Clinical Advice to Cancer Alliances for the Provision of Breast Cancer Services

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Prepared by:
This Clinical Advice to Cancer Alliances for the Provision of Breast Cancer Services was prepared by the Breast Cancer Clinical Expert Group (CEG), whose Chair is Professor Ian Smith and Vice-chair is Professor Chris Holcombe. The Breast Cancer CEG has a wide geographical and multi-disciplinary representation from the full range of professionals involved in delivering breast cancer services, as well as patient representatives and groups. The CEG's secretariat is provided by Breast Cancer Now.

Audience:
Both the initial diagnosis and treatment of breast cancer and the treatment of breast cancer when it has spread elsewhere is changing and improving rapidly.

This document gives a summary of current best practice and can be used as a 'check list' against which to measure a local service, to be used by:

- ***Commissioners***
- ***Acute Trusts***
- ***Cancer Alliances***
- ***Patients***

Commissioners can and should commission in reference to this document.
Acute trusts and others providing care should make sure all elements of the service described herein are provided.
Cancer Alliances should have a role in coordinating with commissioners and providers to ensure all elements of the service described herein are provided within their geographical footprint.
Patients can know whether or not their local service is up to scratch.

Groups consulted:
The Chemotherapy and Radiotherapy Clinical Reference Groups, the Association of Breast Surgeons and the UK Breast Cancer Group have reviewed this clinical advice.

Purpose:

- This clinical advice covers essential services for patients with early, and recurrent (local/regional and metastatic) breast cancer.

- It is provided to support the commissioning of clinical breast cancer services at national and local level.

- This document gives a summary of current best practice and can be used as a 'check list' against which to measure a local service.

Contents

1 Executive summary

This Clinical Advice to Cancer Alliances for the Provision of Breast Cancer Services gives a summary of current best practice, and highlights areas where there have been recent advances and changes in patient management.

Commissioners should be asking the following key questions of their local service:

Are relevant data collected shared and acted upon?
Good data are needed for service provision and improvement. Collection of the cancer outcomes and services dataset (COSD) is mandatory at diagnosis and on recurrence. 5.2.7

Do all patients have optimal treatment planning?
Patients with invasive breast cancer should have tumour ER and HER2 status available as soon as possible and certainly within two weeks to allow treatment planning. 5.2.4

Are breast cancer patients offered the best treatment regardless of their age?
Breast cancer treatment should be based on clinical need and fitness for treatment and not age. 5.2.15

Are appropriate patients offered breast cancer treatment as a day case?
Offering appropriate patients to have their breast cancer treated as a day case or on a 23 hour stay pathway, can significantly improve their experience of care. 5.2.24

Are patients with recurrent breast cancer being discussed at a MDT meeting?
MDT working has led to improved decision-making and it is advised that all patients at first relapse (local or metastatic) are added to MDM so this event is recorded 5.2.51

Do patients with recurrent breast cancer have a named clinical nurse specialist?
The single most important factor associated with high patient satisfaction is access to a named clinical nurse specialist in charge of their care. 5.2.52

Following treatment for breast cancer, are patients given lifestyle advice?
Patients who maintain a healthy weight and take regular exercise can reduce the risk of breast cancer recurrence by approximately 30%. 5.2.50

Are patients considered for referral to genetics services?
Women who meet current guidelines for genetic testing should be given appropriate information and have the opportunity to access such testing. 5.2.19

Are appropriate patients offered adjuvant bisphosphonate therapy?
Adjuvant bisphosphonate therapy should be offered to most postmenopausal women with early breast cancer to reduce the risk of bone recurrence and fractures, and to improve breast cancer survival. 5.2.49

Are appropriate patients offered Open Access Follow Up?
Stratified Open Access Follow Up including supported self-management should be strongly considered for patients with early breast cancer. 5.2.60

2 Key breast statistics

- Breast cancer is the most common cancer in England with around 46,000 women diagnosed each year[1].
- Around 300 men are diagnosed with breast cancer every year in England[1].
- In 2015, the incidence rate for female breast cancer in the UK was 170.2 per 100,000 population[1].
- It is estimated that there are almost 600,000 people living with and beyond breast cancer in the UK[2].
- An estimated five out of six women diagnosed with breast cancer in England and Wales survive for at least five years[1].
- Over 9,500 women die of breast cancer every year in England[1].

