

Early and locally advanced breast cancer: diagnosis and management

Supplement 1: Health economics literature review

NICE guideline tbc

Evidence reviews

January 2018

Draft for Consultation

Supplementary materials were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the [Welsh Government](#), [Scottish Government](#), and [Northern Ireland Executive](#). All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© National Institute for Health and Care Excellence, 2018. All rights reserved. Subject to [Notice of Rights](#).

ISBN:

Contents

Health economics literature review	5
Information sources and eligibility criteria	5
Literature search strategies for health economic evidence	5
Database: Medline	5
Database: Health Technology Assessment Database via Wiley Online	7
Database: NHS Economic Evaluation Database	7
Database: Embase	8
Economic evidence study selection	9
Economic evidence tables	11
Economic evidence	15
Included studies	15
Excluded studies	15

1 Health economics literature review

2 A literature search was carried out across all guideline topics for any health economic studies
3 relating to the management of early and invasive breast cancer. This supplement contains
4 details of this evidence search and the systematic review process.

5 Information sources and eligibility criteria

6 The following databases were searched for economic evidence relevant to the PICO:
7 MEDLINE, EMBASE, COCHRANE, NHS EED and HEED. Studies were selected for
8 inclusion in the evidence review if the following criteria were met:

- 9 • both cost and health consequences of interventions reported (that is, true cost-
10 effectiveness analyses)
- 11 • conducted in an OECD country
- 12 • incremental results are reported or enough information is presented to allow incremental
13 results to be derived
- 14 • studies that matched the population, interventions, comparators and outcomes specified
15 in PICO
- 16 • studies that meet the applicability and quality criteria set out by NICE, including relevance
17 to the NICE reference case and UK NHS.

18 Note that studies that measured effectiveness using quality of life based outcomes (for
19 example, quality adjusted life years [QALYs]) were desirable but, where this evidence was
20 unavailable, studies using alternative effectiveness measures (for example, life years) were
21 considered.

22 Literature search strategies for health economic evidence

23 Database: Medline

24 Last searched on **Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid**
25 **MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present.**

26 Date of last search: 29 September 2017.

#	Searches
1	exp Breast Neoplasms/
2	exp "Neoplasms, Ductal, Lobular, and Medullary"/
3	Carcinoma, Intraductal, Noninfiltrating/
4	Carcinoma, Lobular/
5	Carcinoma, Medullary/
6	1 or 2 or 3 or 4 or 5
7	exp Breast/
8	breast.tw.
9	7 or 8
10	(breast adj milk).tw.
11	(breast adj tender\$.tw.
12	10 or 11
13	9 not 12
14	exp Neoplasms/
15	13 and 14

#	Searches
16	(breast\$ adj5 (neoplasm\$ or cancer\$ or tumor\$ or carcinoma\$ or adenocarcinoma\$ or sarcoma\$ or leiomyosarcoma\$ or dcis or duct\$ or infiltrat\$ or intraduct\$ or lobul\$ or medullary or tubular)).mp.
17	(mammary\$ adj5 (neoplasm\$ or cancer\$ or tumor\$ or carcinoma\$ or adenocarcinoma\$ or sarcoma\$ or leiomyosarcoma\$ or dcis or duct\$ or infiltrat\$ or intraduct\$ or lobul\$ or medullary or tubular)).mp.
18	Paget's Disease, Mammary/
19	(paget\$ and (breast\$ or mammary or nipple\$)).tw.
20	15 or 16 or 17 or 18 or 19
21	6 or 20
22	Economics/
23	"costs and cost analysis"/
24	Cost allocation/
25	Cost-benefit analysis/
26	Cost control/
27	Cost savings/
28	Cost of illness/
29	Cost sharing/
30	"deductibles and coinsurance"/
31	Medical savings accounts/
32	Health care costs/
33	Direct service costs/
34	Drug costs/
35	Employer health costs/
36	Hospital costs/
37	Health expenditures/
38	Capital expenditures/
39	Value of life/
40	exp economics, hospital/
41	exp economics, medical/
42	Economics, nursing/
43	Economics, pharmaceutical/
44	exp "fees and charges"/
45	exp budgets/
46	(low adj cost).mp.
47	(high adj cost).mp.
48	(health?care adj cost\$).mp.
49	(fiscal or funding or financial or finance).tw.
50	(cost adj estimate\$).mp.
51	(cost adj variable).mp.
52	(unit adj cost\$).mp.
53	(economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.
54	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53
55	letter.pt.
56	editorial.pt.

