

Early and locally advanced breast cancer
Advanced breast cancer

Costing report

Implementing NICE guidance

February 2009

This costing report accompanies the clinical guidelines: 'Early and locally advanced breast cancer: diagnosis and treatment' (available online at www.nice.org.uk/CG80) and 'Advanced breast cancer: diagnosis and treatment' (available online at www.nice.org.uk/CG81).

Issue date: February 2009

This guidance is written in the following context

This report represents the view of NICE, which was arrived at after careful consideration of the available data and through consulting healthcare professionals. It should be read in conjunction with the NICE guidelines. The report and templates are implementation tools and focus on those areas that are considered to have significant impact on resource utilisation.

The cost and activity assessments in the report are estimates based on a number of assumptions. They provide an indication of the likely impact of the principal recommendations and are not absolute figures. Assumptions used in the report are based on assessment of the national average. Local practice may be different from this, and the template can be amended to reflect local practice to estimate local impact.

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This is a revised costing report issued in June 2009 to correct the cost per patient for trastuzumab, following feedback on the original costing tools.

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Executive summary

This costing report looks at the resource impact of implementing the NICE guidelines 'Early and locally advanced breast cancer: diagnosis and treatment' and 'Advanced breast cancer: diagnosis and treatment' in England.

One costing report and costing template has been developed for both guidelines because they are likely to be implemented by the same team.

The costing method adopted is outlined in appendix A; it uses the most accurate data available, was produced in conjunction with key clinicians, and reviewed by clinical and financial professionals.

Supporting implementation

The NICE clinical guidelines on Early and locally advanced breast cancer and Advanced breast cancer are supported by a range of implementation tools available on our website (www.nice.org.uk/CG80 for Early and locally advanced breast cancer and www.nice.org.uk/CG81 for Advanced breast cancer) and detailed in the main body of this report.

Significant resource-impact recommendations

Because of the breadth and complexity of the guidelines, this report focuses on recommendations that are considered to have the greatest resource impact and therefore require the most additional resources to implement or can potentially generate savings. They are:

- Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered (Early and locally advanced breast cancer).
- For patients who are receiving treatment with trastuzumab¹ for advanced breast cancer, discontinue treatment with trastuzumab at the time of

¹ Recommendations on the use of trastuzumab are covered by NICE technology appraisal guidance 34 (2002) which will be updated.

disease progression outside the central nervous system. Do not discontinue trastuzumab if disease progression is within the central nervous system alone (Advanced breast cancer).

- Consider offering bisphosphonates to patients newly diagnosed with bone metastases, to prevent skeletal-related events and reduce pain (Advanced breast cancer).

Total cost impact

The annual changes in revenue costs arising from fully implementing the guidelines are summarised in the table below.

Estimated recurrent costs of implementation

Recommendations	Costs (000s)
Costs	
Bisphosphonates for patients newly diagnosed with bone metastases	2,130
Savings	
Pretreatment ultrasound evaluation of the axilla	-1,291
Treatment with trastuzumab	-11,717
Total savings	-13,008
Net implementation costs/savings (-)	-10,878

The time it takes to implement these guidelines will vary depending on local practice. Based on clinical opinion it is believed that most of the recommendations covered in the guidelines are already in practice. However, there is evidence of variation across the country and of patchy availability of treatments and procedures. The guidelines help to address these issues and offer guidance on best practice.

Some of the recommendations in the guidelines, for example, mammography screening, magnetic resonance imaging (MRI) and positron emission tomography fused with computed tomography (PET-CT) might have an impact in some local areas. Organisations should assess the local costs associated with these recommendations and consider them together with those that have

a significant impact on resources at a national level. Where there are opportunities for making savings from reducing expenditure on drugs, organisations are encouraged to redirect these savings to other areas within the guidelines that may require additional resources.

Benefits and savings

Implementing the clinical guidelines will bring the following benefits:

- Best practice in the diagnosis of the disease; identification of the correct and optimal treatment pathway will lead to fewer mortalities and increased survival rates in patients suffering from breast cancer.
- There are likely to be savings when patients avoid undergoing two separate surgical procedures to the axilla as a result of improved preoperative ultrasound evaluation.
- There is likely to be a reduction in hospital beds occupied as a result of an improvement in the treatment of patients with bone metastases. Bone metastases account for over a third of all nights occupied in hospital in advanced breast cancer care (Royal College of Nursing 2005).
- There are likely to be savings if patients discontinue treatment with trastuzumab at the time of disease progression outside the central nervous system. The annual cost of trastuzumab per patient is approximately £15,080. See the table above for the estimated annual savings.

Local costing template

The costing template produced to support these guidelines enables organisations in England, Wales and Northern Ireland to estimate the impact locally and replace variables with ones that depict the current local position. A sample calculation using this template showed that savings of approximately £12,000 could be achieved for a population of 100,000.

1 Introduction

1.1 *Supporting implementation*

1.1.1 The NICE clinical guidelines on Early and locally advanced breast cancer and Advanced breast cancer are supported by the following implementation tools available on our website (www.nice.org.uk/CG80 for Early and locally advanced breast cancer and www.nice.org.uk/CG81 for Advanced breast cancer):

- costing tools
 - a national costing report; this document
 - a local costing template; a simple spreadsheet that can be used to estimate the local cost of implementation.
- a slide set; key messages for local discussion
- audit support.

