Review protocol for 8.2 Is there a subgroup of people with early invasive breast cancer who do not need breast radiotherapy after breast-conserving surgery?

Field (based on PRISMA-P)	Content
Review question	Is there a subgroup of people with early invasive breast cancer who do not need 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 who are at such low risk of local recurrence after breast conserving surgery that the benefits of radiotherapy are unlikely to outweigh the risks. Recommendations will aim to cover groups of women where the option of omission of radiotherapy should be discussed as an alternative to whole breast radiotherapy.
Eligibility criteria – population/disease/condition/issue/domain	Women (18 or over) with invasive breast cancer (M0) who have undergone breast conserving surgery
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	No breast radiotherapy
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: GRADE default values], lung cancer [MID: any statistically significant difference]) any • HRQoL (MID: values from the literature where available, otherwise GRADE default values) 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) 10 year follow-up periods will be prioritised when multiple time points are reported. MID values from the literature: • HRQoL:

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	• 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: T Stage N stage Age (<65, 65 and over) Adjuvant systemic therapy (whether or not received therapy) Grade Margins (+/- note definitions in the studies) ER status HER-2 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 will not be performed for this review question as it is a straightforward intervention review limited to RCTs.
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 OVID. Additionally Web of Science may be searched and consideration will be given to subject-specific databases and used as appropriate.

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	Searches will be undertaken from 2008 onwards as it is an update from the previous version of this guideline. 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	Previous question: What are the indications for radiotherapy after breast conserving surgery? Date of search: 28/02/2008 Relevant recommendation(s) from previous guideline: 1) Patients with early invasive breast cancer who have had breast conserving surgery with clear margins should have breast radiotherapy.
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

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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. 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 of the full guideline.
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 receptor; 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