#	Searches
57	historical article.pt.
58	55 or 56 or 57
59	54 not 58
60	21 and 59

1 Database: Health Technology Assessment Database via Wiley Online

2 Last searched on **Health Technology Assessment Database: Issue 4 of 4, October 2016**
3 via Wiley Online.

4 Date of last search: 29 September 2017.

#	Searches
#1	MeSH descriptor: [Breast Neoplasms] explode all trees
#2	MeSH descriptor: [Neoplasms, Ductal, Lobular, and Medullary] explode all trees
#3	MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] explode all trees
#4	MeSH descriptor: [Carcinoma, Lobular] this term only
#5	MeSH descriptor: [Carcinoma, Medullary] this term only
#6	#1 or #2 or #3 or #4 or #5
#7	MeSH descriptor: [Breast] explode all trees
#8	breast:ti,ab,kw (Word variations have been searched)
#9	#7 or #8
#10	(breast next milk):ti,ab,kw (Word variations have been searched)
#11	(breast next tender*):ti,ab,kw (Word variations have been searched)
#12	#10 or #11
#13	#9 not #12
#14	MeSH descriptor: [Neoplasms] explode all trees
#15	#13 and #14
#16	(breast* near/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular)):ti,ab,kw (Word variations have been searched)
#17	(mammar* near/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular)):ti,ab,kw (Word variations have been searched)
#18	MeSH descriptor: [Paget's Disease, Mammary] this term only
#19	(paget* and (breast* or mammary or nipple*)):ti,ab,kw (Word variations have been searched)
#20	#15 or #16 or #17 or #18 or #19
#21	#6 or #20

5 Database: NHS Economic Evaluation Database

6 Last searched on **NHS Economic Evaluation Database: Issue 2 of 4, April 2015** via Wiley
7 Online.

8 Date of last search: 29 September 2017.

#	Searches
#1	MeSH descriptor: [Breast Neoplasms] explode all trees
#2	MeSH descriptor: [Neoplasms, Ductal, Lobular, and Medullary] explode all trees
#3	MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] explode all trees

#	Searches
#4	MeSH descriptor: [Carcinoma, Lobular] this term only
#5	MeSH descriptor: [Carcinoma, Medullary] this term only
#6	#1 or #2 or #3 or #4 or #5
#7	MeSH descriptor: [Breast] explode all trees
#8	breast:ti,ab,kw (Word variations have been searched)
#9	#7 or #8
#10	(breast next milk):ti,ab,kw (Word variations have been searched)
#11	(breast next tender*):ti,ab,kw (Word variations have been searched)
#12	#10 or #11
#13	#9 not #12
#14	MeSH descriptor: [Neoplasms] explode all trees
#15	#13 and #14
#16	(breast* near/5 (neoplasm* or cancer* or tumor?* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular)):ti,ab,kw (Word variations have been searched)
#17	(mammar* near/5 (neoplasm* or cancer* or tumor?* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular)):ti,ab,kw (Word variations have been searched)
#18	MeSH descriptor: [Paget's Disease, Mammary] this term only
#19	(paget* and (breast* or mammary or nipple*)):ti,ab,kw (Word variations have been searched)
#20	#15 or #16 or #17 or #18 or #19
#21	#6 or #20

1 Database: Embase

2 Last searched on **OID Embase** 1974 to 2017 September 28.

3 Date of last search: 29 September 2017.

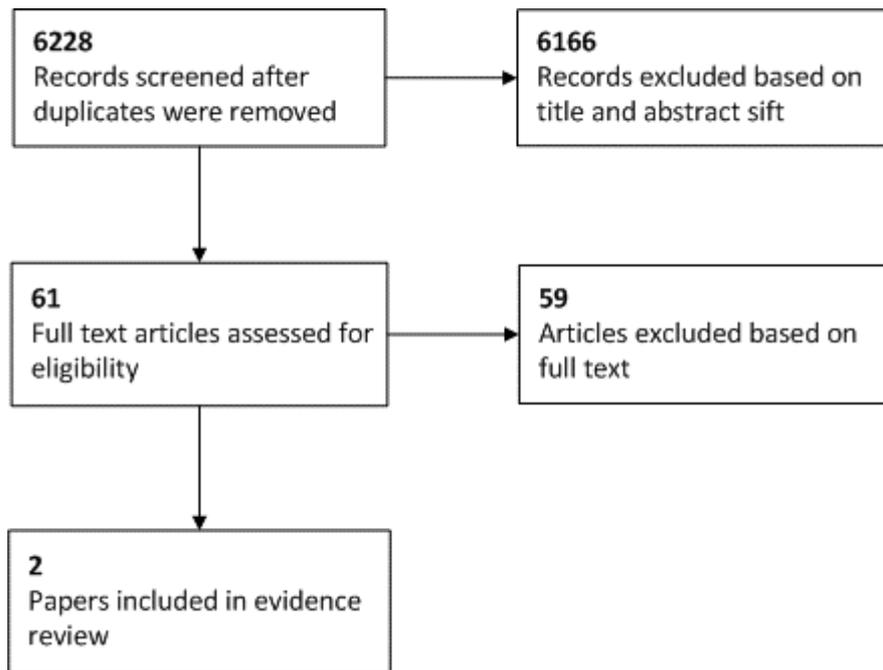
#	Searches
1	exp breast cancer/
2	exp breast carcinoma/
3	exp medullary carcinoma/
4	exp intraductal carcinoma/
5	exp breast tumor/
6	1 or 2 or 3 or 4 or 5
7	exp breast/
8	breast.tw.
9	7 or 8
10	(breast adj milk).tw.
11	(breast adj tender\$.tw.
12	10 or 11
13	9 not 12
14	exp neoplasm/
15	13 and 14
16	(breast\$ adj5 (neoplasm\$ or cancer\$ or tumor?\$ or carcinoma\$ or adenocarcinoma\$ or sarcoma\$ or leiomyosarcoma\$ or dcis or duct\$ or infiltrat\$ or intraduct\$ or lobul\$ or medullary or tubular)).tw.