1.1.2 A practical guide to implementation, 'How to put NICE guidance into practice: a guide to implementation for organisations' is also available to download from the NICE website. It includes advice on establishing organisational level implementation processes as well as detailed steps for people working to implement different types of guidance on the ground.

1.2 *What is the aim of this report?*

1.2.1 This report provides estimates of the national cost impact arising from implementation of guidance on early and locally advanced breast cancer and advanced breast cancer in England. These estimates are based on assumptions made about current practice and predictions of how current practice might change following implementation.

1.2.2 This report aims to help organisations plan for the financial implications of implementing NICE guidance.

- 1.2.3 This report does not reproduce the NICE guidelines on Early and locally advanced breast cancer and Advanced breast cancer and should be read in conjunction with them (see www.nice.org.uk/CG80 for Early and locally advanced breast cancer and www.nice.org.uk/CG81 for Advanced breast cancer).
- 1.2.4 The costing template that accompanies this report is designed to help those assessing the resource impact at a local level in England, Wales or Northern Ireland. NICE clinical guidelines are developmental standards in the Department of Health's document '[Standards for better health](#)'. The costing template may help inform local action plans demonstrating how implementation of the guideline will be achieved.

1.3 *Epidemiology of early and locally advanced breast cancer and advanced breast cancer*

- 1.3.1 The number of people diagnosed with breast cancer in England in 2006 was approximately 42,689. Of these 42,386 were women and 303 were men (Office for National Statistics 2008).
- 1.3.2 Approximately 90% of all diagnosed breast cancer is invasive (Office for National Statistics 2008).
- 1.3.3 Ninety-five per cent of the invasive breast cancer was early and locally advanced (stages 1, 2 and 3) and 5% was advanced breast cancer (stage 4). In addition to people whose breast cancer is advanced at diagnosis, approximately 35% of those with early and locally advanced breast cancer will progress to advanced breast cancer.
- 1.3.4 There are currently 550,000 people alive in the UK who have had a diagnosis of breast cancer. This includes people who are cancer free or living with the disease (Maddams et al, 2008).

Table 1 Annual incidence and analysis of early, locally advanced and advanced breast cancer in England

Details	%	Number of patients
Women aged ≥15 years		21,414,220
Breast cancer diagnosed 2006		42,386
Invasive breast cancer	90%	38,147
Non-invasive breast cancer	10%	4,239
Early and locally advanced breast cancer – stages 1, 2 and 3	95%	36,240
Advanced breast cancer – stage 4	5%	1,907
Early and locally advanced breast cancer patients who progress to advanced stage	35%	8,879

1.4 Models of care

- 1.4.1 The NICE cancer service guidance ‘Improving supportive and palliative care for adults with cancer’ (2004; available from www.nice.org.uk/csgsp) contains recommendations on management, follow-up and minimising delays for a patient receiving treatment or supportive intervention. It also recommends a review of services for screened and symptomatic patients.
- 1.4.2 The NICE clinical guideline ‘Referral guidelines for suspected cancer’ (2005; available from www.nice.org.uk/CG27) contains specific recommendations relating to breast cancer and offers advice about best practice on referral for suspected cancer in adults and children.
- 1.4.3 NICE interventional procedure guidance ‘Endoscopic axillary lymph node retrieval for breast cancer’ (2005; available from www.nice.org.uk/IPG147) contains recommendations on removing the lymph nodes in the armpit (axilla) in people with breast cancer.

2 Costing methodology

2.1 Process

2.1.1 We use a structured approach for costing clinical guidelines (see appendix A).

2.1.2 Although much information is available regarding breast cancer diagnosis and some of the treatments undertaken, some detail needed to inform the costing template was lacking. To overcome this limitation, we had to make assumptions in the costing model. We developed these assumptions and tested them for reasonableness with members of the two Guideline Development Groups (GDG) and key clinical practitioners in the NHS.

2.2 Scope of the cost-impact analysis

2.2.1 The guidelines offer best practice advice on the care of adults who are suspected of having, or are diagnosed with, early and locally advanced breast cancer and advanced breast cancer.

2.2.2 The guideline on early and locally advanced breast cancer covers:

- Women with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1 and 2. This is where the primary tumour is less than 5 cm in diameter and there is no sign of spread between the breast and the axillary lymph nodes.
- Women with adenocarcinoma of the breast of clinical stage 3. This includes primary tumours which may be larger than 5 cm in diameter (and includes inflammatory carcinoma).
- Men with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1, 2 and 3.
- Women with newly diagnosed ductal carcinoma in situ and women with Paget's disease of the breast.

2.2.3 The guideline does not cover the following, which are therefore outside the scope of the costing model:

- Women and men with invasive adenocarcinoma of the breast of clinical stage 4 (this is covered by 'Advanced breast cancer: diagnosis and treatment' NICE clinical guideline 81 [2009]).
- Women and men with rare breast tumours (for example, angiosarcoma, lymphoma).
- Women and men with benign breast tumours (for example, fibroadenoma, phyllodes tumour).
- Women with lobular carcinoma in situ.
- Women with an increased risk of breast cancer due to family history. This population is covered by 'Familial breast cancer' (NICE clinical guideline 41 [2006]).