3 Outcomes

Breast cancer is the most common cancer in England affecting mainly women and a very small proportion of men. Although survival has improved greatly over the last 20 years, breast cancer outcomes in England remain inferior to the best in Europe. Breast cancer is the second biggest cause of cancer death for women after lung cancer.

This may be because more patients are diagnosed when their cancer is already in the advanced stage, and has spread significantly within the breast or to other organs of the body (stage 3 or 4 disease). It may also be because there are variations in the quality and appropriateness of care that breast cancer patients receive.

It is estimated that almost 600,000 people are alive in England after a diagnosis of breast cancer, but it is unknown how many of them have recurrent or metastatic disease. Dealing with recurrent and metastatic breast cancer remains a significant and challenging medical problem, exacerbated by the lack of information about this specific group of patients.

Despite significant improvements in survival, there are variations in the quality of care that breast cancer patients receive. This Clinical Advice focuses specifically on areas where significant improvements are needed to improve breast cancer outcomes as well as to ensure patients have the best possible experience throughout their care.

4 Key themes

Relevant sections mapped against the NHS Outcomes Framework Domains are included in appendix 1.

Are relevant data collected and shared so that appropriate action can be taken?

At diagnosis, the provision of the cancer outcomes and services dataset (COSD) is mandatory. This should include tumour, node and metastasis (TNM) staging information for all new diagnoses of breast cancer, in order to provide the data needed to assess whether progress is being made on improving survival rates

through earlier diagnosis. All diagnoses of recurrent and/or metastatic breast cancer should be recorded via the COSD, to enable improved service planning for these patients (section 5.2.7 – Domain 1; Cancer Strategy recommendation 90).

Do all patients have optimal treatment planning?

All patients with invasive breast cancer should have tumour ER and HER2 status assessed on the diagnostic core biopsy to allow optimal multimodality treatment sequencing and planning. Results should be available as soon as possible; if these tests are performed locally the immunohistochemical results should be available within one week. If these receptor assays are submitted to a central laboratory for assessment, immunohistochemical results should be available, as a minimum, within two weeks.

This will also improve patients' experience of care as they are not left waiting for a significant length of time for a treatment plan (section 5.2.4 – Domains 1, 4 & 5).

Are breast cancer patients offered the best possible treatment regardless of their age?

A third of breast cancers in the UK occur in women over the age of 70 and breast cancer in older women is expected to quadruple over the next three decades. However, evidence suggests that older people do not always receive the same standard of treatment as younger patients[3]. Older women are less likely to be assessed for HER2 status and less likely to receive optimal treatment. Breast cancer treatment should be based on clinical need and fitness for treatment, rather than age alone (section 5.2.15 – Domains 1 & 4; Cancer Strategy recommendation 41).

Are appropriate patients offered breast cancer treatment as a day case or on a 23 hour stay pathway?

Offering appropriate patients to have their breast cancer treated as a day case or on a 23 hour stay pathway, can significantly improve their experience of care and reduce their length of stay in hospital (section 5.2.24 – Domain 3, 4 & 5).

Are patients with recurrent or metastatic breast cancer being discussed at a MDT meeting?

MDT working has led to improved decision-making, more coordinated patient care and improvement in overall quality of care. A survey of 2,050 MDT members in September 2009 found that there is an overwhelming consensus that MDTs are beneficial to patient care and should remain the cornerstone of cancer treatment[4]. However, evidence suggests that many patients with recurrent or metastatic breast cancer do not have their treatment and care discussed in this way. It is advised that all patients at first relapse (local or metastatic) are added to MDM so this event is recorded. Cancer Research UK have also recently commissioned research into the MDT and have suggested streamlining the MDT meeting, and improving the quality of discussions, especially for complex patients who would benefit most from this[5] (section 5.2.51; Cancer Strategy recommendation 46).