#	Searches
17	(mammar\$ adj5 (neoplasm\$ or cancer\$ or tumo?r\$ or carcinoma\$ or adenocarcinoma\$ or sarcoma\$ or leiomyosarcoma\$ or dcis or duct\$ or infiltrat\$ or intraduct\$ or lobul\$ or medullary or tubular)).tw.
18	exp Paget nipple disease/
19	(paget\$ and (breast\$ or mammary or nipple\$)).tw.
20	15 or 16 or 17 or 18 or 19
21	6 or 20
22	"Cost Benefit Analysis"/
23	"Cost Effectiveness Analysis"/
24	"Cost Minimization Analysis"/
25	"Cost of Illness"/
26	"Cost Control"/
27	"Cost Utility Analysis"/
28	Economic Aspect/
29	"COST"/
30	Financial Management/
31	"Health Care Cost"/
32	exp "Hospital Cost"/
33	Economic Evaluation/
34	Health Economics/
35	(fiscal or financial or finance\$ or funding).tw.
36	(cost adj estimate\$).tw.
37	(cost adj variable\$).tw.
38	(unit adj cost\$).tw.
39	(health?care adj cost\$).tw.
40	(economic\$ or price\$ or pricing).tw.
41	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42	letter.pt.
43	editorial.pt.
44	42 or 43
45	41 not 44
46	21 and 45

1 Economic evidence study selection

- 2 The literature search results were screened by checking the titles and abstracts for relevance
- 3 to the review question. The full articles of non-excluded studies were then obtained for
- 4 appraisal and compared against the inclusion criteria specified above. Figure 1 shows the
- 5 search results and study selection process.

1 **Figure 1: Summary of health-economic evidence search and sifting process**



2

3 It can be seen that 6,228 possibly relevant papers were identified. Of these, 6,166 papers
4 were excluded at the initial sifting stage based on the title and abstract while 61 full papers
5 were obtained for appraisal. A further 59 papers were excluded based on the full text as they
6 were not applicable to the PICO or did not include an incremental analysis of both costs and
7 health effects. Therefore, 2 papers were included in the systematic review of the economic
8 evidence; Erman 2014 and Shah 2013. Both studies included a cost-effectiveness analysis
9 where effectiveness was measured using QALYs, that is a cost-utility analysis.

10 The identified studies were applicable to 2 review questions in the guideline. The applicable
11 studies under each of these review questions are described below.

12

Economic evidence tables

Table 1: Summary table showing the included health economic evidence for the optimal duration of adjuvant endocrine therapy for people with oestrogen-receptor positive breast cancer (review question 4.1, see evidence report [D] for full details)