2.2.4 The advanced breast cancer guideline covers:

- Women and men with invasive adenocarcinoma of the breast of clinical stage 4 (that is, with known metastatic disease).

2.2.5 The guideline does not cover:

- Women and men with invasive adenocarcinoma of the breast of clinical stages 1, 2 and 3 (this is covered by the NICE guideline on 'Early and locally advanced breast cancer: diagnosis and treatment').
- Women and men with metastases to the breast from other primary tumours.
- Women and men with rare breast tumours (for example, angiosarcoma, lymphoma).

- Women and men with benign breast tumours (for example, fibroadenoma, benign phyllodes tumours).

2.2.6 For costing purposes, we have only considered the female population because the number of men diagnosed with breast cancer is very small (0.7% of all new cases in 2006). However, the clinical guidelines apply to both men and women.

2.2.7 Due to the breadth and complexity of the guidelines, we worked with the GDGs and other professionals to identify the recommendations that would have the most significant resource-impact (see table 2). Costing work has focused on these recommendations.

Table 2 Recommendations with a significant resource impact

High-cost recommendations	Recommendation number	Key priority?
Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.	1.1.3; Early and locally advanced breast cancer guideline	✓
For patients who are receiving treatment with trastuzumab ² for advanced breast cancer, discontinue treatment with trastuzumab at the time of disease progression outside the central nervous system. Do not discontinue trastuzumab if disease progression is within the central nervous system alone.	1.3.12; Advanced breast cancer guideline	✓
Consider offering bisphosphonates to patients newly diagnosed with bone metastases, to prevent skeletal-related events and reduce pain.	1.5.12; Advanced breast cancer guideline	✓

2.2.8 A total of 20 recommendations in the guidelines have been identified as key priorities for implementation, and three of these are also among the recommendations considered to have significant resource impact. See appendix C for details of other key priorities for implementation that have not been included in the costing template.

² Recommendations on the use of trastuzumab are covered by NICE technology appraisal guidance 34 (2002) which will be updated.

2.2.9 The Department of Health has indicated that the following recommendations might have a large impact on resources in some local areas.

- Offer MRI of the breast to patients with invasive breast cancer:
 - if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
 - if breast density precludes accurate mammographic assessment
 - to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer. (1.1.2; Early and locally advanced breast cancer guideline)
- Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:
 - are starting adjuvant aromatase inhibitor treatment
 - have treatment-induced menopause
 - are starting ovarian ablation/suppression therapy. (1.10.1; Early and locally advanced breast cancer guideline)
- Offer annual mammography to all patients with early breast cancer, including ductal carcinoma in situ (DCIS), until they enter the NHS Breast Screening Programme (NHSBSP)/Breast Test Wales Screening Programme (BTWSP). Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years. (1.14.1; Early and locally advanced breast cancer guideline)
- Positron emission tomography fused with computed tomography (PET-CT) should only be used to make a new diagnosis of metastases for patients with breast cancer whose imaging is suspicious but not diagnostic of metastatic disease. (1.1.5; Advanced breast cancer guideline)

- A breast cancer multidisciplinary team should assess all patients presenting with uncontrolled local disease and discuss the therapeutic options for controlling the disease and relieving symptoms. (1.5.9; Advanced breast cancer guideline)

2.2.10 Local organisations will need to assess the local costs associated with these recommendations and consider them together with those that have a significant impact on resources at a national level. Where there are opportunities for making savings from the surgery avoided and the discontinuance of using trastuzumab organisations are encouraged to redirect these savings to the areas identified in these recommendations.

2.3 *General assumptions made*

- 2.3.1 The costing model is based on annual incidence and population estimates (see table 1 in section 1.3 above).
- 2.3.2 The number of men with breast cancer is very low, so we have considered only the female population in the costing model.

2.4 *Basis of unit costs*

- 2.4.1 The way the NHS is funded has undergone reform with the introduction of 'Payment by results' based on a national tariff. The national tariff will be applied to all activity for which Healthcare Resource Groups (HRGs) or other appropriate case-mix measures are available. Where a national tariff price or indicative price exists for an activity this has been used as the unit cost; this has then been inflated by the national average market forces factor.
- 2.4.2 Using these prices ensures that the costs in the report are the cost to the primary care trust (PCT) of commissioning predicted

changes in activity at the tariff price, but may not represent the actual cost to individual trusts of delivering the activity.

- 2.4.3 For new or developing services, where there is no national average unit cost, organisations already undertaking this activity have been asked their current unit cost.