Do patients with recurrent or metastatic breast cancer have access to a clinical nurse specialist?

Analysis of Cancer Patient Experience Survey data shows that the single most important factor associated with high patient scores is patients being given the name of a clinical nurse specialist in charge of their care. However, access to such support varies and people with metastatic breast cancer have less access to support from clinical nurse specialists than patients undergoing primary treatment, at a time when they need it most (section 5.2.52 – Domains 2 & 4; Cancer Strategy recommendation 61).

Following treatment for breast cancer, are patients given lifestyle advice?

Evidence shows that patients who maintain a healthy weight and take regular exercise can reduce the risk of breast cancer recurrence, sometimes to the same degree as with adjuvant medical treatment – a reduction in risk of recurrence of approximately 30%. Currently, however, there is uncertainty about how many patients are being given this crucial lifestyle advice (section 5.2.50 - Domains 1, 2 & 3; Cancer Strategy recommendation 8).

Following treatment for breast cancer, are patients considered for referral to genetics services?

A small proportion of women diagnosed with breast cancer (<3% overall) have a mutation to one of the high risk breast cancer genes, BRCA1 or BRCA2. This gives a much greater risk of developing a new primary cancer (breast and ovary). Women who meet current guidelines for genetic testing should be given appropriate information and have the opportunity to access such genetic testing.[6] Furthermore, this should be offered as soon as possible after diagnosis since it may alter both surgical and medical treatment options (section 5.2.19; Cancer Strategy recommendation 36).

Are appropriate patients offered adjuvant bisphosphonate therapy?

Adjuvant bisphosphonate therapy with zoledronate or ibandronate should be offered to most postmenopausal women with early breast cancer to reduce the risk of bone recurrence and fractures, and improve breast cancer survival (section 5.2.49 - Domain 1; Cancer Strategy recommendation 47).

Are appropriate patients offered Open Access Follow Up?

There is no evidence of benefit for routine clinical follow up. Stratified Open Access Follow Up including self-management and supported self-management should be strongly considered for patients with early breast cancer, on the basis of established patient satisfaction and resource savings (sections 5.2.60 - Domains 2, 3 & 4; Cancer Strategy recommendation 67).

5 Clinical Advice to Cancer Alliances for the Provision of Breast Cancer Services

5.1 Purpose

5.1.1 This Clinical Advice for the Provision of Breast Cancer Services covers essential services for patients with early, and recurrent (local/regional and metastatic) breast cancer. It is provided to support the commissioning of clinical breast cancer services at national and local level (see appendix 2 for example breast pathways). There is already a detailed range of documentation on the provision of breast cancer services (appendix 3), which have been cross-referenced in this document.

5.1.2 Breast screening services are not included in the Clinical Advice but are commissioned by Public Health England via a mandate to NHS England[7]. However, the NHS Breast Screening Programme excludes services for women with a significant risk of familial breast cancer, except for the minority categorised at very high risk. Commissioning policies developed by the Medical Genetics Clinical Reference Group (which covers family history services)[8], Chemotherapy Clinical Reference Group[9] and Radiotherapy Clinical Reference Group[10] will also be relevant when commissioning breast cancer services. Statements from the Breast Cancer Quality Standard[11] have been incorporated into this Clinical Advice where appropriate. A number of the essential services detailed in this document are also directly related to improvement areas in the CCG Outcomes Indicator Set 2015/16[12]. When these essential services are delivered collectively they will contribute to improving the effectiveness, safety and experience of care for patients with breast cancer across the NHS Outcomes Framework Domains (appendix 1)[13].

5.1.3 This Clinical Advice supports a more integrated approach to commissioning as recommended by the Independent Cancer Taskforce in their report "*Achieving world-class cancer outcomes: a Strategy for England 2015-2020*"[14].

5.2 Essential services

DIAGNOSIS and STAGING

5.2.1 Standard triple assessment should be undertaken at a single visit to enable accurate and timely diagnosis or exclusion of BC. This is convenient, cost efficient, and gives the patient a positive experience of their care[15]. MRI should not be used as routine imaging but reserved for specific indications[16] and reasons documented in the notes (Domain 4 & 5).