Study	Population	Comparators	Costs	Effects	Incr costs	Incr effects	ICER	Uncertainty	Applicability and limitations	
Erman 2014	Post-menopausal women with early stage (stage I-III) HR+ breast cancer.	Comparison against standard tamoxifen							A series of one-way sensitivity analyses were conducted exploring changes in costs and clinical inputs. The result was found to be sensitive to changes in the cost of aromatase inhibitors and the probability of recurrence when taking aromatase inhibitors or tamoxifen. Probabilistic sensitivity analysis was conducted. At the conventional threshold of \$50,000 (CAD) per QALY, the probability of being cost-effective was 70% for extended aromatase inhibitors, 30% for extended tamoxifen and 0.003% for standard tamoxifen.	The study was deemed to be only partially applicable to the UK because it considered the perspective of the Canadian health care system. The study was generally thought to be of good quality but some potentially serious limitations were noted such as the absence of some potentially key parameters from sensitivity analysis (utility weights).
		Standard tamoxifen	\$9,343.66 (CAD)	10.12 QALYs	Reference					
		Extended tamoxifen	\$8,623.06 (CAD)	10.38 QALYs	-\$720.60 (CAD)	0.26 QALYs	Dominant			
		Extended aromatase inhibitors	\$9,432.73 (CAD)	10.62 QALYs	\$89.07 (CAD)	0.50 QALYs	\$178.14 (CAD)			
		Dominance rank								
		Extended tamoxifen	\$8,623.06 (CAD)	10.38 QALYs	Reference					
		Standard tamoxifen	\$9,343.66 (CAD)	10.12 QALYs	\$720.60 (CAD)	-0.26 QALYs	Dominated			
		Extended aromatase inhibitors	\$9,432.73 (CAD)	10.62 QALYs	\$809.66 (CAD)	0.24 QALYs	\$3,402.38 (CAD) per QALY			
<p>Comments: Strategies compared using 'dominance rank' approach to determine optimal strategy overall. Strategies are first ranked in terms of cost (least costly to most costly). The second intervention in the list is then compared against the first strategy. Subsequent strategies are then compared against the previous strategy that was found to be cost-effective.</p> <p>Strategies compared against standard tamoxifen were not reported in study but have been estimated here as they were of most relevance to the review question.</p>										

Table 2: Economic evidence table showing the included health economic evidence for the optimal duration of adjuvant endocrine therapy for people with oestrogen-receptor positive breast cancer (review question 8.3, see evidence report [H] for full details)

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
<p>Author & year: Shah 2013</p> <p>Country: United States of America (USA)</p> <p>Type of economic analysis: Cost-utility analysis</p> <p>Source of funding: Not reported.</p>	<p>Accelerated partial breast radiotherapy (APBRT) techniques were compared against whole beam radiotherapy (WBRT) techniques. Various APBRT and WBRT techniques were considered:</p> <p>APBRT techniques</p> <p>3D Conformal radiotherapy (CT)</p> <p>Intensity modulated radiotherapy (IMRT)</p> <p>Single lumen (SL)</p> <p>Multi lumen (ML)</p> <p>Interstitial</p> <p>WBRT techniques</p> <p>3D Conformal radiotherapy (CT)</p> <p>Intensity modulated radiotherapy (IMRT)</p>	<p>Population characteristics: Women with invasive early stage (breast cancer).</p> <p>Modelling approach: Cost-efficacy analysis and cost-utility analysis (results reported here reflect cost-utility analysis).</p> <p>Source of base-line and effectiveness data: Matched pair analyses of cohort data for patients treated with APBI and WBI was used to inform analysis. It was assumed that WBI and APBI effectiveness was the same regardless of technique. WBI effectiveness was based on data from traditional techniques (2D and 3D CRT) and this was extended to newer techniques (IMRT). APBI effectiveness was based on data from interstitial technique and it was assumed to be equivalent to all other APBI techniques (based on a trial which found no difference in outcome between techniques).</p> <p>Source of cost data: Costs were based on reimbursement</p>	<p>APBRT techniques compared against WBRT – 3D CRT</p> <p>Mean (and incremental) cost per patient</p> <p>WBRT – 3D CRT: \$11,726</p> <p>APBRT – 3DCRT: \$6,578 (-\$5,148)</p> <p>APBRT –IMRT: \$10,547 (-\$1,179)</p> <p>APBRT –SL: \$12,602 (\$876)</p> <p>APBRT –ML: \$16,439 (\$4,713)</p> <p>APBRT –Interstitial: \$11,765 (\$39)</p> <p>-</p> <p>Mean (and incremental) QALYs per patient:</p> <p>WBRT – 3D CRT: 10.84 QALYs</p> <p>APBRT – 3DCRT: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –IMRT: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –SL: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –ML: 10.91 QALYs (0.07 QALYs)</p>	<p>Perspective: Multiple perspectives were considered as various costs were included. Results reported here focus on reimbursement costs and therefore reflect the US health care payer perspective.</p> <p>Currency: US dollars (\$)</p> <p>Cost year: 2011.</p> <p>Time horizon: Not reported</p> <p>Discounting: Not reported.</p> <p>Applicability: The analysis was only partially applicable to</p>