3 Cost of significant resource-impact recommendations

3.1 *Preoperative staging of the axilla*

Recommendation

- 3.1.1 Pre-treatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered. (1.1.3; Early and locally advanced breast cancer guideline)

Background

- 3.1.2 For patients with early invasive breast cancer, staging of the ipsilateral axilla is essential for deciding which local and systemic treatments are subsequently required. The axilla can be staged using limited axillary surgery carried out at the same time as the breast surgery, but a second operation may be required if nodal disease is found. A preoperative diagnosis of nodal metastasis enables definitive surgical staging of the axilla at the time of breast surgery. The majority of patients with axillary lymph node disease do not have clinically obvious node involvement, but imaging of the axilla can detect impalpable lymph nodes that may contain metastatic disease.

Assumptions made

- 3.1.3 The costing model considers the cost of ultrasound-guided needle sampling only. The commissioning cost of pre-treatment ultrasound

evaluation of the breast and axilla is the same as that of the breast only. In practice it takes only a few minutes more to scan the axilla and this could be absorbed as part of the appointment. However, some units with a significant volume of activity may require additional resources to ensure sufficient time to scan the axilla for each patient.

- 3.1.4 Based on clinical opinion we have assumed that 60% (21,744) of women with early invasive breast cancer are currently offered ultrasound evaluation of both the breast and the axilla.
- 3.1.5 Based on clinical opinion approximately 33% of women with early invasive breast cancer have morphologically abnormal lymph nodes identified after an ultrasound. This proportion proceeds to ultrasound-guided needle sampling to confirm metastases before they are offered breast surgery.
- 3.1.6 In future we predict that 100% of women with early invasive breast cancer would receive pre-treatment ultrasound evaluation of the breast and axilla.
- 3.1.7 Based on clinical opinion, we have assumed that 20% of patients offered ultrasound-guided needle sampling benefit from avoiding additional surgical procedures where nodal disease is only identified at initial surgery.
- 3.1.8 The unit cost for ultrasound-guided needle sampling is £240. The cost is based on the 08/09 national tariffs (currency code OPFND – Fine needle biopsy).
- 3.1.9 The unit cost for breast surgery is £2,549. The cost is based on the 08/09 national tariffs, HRG J11 – Lymph node dissection.

Cost summary

- 3.1.10 The estimated cost for providing ultrasound-guided needle sampling of morphologically abnormal lymph nodes is £1.1 million

and the associated saving resulting from patients avoiding second surgery is approximately £2.4 million, as shown in table 3.

Table 3 Estimated cost of ultrasound-guided needle sampling of abnormal lymph nodes

Details	Unit cost	Current		Proposed		Change	
		Number of patients	Cost (£000)	Number of patients	Cost (£000s)	Number of patients	Cost (£000s)
Ultrasound-guided needle sampling	£240	7,176	1,722	11,959	2,870	4,783	1,148
Savings from avoiding second surgery ³	£2,549	1,435	-3,658	2,392	-6,097	957	-2,439
Totals			-1,936		-3,227		-1,291

Other considerations

3.1.11 The costing assumes a patient being offered one ultrasound-guided needle sampling test per year, although some patients may receive more than one depending on circumstances.

3.2 *Patients receiving treatment with trastuzumab*

Recommendation

3.2.1 For patients who are receiving treatment with trastuzumab⁴ for advanced breast cancer, discontinue treatment with trastuzumab at the time of disease progression outside the central nervous system. Do not discontinue trastuzumab if disease progression is within the central nervous system alone. (1.3.12; Advanced breast cancer guideline)

Background

3.2.2 Trastuzumab is only used in patients whose tumours have either human epidermal growth receptor 2 (HER2) protein over-

³ Reduction in surgery applies to only the increased number receiving ultrasound-guided needle sampling, not to 20% of all patients.

⁴ Recommendations on the use of trastuzumab are covered by NICE technology appraisal guidance 34 (2002) which will be updated.

expression or HER2 gene amplification as determined by an accurate and validated test. Approximately 25% of patients with advanced breast cancer have tumours that over-express HER2. Because trastuzumab does not cross the blood–brain barrier it is not effective in treating metastatic disease of the central nervous system.

Assumptions made

- 3.2.3 The latest Department of Health guidance requires all breast cancer patients to be tested for HER2 status (Department of Health 2005).
- 3.2.4 It is estimated that 25% (2,697) of patients with advanced breast cancer are HER2 positive and will be considered for treatment with trastuzumab.
- 3.2.5 Based on clinical opinion we have assumed that of patients for whom trastuzumab is considered, it will be unsuitable for 10% (270) because of the risk of adverse events.
- 3.2.6 Based on clinical opinion, it is assumed that of patients with advanced breast cancer for whom treatment with trastuzumab is suitable, 80% (1,942) are currently receiving the drug.
- 3.2.7 Based on clinical opinion, it is assumed that 80% (1,554) of patients currently taking trastuzumab will have disease progression outside the central nervous system.
- 3.2.8 Based on clinical opinion, it is assumed that 50% (777) who have disease progression outside the CNS continue taking trastuzumab. It is in this group that trastuzumab treatment will be discontinued.
- 3.2.9 The cost per patient of trastuzumab treatment is £15,080 including administration and cardiac monitoring costs. The cost of trastuzumab is based on British National Formulary 56th Edition (BNF 56).

Cost summary

3.2.10 The estimated annual saving resulting from the discontinuance of treatment with trastuzumab in patients whose disease has progressed outside the central nervous system is approximately £11.7 million as shown in table 4.

