None	83	85	-	MD 0.02 lower (0.1 lower to 0.06 higher)	LOW	CRITICAL
HRQoL - reduction in scores on Breast Cancer Chemotherapy Questionnaire (all patients N stage 0, negative margins; 2 month follow-up)												
1	Randomised trials	[6]	No serious inconsistency	7	Serious3	None	60/376 (16%)	93/344 (27%)	RR 0.59 (0.44 to 0.79)	111 fewer per 1000 (from 57 fewer to 151 fewer)		CRITICAL

CI: Confidence interval; EQ5D, EuroQol Research Foundation measure of general health status; HADS: Hospital Anxiety and Depression Scale; HR: Hazard ratio; HRQoL: Health related quality of life; RR: Risk ratio;

[1] <300 events

[2] Random effects model with significant heterogeneity - I squared value 74% - not possible to investigate heterogeneity as additional subgroups of interest identified by the GC were not reported for the trials that contributed to this estimate. All estimated effects were in the same direction

[3] *Total events <300*
[4] *<300 events and 95% CI crosses both thresholds for minimally important difference based on GRADE default values (0.80 and 1.25)*
[5] *N<400*
[6] *Insufficient evidence available to rate risk of bias*
[7] *Insufficient information available to judge whether evidence is indirect*
[8] *total events<300; not downgraded based on 95% CI due to very small differences in absolute risk*