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
		<p>costs from Medicare schedules for each treatment technique. Costs associated with recurrence and distant disease were sourced from a published cost analysis. Follow-up costs were not considered in the analysis because of the similarity in follow-up between treatment strategies.</p> <p>In some scenarios, non-medical costs were incorporated based on costs from a previous analysis.</p> <p>Source of QoL data:</p> <p>QoL values were sourced from a previous cost-effectiveness analysis. QoL values were applied for three health states (no recurrence, recurrence and distant metastases).</p>	<p>APBRT –Interstitial: 10.91 QALYs (0.07 QALYs)</p> <p>ICERs:</p> <p>APBRT – 3DCRT: Dominant</p> <p>APBRT –IMRT: Dominant</p> <p>APBRT –SL: \$12,514 per QALY</p> <p>APBRT –ML: \$67,329 per QALY</p> <p>APBRT –Interstitial: \$557 per QALY</p> <p>APBRT techniques compared against WBRT – IMRT</p> <p>Mean (and incremental) cost per patient</p> <p>WBRT – IMRT: \$20,637</p> <p>APBRT – 3DCRT: \$6,578 (-\$14,059)</p> <p>APBRT –IMRT: \$10,547 (-\$10,090)</p> <p>APBRT –SL: \$12,602 (-\$8,035)</p> <p>APBRT –ML: \$16,439 (-\$4,198)</p> <p>APBRT –Interstitial: \$11,765 (-\$8,872)</p> <p>-</p> <p>Mean (and incremental) QALYs per patient:</p> <p>WBRT – IMRT: 10.84 QALYs</p> <p>APBRT – 3DCRT: 10.91 QALYs (0.07</p>	<p>the UK context since it considered the US health care system.</p> <p>Limitations:</p> <p>Serious limitations were identified in the analysis. Most notably, uncertainty around the base case estimates was not assessed as no deterministic or probabilistic sensitivity analyses were conducted. Also the modelled time horizon was not clear and the discount rate was not reported (possible that no discount rates were used).</p> <p>Other comments:</p> <p>Incremental costs and QALYs were not reported in the study. Incremental values above have therefore been estimated as the difference between the absolute values reported in the study.</p> <p>Note also that the study presents costs under numerous scenarios. The costs presented</p>

Study details	Treatment strategies	Study population, design and data sources	Results	Comments
			<p>QALYs)</p> <p>APBRT –IMRT: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –SL: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –ML: 10.91 QALYs (0.07 QALYs)</p> <p>APBRT –Interstitial: 10.91 QALYs (0.07 QALYs)</p> <p>ICERs:</p> <p>APBRT – 3DCRT: Dominant</p> <p>APBRT –IMRT: Dominant</p> <p>APBRT –SL: Dominant</p> <p>APBRT –ML: Dominant</p> <p>APBRT –Interstitial: Dominant</p> <p>Subgroup analysis:</p> <p>Not conducted.</p> <p>Sensitivity analysis:</p> <p>No deterministic or probabilistic sensitivity analyses were conducted.</p>	<p>above are for reimbursement costs only as it was thought to best reflect the third party perspective (other scenarios reported in the analysis included ‘non-medical’ costs which possibly include costs more applicable to the societal perspective).</p>

1 Economic evidence

2 Included studies

3 Erman 2014

4 Erman, A., et al., Cost-effectiveness analysis of extended adjuvant endocrine therapy
5 in the treatment of post-menopausal women with hormone receptor positive breast
6 cancer. *Breast Cancer Research & Treatment*, 2014. 145(2): p. 267-79.

7 Shah 2013

8 Shah, C., et al., Cost-efficacy of acceleration partial-breast irradiation compared with
9 whole-breast irradiation. *Breast Cancer Research & Treatment*, 2013. 138(1): p. 127-
10 35.