Table 4 Annual savings from the discontinuance of trastuzumab

		Current		Proposed		Change	
Details	Unit cost	Number of patients	Cost (£000s)	Number of patients	Cost (£000s)	Number of patients	Cost (£000s)
Trastuzumab treatment	£15,080	1,554	23,434	777	11,717	-777	-11,717

3.2.11 The savings achieved annually will vary as disease progression will differ from patient to patient.

3.3 *Bisphosphonates for patients newly diagnosed with bone metastases*

Recommendation

3.3.1 Consider offering bisphosphonates to patients newly diagnosed with bone metastases, to prevent skeletal-related events and reduce pain. (1.5.12; Advanced breast cancer guideline)

Background

3.3.2 Modern systematic anticancer treatment may result in patients with breast cancer living with bone metastases for a long time. In order to relieve pain patients can be managed by preventing skeletal events, controlling pain and treating complications such as fracture, immobility and spinal cord compression.

Assumptions made

3.3.3 We have estimated the total number of patients with advanced breast cancer including those with early and locally advanced

breast cancer who progress to advanced breast cancer to be 10,786.

- 3.3.4 It is estimated that 74% (7,982) of patients with advanced breast cancer will develop bone metastases (Lipton and Milton 2006; Kozlow and Guise 2005).
- 3.3.5 Based on clinical opinion, it is estimated that 55% (4,390) of patients with bone metastases are currently offered bisphosphonates.
- 3.3.6 Based on clinical opinion, it is estimated that in future, 65% (5,189) of patients with bone metastases would be offered bisphosphonates.
- 3.3.7 Bisphosphonates that are currently offered include oral sodium clodronate, ibandronic acid, zoledronic acid and pamidronate.
- 3.3.8 Based on clinical opinion, it is assumed that 50% of patients receive oral clodronate and oral ibandronic acid. The other 50% receive intravenous zoledronic acid or pamidronate.
- 3.3.9 The annual cost for oral sodium clodronate is £1,791.00 and for oral ibandronic acid is £2,541.96. The price of the drugs is based on BNF 56.
- 3.3.10 The annual cost for zoledronic acid is £3,208.00 and for pamidronate is £2,848.00. These are inclusive of administration costs. The price of the drugs is based on BNF 56.

Cost summary

- 3.3.11 The estimated annual cost for bisphosphonates treatment is approximately £2.1 million as shown in table 5.

Table 5 Annual cost of bisphosphonates treatment

	Current		Proposed		Change	
Details	Number of patients	Cost (£000s)	Number of patients	Cost (£000s)	Number of patients	Cost (£000s)
Bisphosphonates for patients with bone metastases	4,390	11,728	5,189	13,858	799	2,130

4 Sensitivity analysis

4.1 Methodology

- 4.1.1 There are a number of assumptions in the model for which no empirical evidence exists. Because of the limited data, the model developed is based mainly on discussions of typical values and predictions of how things might change as a result of implementing the guidance and is therefore subject to a degree of uncertainty.
- 4.1.2 As part of discussions with practitioners, we discussed possible minimum and maximum values of variables, and calculated their impact on costs across this range.
- 4.1.3 Wherever possible we have used the national tariff plus market forces factor to determine cost. We used the variation of costs for the 25th and 75th percentiles from reference costs compared with the reference cost national average as a guide to inform the maximum and minimum range of costs.
- 4.1.4 It is not possible to arrive at an overall range for total cost because the minimum or maximum of individual lines would not occur simultaneously. We undertook one-way simple sensitivity analysis, altering each variable independently to identify those that have greatest impact on the calculated total cost.

4.1.5 Appendix B contains a table detailing all variables modified and the key conclusions drawn are discussed below.

4.2 *Impact of sensitivity analysis on costs*

Cost of trastuzumab

4.2.1 From appendix B, it can be seen that varying the cost of trastuzumab between a minimum of £15,080 and a maximum of £30,041 brings about savings in implementing the guidance from a minimum of £10.9 million to a maximum of £22.5 million.

HER2-positive women eligible for trastuzumab

4.2.2 From appendix B, it can be seen that varying the number of patients eligible for trastuzumab between a minimum of 20% and a maximum of 30% brings about savings in implementing the guidance from a minimum of £8.5 million to a maximum of £13.2 million.

HER2-positive women currently receiving trastuzumab

4.2.3 From appendix B, it can be seen that varying the percentage of patients currently receiving trastuzumab treatment for bone metastases between the limits 60% and 100% brings about savings in implementing the guidance from a minimum of £8.0 million to a maximum of £13.8 million.

5 Impact of guidance for commissioners

5.1.1 The diagnosis and some of the treatment of both early and locally advanced breast cancer and advanced breast cancer fall under the scope of 'Payment by results'. However, although prescribing of bisphosphonates may be initiated in secondary care, it is likely to be mainly carried out in primary care and hence to fall outside the scope of 'Payment by results'.

5.1.2 The costs for breast cancer treatment fall under programme budgeting category code 202F (cancers and tumours – breast).