5.2.2 Pre-operative radiology staging for early breast cancer should follow standard guidelines. This should include assessment of the axilla by ultrasound and guided fine needle aspirate or core biopsy of nodes which are suspicious on imaging. Radiology staging investigations for metastatic disease (e.g. CT scan, isotopic bone scan) should not be used in all patients but only those at high risk (e.g. 4 or more nodes involved, T3 >5cm cancers)[17]. PET-CT should

likewise not be used as a routine investigation but reserved for specific indications[18] (Domain 1, 4 & 5).

5.2.3 Patients should be informed of the histological result of the diagnostic core biopsy within 7 days[19] (Domain 4).

5.2.4 ER and HER2 status of invasive breast cancer should also be assessed on the core biopsy sample of every patient. Results should be available as soon as possible; if these tests are performed locally the immunohistochemical results should be available within one week. If these receptor assays are submitted to a central laboratory for assessment, immunohistochemical results should be available, as a minimum, within two weeks. This will allow optimal multimodality treatment planning and sequencing by the MDT[20]. Routine repeat receptor status assessment on the excised tumour is not required[21]. Assessment of progesterone receptor status and Ki67 levels is regarded as optional (Domain 1, 4 & 5).

5.2.5 All breast cancer specimens should be handled and reported as per UK NHS Breast Screening Programme and Royal College of Pathologists guidelines, including provision of the pathology minimum datasets.

MULTI-DISCIPLINARY TEAM (MDT)

5.2.6 Patients with newly diagnosed breast cancer should be discussed at a full MDT meeting before any treatment and a record of this discussion kept in the notes[22] (Domain 5).

5.2.7 The provision of the cancer outcomes and services dataset (COSD) is mandatory. This includes TNM staging information for all new diagnoses of breast cancer, including recurrence and metastases, in order to provide data needed to assess whether progress is being made on improving survival rates through earlier diagnosis. This should be captured electronically at MDT meetings (Domain 1).

5.2.8 All units are encouraged to recruit to clinical trials; many are now open in the window of opportunity before surgery and should be offered at this point**.**

GENERAL SUPPORT

5.2.9 All patients must have access to a clinical nurse specialist at all stages in their treatment pathway. This specifically includes patients with recurrent/metastatic disease. This should be recorded in the notes and the name and contact details given to the patient. Analysis of Cancer Patient Experience Survey data shows that the single most important factor associated with high patient scores is the patient being given the name of a clinical nurse specialist in charge of their care[23] (Domain 2 & 4).

5.2.10 Every patient should be offered a Holistic Needs Assessment (HNA) at key pathway points, including at diagnosis, the start of treatment and at the end of

primary treatment. A formal care plan should be developed. It should be ensured that the results of patients' HNAs are taken into account in MDT decision making and that patients are referred to other services as appropriate[24] (Domain 2 & 4).

5.2.11 All patients having treatment for newly diagnosed, or recurrent breast cancer should be offered psychological support. This may be formal psychology or psychiatry appointments or may include face-to-face or online peer support from other patients, local support groups, online support groups and helplines (Domain 2, 3 & 4).

5.2.12 All patients should be offered quality mark accredited written information tailored to their individual circumstances (Domain 2 & 4). This should include (but not limited to):

- Before starting treatment: Information on all appropriate treatment options available to them and the potential benefits and risks of these treatments.
- During and after any treatment: Specific information on managing any side effects of treatment including fatigue, menopausal symptoms, and joint pain and details of how to contact a named healthcare professional[25].

5.2.13 All patients should be offered information on lymphoedema and physiotherapy, and referral to these specialised services if required (Domain 3).

5.2.14 There should be appropriate assessment of patients' rehabilitative and re-enablement needs across the pathway including signposting as appropriate to fertility specialists, wig and prosthesis providers and physiotherapists for post-operative exercises (Domain 2, 3 & 4).