11 Excluded studies

12 Table 3: Excluded studies health economic evidence.

Excluded studies - health economic evidence for early and locally advanced breast cancer	
Study	
Ali, A.A., et al., (2017) Comparative cost-effectiveness of early-stage breast cancer treatments in the elderly. <i>Value in Health</i> , 20 (5), A9.	
Amadio, G., et al., (2016) Bilateral salpingo-oophorectomy versus GNRH analogue in the adjuvant treatment of premenopausal breast cancer patients: Cost-effectiveness evaluation of breast cancer outcome. <i>International Journal of Gynecological Cancer</i> , 26, 259.	
Al-Khudairi, R., et al., (2017) Systematic review of the economic impact of re-operation in breast-conserving surgery: Assessment of quality using the QHES instrument. <i>European Journal of Surgical Oncology</i> , 43 (5), S30.	
Ansaripour, A., C.A. Uyl-de Groot, and W.K. Redekop, (2107) Adjuvant Trastuzumab Therapy for Early HER2-Positive Breast Cancer in Iran: A Cost-Effectiveness and Scenario Analysis for an Optimal Treatment Strategy. <i>PharmacoEconomics</i> , 1-13.	
Attard, C.L., et al., (2015) Cost-effectiveness analysis of neoadjuvant pertuzumab and trastuzumab therapy for locally advanced, inflammatory, or early HER2-positive breast cancer in Canada. <i>Journal of Medical Economics</i> ,18(3), 173-88.	
Bhattacharya, K. and Y. Yang, (2016) A cost-effectiveness analysis of palbociclib and other aromatase inhibitors for treatment of advanced breast cancer. <i>Value in Health</i> , 19 (3), A150.	
Bonastre, J., et al., (2014) Cost effectiveness of molecular profiling for adjuvant decision making in patients with node-negative breast cancer. <i>Journal of Clinical Oncology</i> , 32(31), 3513-9.	
Chagpar, A.B., et al., (2017) Economic Impact of Routine Cavity Margins Versus Standard Partial Mastectomy in Breast Cancer Patients: Results of a Randomized Controlled Trial. <i>Annals of Surgery</i> , 265(1), 39-44.	
Chatterjee, A., et al., (2017) A cost-utility analysis comparing large volume displacement oncoplastic surgery to mastectomy with single stage implant reconstruction in the treatment of breast cancer. <i>Annals of Surgical Oncology</i> , 24 (2 Supplement 1), 239-240.	
Clarke, C.S., et al., (2017) Multi-arm Cost-Effectiveness Analysis (CEA) comparing different durations of adjuvant trastuzumab in early breast cancer, from the English NHS payer perspective. <i>PLoS ONE [Electronic Resource]</i> , 12(3), e0172731.	
Colomer, R., et al., (2016) Cost-utility analysis of neoadjuvant chemotherapy with pertuzumab, trastuzumab and docetaxel in patients with HER2+ breast cancer in	

Excluded studies - health economic evidence for early and locally advanced breast cancer

Study

spaincost-utility analysis of neoadjuvant chemotherapy with pertuzumab, trastuzumab and docetaxel in patients with HER2+ breast cancer in Spain. *Value in Health*, 19 (7), A740.

Das, R., et al., (2013) Economic evaluation of fulvestrant 500 mg versus generic nonsteroidal aromatase inhibitors in patients with advanced breast cancer in the United Kingdom. *Clinical Therapeutics*, 35(3), 246-260.e5.

Deshmukh, A.A., et al., (2017) Cost-effectiveness Analysis Comparing Conventional, Hypofractionated, and Intraoperative Radiotherapy for Early-Stage Breast Cancer. *Journal of the National Cancer Institute*, 109 (11).

Djalalov, S., et al., (2015) Economic evaluation of hormonal therapies for postmenopausal women with estrogen receptor-positive early breast cancer in Canada. *Current Oncology*, 22(2), 84-96.

Frederix, G.W., et al., (2014) The impact of structural uncertainty on cost-effectiveness models for adjuvant endocrine breast cancer treatments: the need for disease-specific model standardization and improved guidance. *Pharmacoeconomics*, 32(1), 47-61.

Gordon, L.G., et al., (2017) Cost-effectiveness of a pragmatic exercise intervention for women with breast cancer: results from a randomized controlled trial. *Psycho-Oncology*, 26(5), 649-655.

Goto, R., et al., (2017) Cost analysis of leuprorelin acetate in Japanese pre-menopausal breast-cancer patients: comparison between 6-month and 3-month depot formulations. *Journal of Medical Economics*, 1-7.

Greenup, R.A., et al., (2017) Cost implications of an evidence-based approach to radiation treatment after lumpectomy for early-stage breast cancer. *Journal of Oncology Practice*, 13(4), e283-e290.

Han, K., et al., (2016) Omission of Breast Radiotherapy in Low-risk Luminal A Breast Cancer: Impact on Health Care Costs. *Clinical Oncology (Royal College of Radiologists)*, 28(9), 587-93.

Harat, A., M. Harat, and R. Makarewicz, (2016) Whole breast irradiation vs. APBI using multicatheter brachytherapy in early breast cancer - simulation of treatment costs based on phase 3 trial data. *Journal of Contemporary Brachytherapy*, 8(6), 505-511.

Ignatyeva, V. and G. Khachatryan, (2016) Cost-utility analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early HER-2 positive breast cancer. *Value in Health*, 19 (7), A739-A740.

Jahn, B., et al., (2015) Cost effectiveness of personalized treatment in women with early breast cancer: the application of OncotypeDX and Adjuvant! Online to guide adjuvant chemotherapy in Austria. *Springerplus*, 4, 752.