6 Conclusion

6.1 Total national cost for England

6.1.1 Using the significant resource impact recommendations shown in table 1 and assumptions specified in section 3 we have estimated the annual saving of fully implementing the guidelines in England to be approximately £10.9 million. Table 6 shows the breakdown of cost of each significant resource-impact recommendation.

Table 6 Estimated recurrent costs of implementation

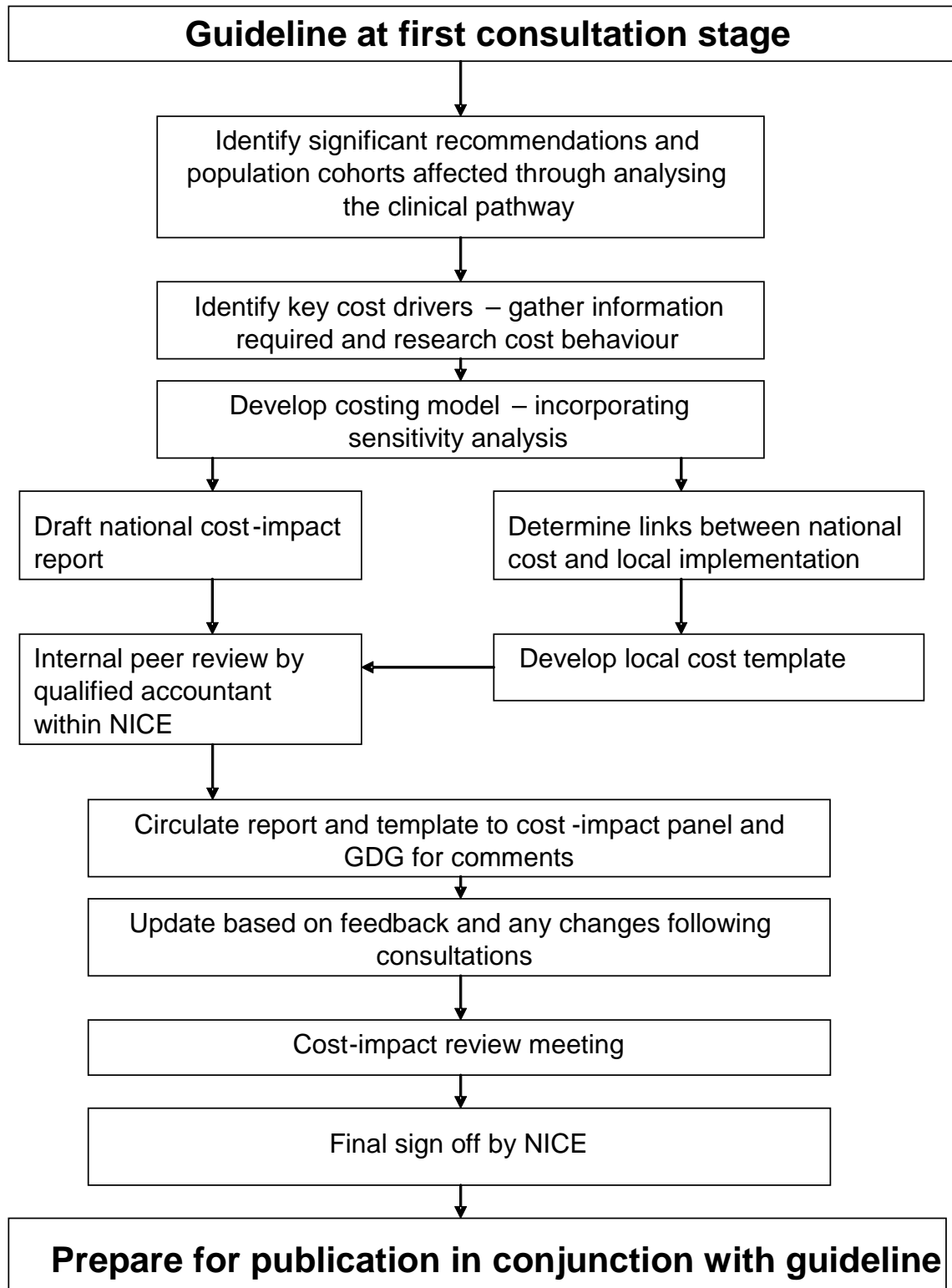
Recommendations	Costs (000s)
Costs	
Bisphosphonates for patients newly diagnosed with bone metastases	2,130
Savings	
Pretreatment ultrasound-guided needle sampling of the axilla	-1,291
Treatment with trastuzumab	-11,717
Net implementation costs/savings (-)	-10,878

6.1.2 We applied reality tests against existing data wherever possible, but this was limited by the availability of detailed data. We consider this assessment to be reasonable, given the limited detailed data regarding diagnosis and treatment paths and the time available. However, the costs presented are estimates and should not be taken as the full cost of implementing the guideline.

6.2 Next steps

6.2.1 The local costing template produced to support this guideline enables organisations such as primary care trusts (PCTs) or health boards in Wales and Northern Ireland to estimate the impact locally and replace variables with ones that depict the current local position. A sample calculation using this template showed that a population of 100,000 could expect to incur additional savings of approximately £12,000. Use this template to calculate the cost of implementing this guidance in your area.

