Review protocol for 8.3 Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery?

Field (based on PRISMA-P)	Content
Review question	Is there a subgroup of women with early invasive breast cancer for whom partial breast radiotherapy is an equally effective alternative to whole breast radiotherapy after breast-conserving surgery?
Type of review question	Intervention review
Objective of the review	This review of evidence seeks to establish whether there is a subgroup of women with early breast cancer for whom partial breast radiotherapy is an equally effective treatment strategy, with less potential side effects, than whole breast radiotherapy. Recommendations will aim to cover which group of women should be offered partial breast radiotherapy.
Eligibility criteria – population/disease/condition/issue/domain	Women (18 or over) with HER2 - invasive breast cancer (M0) who have undergone breast conserving surgery (with clear margins) and are recommended radiotherapy
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Partial breast radiotherapy: Brachytherapy Intrabeam RT (removed as it is the subject of a separate NICE Technology Appraisal) 3D-Conformal RT Intensity modulated RT
Eligibility criteria – comparator(s)/control or reference (gold) standard	Whole breast radiotherapy
Outcomes and prioritisation	Critical (up to 3 outcomes) • Local recurrence rate (MID: any statistically significant difference) • Treatment-related morbidity(e.g., pulmonary toxicity [MID: any statistically significant difference], lung cancer [MID: any statistically significant difference]) • HRQoL(MID: values from the literature where available; GRADE default value for FACT-B endocrine scale) Important but not critical • Overall survival (MID: any statistically significant difference) • Disease-free survival (MID: any statistically significant difference) • Treatment-related mortality (MID: any statistically significant difference)

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	• Unplanned additional radiotherapy (Intrabeam only) 5 year follow-up periods will be prioritised when multiple time points are reported. MID values from the literature: HRQoL: • FACT-G total: 3-7 points • FACT-B total: 7-8 points • TOI (trial outcome index) of FACT-B: 5-6 points • BCS of FACT-B: 2-3 points • WHOQOL-100: 1 point
Eligibility criteria – study design	• Systematic reviews/meta-analyses of RCTs • RCTs
Other inclusion exclusion criteria	Foreign language studies, conference abstracts, and narrative reviews will not routinely be included.
Proposed sensitivity/sub-group analysis, or meta-regression	Subgroups (critical outcomes only – excluding treatment-related morbidity): • T Stage • N stage • Age (<50, >50, >60, >70) • Grade • ER status
Selection process – duplicate screening/selection/analysis	Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the reviewing team. Quality control will be performed by the senior systematic reviewer. Dual sifting not be performed for this review question as it is a straightforward intervention review.
Data management (software)	Study sifting and data extraction will be undertaken in STAR. Pairwise meta-analyses will be performed using Cochrane Reviewer Manager (RevMan 5). GRADEpro will be used to assess the quality of evidence for each outcome.
Information sources – databases and dates	The following key databases will be searched: Cochrane Library (CDSR, DARE, CENTRAL, HTA) through Wiley, Medline & Medline in Process and Embase through

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	OVID. Additionally Web of Science may be searched and consideration will be given to subject-specific databases and used as appropriate. The search will be undertaken from 1996 to capture studies using modern radiotherapy techniques. A general exclusions filter and methodological filters (RCT and systematic review) will also be used as it is an intervention question.
Identify if an update	N/A
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see Section 4.5 of Developing NICE guidelines: the manual
Search strategy	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or appendix H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or appendix H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see Section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see Section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods chapter.
Meta-bias assessment – publication bias, selective reporting bias	For details please see Section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see Sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the NGA and chaired by Dr Jane Barrett in line with section 3 of Developing NICE guidelines: the manual.

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	Staff from NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter.
Sources of funding/support	NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for the NHS in England.
PROSPERO registration number	N/A

BCS, breast cancer subscale; ER, oestrogen recptor; FACT-B, Functional assessment of cancer therapy – Breast cancer; FACT-G, Functional assessment of cancer therapy – General; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HER2, human epidermal growth factor receptor 2; HRQoL, health-related quality of life; MID, minimally important difference; N/A, not applicable; NHS, National Health Service, NICE, National Institute of Health and Care Excellence; NGA, National Guideline Alliance; RCT, randomised controlled trial; RT, radiotherapy; TOI, Trial outcome index; WHOQOL, World Health Organization quality of life