Kee, W., et al., (2016) Cost effectiveness and tolerability of dose dense versus weekly paclitaxel chemotherapy in patients with early breast cancer: A real-world comparison. *Journal of Clinical Oncology. Conference*, 34.

Kwon, J.S., et al., (2017) Costs and benefits of extended endocrine strategies for premenopausal breast cancer. *JNCCN Journal of the National Comprehensive Cancer Network*, 15(8), 1015-1021.

Kwon, J.S., et al., (2015) Long-term-consequences of ovarian ablation for pre-menopausal breast cancer. *Journal of Clinical Oncology*, 33(15 SUPPL. 1).

Lamond, N.W.D., et al., (2013) Should adjuvant zoledronic acid be used in early-stage, endocrine-sensitive breast cancer? *Cancer Research*, 73(24 SUPPL. 1).

Le, Q.A., (2016) Structural Uncertainty of Markov Models for Advanced Breast Cancer: A Simulation Study of Lapatinib. *Medical Decision Making*, 36(5), 629-40.

Le, Q.A., Y.H. Bae, and J.H. Kang, (2016) Cost-effectiveness analysis of trastuzumab emtansine (T-DM1) in human epidermal growth factor receptor 2 (HER2): positive advanced breast cancer. *Breast Cancer Research & Treatment*, 159(3), 565-73.

Excluded studies - health economic evidence for early and locally advanced breast cancer

Study

- Lester-Coll, N.H., C.E. Rutter, and S.B. Evans, (2016) Cost-effectiveness assessment of lumpectomy cavity boost in elderly women with early stage estrogen receptor positive breast cancer receiving adjuvant radiotherapy. *Radiotherapy & Oncology*, 119(1): p. 52-6.
- Leung, W., et al., (2016) Adjuvant Trastuzumab in HER2-Positive Early Breast Cancer by Age and Hormone Receptor Status: A Cost-Utility Analysis. *PLoS Medicine / Public Library of Science*, 13(8), e1002067.
- Loving, V.A., et al., (2014) Monte Carlo simulation to analyze the cost-benefit of radioactive seed localization versus wire localization for breast-conserving surgery in fee-for-service health care systems compared with accountable care organizations. *AJR. American Journal of Roentgenology*, 202(6), 1383-8.
- Mailhot Vega, R.B., et al., (2016) Establishing Cost-Effective Allocation of Proton Therapy for Breast Irradiation. *International Journal of Radiation Oncology, Biology, Physics*, 95(1), 11-8.
- May, A.M., et al., (2017) Cost-effectiveness analysis of an 18-week exercise programme for patients with breast and colon cancer undergoing adjuvant chemotherapy: The randomised PACT study. *BMJ Open*, 7 (3).
- McGuffin, M., et al., (2017) Who Should Bear the Cost of Convenience? A Cost-effectiveness Analysis Comparing External Beam and Brachytherapy Radiotherapy Techniques for Early Stage Breast Cancer. *Clinical Oncology (Royal College of Radiologists)*, 29(3), e57-e63.
- Miquel-Cases, A., et al., (2016) Exploratory Cost-Effectiveness Analysis of Response-Guided Neoadjuvant Chemotherapy for Hormone Positive Breast Cancer Patients. *PLoS ONE [Electronic Resource]*, 11(4), e0154386.
- Miquel-Cases, A., et al., (2015) Early stage cost-effectiveness analysis of a BRCA1-like test to detect triple negative breast cancers responsive to high dose alkylating chemotherapy. *Breast*, 24(4), 397-405.
- Mousa, R., L. Chen, and K. Cheung, (2016) Cost effectiveness of primary endocrine therapy against surgery for older women with primary breast cancer. *Value in Health*, 19 (3), A152.
- Nair, N., G. Kvizhinadze, and T. Blakely, (2016) Cancer Care Coordinators to Improve Tamoxifen Persistence in Breast Cancer: How Heterogeneity in Baseline Prognosis Impacts on Cost-Effectiveness. *Value in Health*, 9(8), 936-944.
- Paget, J.T., K.C. Young, and S.M. Wilson, (2013) Accurately costing unilateral delayed DIEP flap breast reconstruction. *Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*, 66(7), 926-30.
- Perrier, L., et al., (2016) A cost-effectiveness analysis of a 6-month physical activity program versus usual dietary care during adjuvant chemotherapy in breast cancer patients. *Value in Health*, 19 (3), A149.
- Postma, E.L., et al., (2013) Cost-effectiveness of radioguided occult lesion localization (ROLL) versus wire-guided localization (WGL) in breast conserving surgery for nonpalpable breast cancer: results from a randomized controlled multicenter trial. *Annals of Surgical Oncology*, 20(7), 2219-26.
- Quintyne, K.I., et al., (2016) Cost-effectiveness analysis (CEA) of adjuvant trastuzumab therapy use in HER2-positive early-stage breast cancer (EBC). *Annals of Oncology. Conference: 41st European Society for Medical Oncology Congress, ESMO*, 27.
- Razdan, S.N., et al., (2016) Cost-Effectiveness Analysis of Breast Reconstruction Options in the Setting of Postmastectomy Radiotherapy Using the BREAST-Q. *Plastic & Reconstructive Surgery*, 137(3), 510e-7e.
- Reeder-Hayes, K.E., et al., (2014) Cost-effectiveness of alternative adjuvant bisphosphonate regimens in postmenopausal women with early breast cancer. *Journal of Clinical Oncology*, 32(15 SUPPL. 1).