Appendix A. Approach to costing guidelines



Appendix B. Results of sensitivity analysis

Assessment of sensitivity costs to a range of variables							
Parameter varied	Baseline value	Minimum value	Maximum value	Baseline costs (£000s)	Minimum costs (£000s)	Maximum costs (£000s)	Change (£000s)
Women with invasive breast cancer	90.0%	85.0%	95.0%	-10,878	-10,263	-11,467	-1,204
Women in whom the cancer progresses to advanced breast cancer	35.0%	30.0%	40.0%	-10,878	-9,726	-12,014	-2,288
Women currently receiving pre-treatment ultrasound evaluation plus ultrasound-guided needle sampling	60.0%	50.0%	70.0%	-10,878	-11,200	-10,556	644
Women identified with abnormal lymph nodes	33.0%	30.0%	36.0%	-10,878	-11,717	-10,995	722
Women who avoid second surgery as a result of ultrasound-guided needle sampling of the axilla	20.0%	15.0%	25.0%	-10,878	-10,266	-11,487	-1,221
Women HER2-positive who are eligible for trastuzumab	25.0%	20.0%	30.0%	-10,878	-8,510	-13,215	-4,705
Women HER2-positive currently receiving trastuzumab	80.0%	60.0%	100.0%	-10,878	-7,953	-13,804	-5,851
Women HER2-positive who are intolerant of trastuzumab	10.0%	5.0%	15.0%	-10,878	-10,230	-11,526	-1,296
Women in whom the cancer progresses outside the central nervous system	80.0%	70.0%	90.0%	-10,878	-9,400	-12,341	-2,941
Women with advanced breast cancer who develop bone metastases	74.0%	65.0%	80.0%	-10,878	-11,131	-10,707	424
Women with advanced breast cancer currently receiving bisphosphonates	55.0%	50.0%	60.0%	-10,878	-9,810	-11,940	-2,130
Women with bone metastases who are to receive bisphosphonates in future	65.0%	60.0%	70.0%	-10,878	-11,940	-9,812	2,128
Cost of trastuzumab	£15,080	£15,080	£30,041	-10,878	-10,878	-22,503	-11,625

Appendix C. Comments on key priorities for implementation not included in the costing template

Table 7 Early and locally advanced breast cancer: diagnosis and treatment

Recommendation number	Recommendation	Reasons for non-inclusion in costing template
1.1.2	<p>Preoperative assessment of the breast and axilla</p> <p>Offer MRI of the breast to patients with invasive breast cancer:</p> <ul style="list-style-type: none"> • if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment • if breast density precludes accurate mammographic assessment • to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer. 	<p>Based on expert opinion this recommendation could increase costs in line with increased activity. However, the costs are considered to be small and unlikely to have any significant impact on resources at a national level.</p>
1.4.1	<p>Surgery to the axilla</p> <p>Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique.</p>	<p>The recommendation reflects best practice so it is unlikely to have any significant impact on resources. However, it should be considered locally.</p>
1.5.1	<p>Breast reconstruction</p> <p>Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.</p>	<p>The recommendation reflects and emphasises good practice. It aims to speed up breast reconstruction. There could be some savings at a local level if more reconstructions are carried out simultaneously with mastectomy. The savings would include avoided admissions and associated administration costs. However, it is not considered to have any significant impact on resources at a national level.</p>
1.6.8	<p>Adjuvant treatment planning</p> <p>Start adjuvant chemotherapy or radiotherapy</p>	<p>The recommendation focuses on timing and ensuring good practice. Previously, the standard</p>

	as soon as clinically possible within 31 days of completion of surgery ⁵ in patients with early breast cancer having these treatments.	was to start adjuvant chemotherapy within 6 weeks of surgery; now it is within 31 days of surgery. It is considered not to have a significant impact on resources at a national level.
1.7.3	Aromatase inhibitors Postmenopausal women with oestrogen receptor (ER)-positive early invasive breast cancer who are not considered to be at low risk ⁶ should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated.	The recommendation is not considered to have a significant cost impact on resources. The use of aromatase inhibitors is covered in 'Breast cancer (early) – hormonal treatments' (NICE technology appraisal guidance112; available from www.nice.org.uk/TA112).
1.10.1	Assessment of bone loss Patients with early invasive breast cancer should have a baseline DEXA scan to assess bone mineral density if they: <ul style="list-style-type: none"> • are starting adjuvant aromatase inhibitor treatment • have treatment-induced menopause • are starting ovarian ablation/suppression therapy. 	The cost of a DEXA scan is £49. This is based on the 08/09 indicative tariffs, currency code RADX1. The implementation of this recommendation is likely to involve a limited number of patients. The recommendation is therefore not considered to have a significant impact on resources at a national level.
1.12.1	Primary systemic therapy Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.	Quite often older people get oral medication alone, and this recommendation would mean more operations, particularly relevant in the older age group who will have more complications, more comorbidity and longer length of hospital stay. There may be cost implications in some units as operations increase. However, based on clinical opinion, the number of operations is considered too small to have a significant impact on resources at a national level.
1.14.1	Follow-up imaging Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHS (NHSBSP)/ (BTWSP). Patients diagnosed with early breast cancer who are already eligible for screening should have	There is variation in practice across the country; some units offer follow-up annual mammography for 5 years and some for 10 years duration. The incidence of breast cancer in patients aged <50 is 8,000 (see