Excluded studies - health economic evidence for early and locally advanced breast cancer

Study

Schutzer, M.E., D.W. Arthur, and M.S. Anscher, (2016) Time-driven activity-based costing: A comparative cost analysis of whole-breast radiotherapy versus balloon-based brachytherapy in the management of early-stage breast cancer. *Journal of Oncology Practice*, 12(5), e584-e593.

Shah, C., et al., (2014) Evaluating radiotherapy options in breast cancer: does intraoperative radiotherapy represent the most cost-efficacious option? *Clinical Breast Cancer*, 14(2), 141-6.

Shah, C., et al., (2014) Cost-effectiveness of 3-dimensional conformal radiotherapy and applicator-based brachytherapy in the delivery of accelerated partial breast irradiation. *American Journal of Clinical Oncology*, 37(2), 172-6.

Sher, D.J., et al. (2009) Partial-breast irradiation versus whole-breast irradiation for early-stage breast cancer: a cost-effectiveness analysis (Structured abstract). *International Journal of Radiation Oncology, Biology, Physics*, 74, 440-446.

Singer, L., E. Brown, and T. Lanni, Jr., (2016) Margins in breast conserving surgery: The financial cost & potential savings associated with the new margin guidelines. *Breast*, 28, 1-4.

Skedgel, C., D. Rayson, and T. Younis, (2013) Is adjuvant trastuzumab a cost-effective therapy for HER-2/neu-positive T1bN0 breast cancer? *Annals of Oncology*, 24(7), 1834-40.

Squires, H., et al., (2017) Pertuzumab for the Neoadjuvant Treatment of Early-Stage HER2-Positive Breast Cancer: An Evidence Review Group Perspective of a NICE Single Technology Appraisal. *Pharmacoeconomics*, 02, 02.

Squires, H., et al., (2016) Trastuzumab Emtansine for Treating HER2-Positive, Unresectable, Locally Advanced or Metastatic Breast Cancer After Treatment with Trastuzumab and a Taxane: An Evidence Review Group Perspective of a NICE Single Technology Appraisal. *Pharmacoeconomics*, 34(7), 673-680.

Vaidya, A., et al., (2017) Health economics of targeted intraoperative radiotherapy (TARGIT-IORT) for early breast cancer: a cost-effectiveness analysis in the United Kingdom. *BMJ Open*, 7(8), e014944.

Vaidya, J.S., et al., (2016) An international randomised controlled trial to compare TARGITed Intraoperative radioTherapy (TARGIT) with conventional postoperative radiotherapy after breast-conserving surgery for women with early-stage breast cancer (the TARGIT-A trial). *Health Technology Assessment (Winchester, England)*, 20(73),1-188.

Vaidya, A., et al., (2014) Cost effectiveness analysis of targeted intraoperative radiotherapy alone (TARGIT-A) in early breast cancer patients. *Value in Health*, 17(7), A640.

VandenBussche, C.J., et al., (2016) Reflex Estrogen Receptor (ER) and Progesterone Receptor (PR) Analysis of Ductal Carcinoma In Situ (DCIS) in Breast Needle Core Biopsy Specimens: An Unnecessary Exercise That Costs the United States \$35 Million/y. *American Journal of Surgical Pathology*, 40(8), 1090-9.

Webber-Foster, R., et al., (2014) Cost-effectiveness analysis of docetaxel versus weekly paclitaxel in adjuvant treatment of regional breast cancer in New Zealand. *Pharmacoeconomics*, 32(7), 707-24.

Xie, J., et al., (2015) Economic Evaluations of Everolimus Versus Other Hormonal Therapies in the Treatment of HR+ HER2+ Advanced Breast Cancer from a US Payer Perspective. *Clinical Breast Cancer*, 15(5), e263-e276.

Yu, J., et al., (2017) Cost Analysis of a Surgical Consensus Guideline in Breast-Conserving Surgery. *Journal of the American College of Surgeons*, 225(2), 294-301.