⁵ Department of Health (2007) Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)

⁶ Low-risk patients are those in the EPG or GPG (excellent prognostic group or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have a similar prediction using Adjuvant! Online.

	annual mammography for 5 years.	Step 2: Costing template – incidence of breast cancer). Most of these patients are aged ≥ 40 . A significant number will be covered under the current practice. Any additional cost, however, is unlikely to have a significant impact on resources at a national level. Local organisations should assess the impact locally.
1.14.6	<p>Clinical follow-up</p> <p>Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:</p> <ul style="list-style-type: none"> • designated named healthcare professionals • dates for review of any adjuvant therapy • details of surveillance mammography • signs and symptoms to look for and seek advice on • contact details for immediate referral to specialist care, and • contact details for support services, for example support for patients with lymphoedema. 	The recommendation reinforces and reflects current practice. There could be additional costs involved in those units where practice falls short of the recommendation. However, the recommendation is not considered to have a significant impact on resources.

Table 8 Advanced breast cancer: diagnosis and treatment

1.1.5	<p>Diagnosis and assessment</p> <p>PET-CT should only be used to make a new diagnosis of metastases for patients with breast cancer whose imaging is suspicious but not diagnostic of metastatic disease.</p>	Based on clinical opinion there are very few cases where imaging is suspicious but not diagnostic of metastatic disease. Suggestions are that the number of such cases is likely to be less than 10 per year at any given breast cancer centre/unit. The recommendation is not considered to have a significant cost impact at a national level and may be cost saving if present local practice uses PET-CT appropriately.
1.1.8	Assess ER and HER2 status at the time of disease recurrence if receptor status was not assessed at the time of initial diagnosis. In the absence of tumour tissue from the primary tumour, and if feasible, obtain a biopsy of a metastasis to assess ER and HER2 status.	The recommendation reinforces good practice; therefore it is not considered to have a significant impact on resources at a national level.
1.3.1	<p>Systemic disease-modifying therapy</p> <p>Offer endocrine therapy as first-line</p>	The recommendation reinforces current practice; therefore it is not considered to have a significant

	treatment for the majority of patients with ER-positive advanced breast cancer.	impact on resources at a national level.
1.3.10	<p>For patients with advanced breast cancer who are not suitable for anthracyclines (because they are contraindicated or because of prior anthracycline treatment either in the adjuvant or metastatic setting), systemic chemotherapy should be offered in the following sequence:</p> <ul style="list-style-type: none"> • first line: single-agent docetaxel • second line: single-agent vinorelbine or capecitabine • third line: single-agent capecitabine or vinorelbine (whichever was not used as second-line treatment). 	The recommendation reinforces current practice; therefore it is not considered to have a significant impact on resources at a national level.
1.4.1	<p>Supportive care</p> <p>Healthcare professionals involved in the care of patients with advanced breast cancer should ensure that the organisation and provision of supportive care services comply with the recommendations made in ‘Improving outcomes in breast cancer: manual update’ (NICE cancer service guidance [2002]) and ‘Improving supportive and palliative care for adults with cancer’ (NICE cancer service guidance [2004]), in particular the following two recommendations:</p> <ul style="list-style-type: none"> • ‘Assessment and discussion of patients’ needs for physical, psychological, social, spiritual and financial support should be undertaken at key points (such as diagnosis; at commencement, during, and at the end of treatment; at relapse; and when death is approaching).’ • ‘Mechanisms should be developed to promote continuity of care, which might include the nomination of a person to take on the role of “key worker” for individual patients.’ 	The recommendation reinforces good practice; therefore it is not considered to have a significant impact on resources at a national level.

1.5.9	<p>Managing complications</p> <p>A breast cancer multidisciplinary team should assess all patients presenting with uncontrolled local disease and discuss the therapeutic options for controlling the disease and relieving symptoms.</p>	<p>This recommendation involves a change in practice as currently the majority of a patient's therapeutic options at this point in their pathway are not discussed by the multidisciplinary team. However, this change is not likely to have a significant impact on resources at a national level.</p>
1.5.14	<p>Use external beam radiotherapy in a single fraction of 8Gy to treat patients with bone metastases and pain.</p>	<p>This reflects best practice and is unlikely to result in a significant change in resources at a national level.</p>
1.5.16	<p>Offer surgery followed by whole brain radiotherapy to patients who have a single or small number of potentially resectable brain metastases, a good performance status and who have no or well-controlled other metastatic disease.</p>	<p>The recommendation reflects current practice in most units around the country. It is therefore unlikely to result in any significant impact on resources at a national level.</p> <p>There are approximately 11,000 patients with advanced breast cancer. About 10% (1,100) develop brain metastases and 6% (66) have resectable brain metastases, good performance status and have no or well-controlled other metastatic disease.</p>

Appendix D. References

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