5.2.15 Patients with newly diagnosed early breast cancer, irrespective of age, should be offered standard surgery, radiotherapy and appropriate systemic therapy, unless clinically inappropriate or significant comorbidity precludes standard of care treatment[26]. Breast cancer treatment should be based on clinical need and fitness for treatment rather than age alone. Formal assessment of fitness for surgery and other neoadjuvant therapy should be considered by the anaesthetist, care of elderly physician or cardiologist as appropriate. This is an area of focus for Quality, Improvement, Productivity and Prevention (QIPP) and Commissioning for Quality and Innovation (CQUIN) (Domain 1 & 4)[27].

5.2.16 Patients with a personal or family history of breast or ovarian cancer, or with triple negative breast cancer under the age of 50 years, should be offered genetic risk assessment and consideration of genetic testing according to local agreements for access to genetic testing[28,29]. Furthermore, this should be offered as soon as possible after diagnosis since it may alter both surgical and medical treatment options.

NEOADJUVANT SYSTEMIC THERAPY

5.2.17 Neoadjuvant chemotherapy or endocrine therapy is being used in increasingly large numbers of patients who have a biologically aggressive tumour, for those who are HER 2 positive and can therefore access pertuzumab or for downsizing to allow for breast conservation, or more limited axillary surgery. Neoadjuvant therapy will also be used within trial protocols where an in vivo assessment of sensitivity to treatment is required[30].

5.2.18 The rationale for primary surgical and medical treatment decisions should always be recorded in the notes (Domain 1).

5.2.19 The option of neoadjuvant chemotherapy (if appropriate) can also be considered in patients who are eligible for genetic testing (based on tumour type, young onset and/or strong family history) when this will allow adequate time to appropriately inform patients about future new primary cancer risk based on family history assessment and genetic test outcome. Information about genetic status may impact on the patient's subsequent choice about breast surgery and reconstruction (Domain 1).

SURGERY

5.2.20 All patients should have all appropriate surgical options discussed in conjunction with their clinical nurse specialist. Oncoplastic conservation procedures should be available, offered and used where appropriate. Most will not require any further adjustment procedures. Neoadjuvant chemotherapy or endocrine therapy should be considered to allow downsizing of the tumour and breast conservation.

5.2.21 Patients requiring mastectomy should have the option of immediate or delayed breast reconstruction[31]. Breast reconstruction is a process rather than a single event, most will require more than one operation. All patients who have breast conservation or reconstruction should have the option of contra-lateral symmetrisation surgery, either simultaneously or as a second procedure, as well as any other secondary procedures to optimise outcomes where appropriate. Patients make decisions at very different speeds so delayed reconstruction or further operative procedures to optimise symmetry should be available without time restrictions. (Domain 4 & 5).

5.2.22 The reasons for surgical treatment choices should be clearly recorded for every patient e.g. why surgery was not carried out in those on primary endocrine therapy, the reasons for mastectomy if this is recommended, and in those having mastectomy without reconstruction, why reconstruction was not performed.

5.2.23 Sentinel node biopsy should be offered to all appropriate (clinically/radiologically node negative) patients[32]. The current standard methodology for localisation is blue dye and radioisotope (Domain 1 & 5).

5.2.24 Since 2007, following the NHS Improvement Transforming Inpatient Care Programme, the length of stay for non-reconstructive breast surgery has

progressively decreased. Day case or one night stay should be regarded as best practice for the majority of women undergoing this type of breast surgery. This is an area of focus for Quality, Improvement, productivity and Prevention (QIPP) and Commissioning for Quality and Innovation (CQUIN) (Domain 3, 4 & 5).

5.2.25 All patients undergoing surgery on their axilla must be given information on risk reduction strategies for lymphoedema. Pathways should be in place for the referral of patients with the condition to specialised lymphoedema services[33] (Domain 2 & 3).

5.2.26 Positive SLNB: micrometastases or isolated tumour cells on sentinel node biopsy do not require further axillary treatment. Patients with one or two sentinel node macrometastases who are postmenopausal, receiving breast conservation and whole breast radiotherapy, are having systemic endocrine or chemotherapy, and who are also T1, G1/2, ER positive and HER2 negative do not require mandatory further axillary treatment (Domain 5). The total number of involved axillary nodes is not usually required for decision-making on adjuvant systemic therapies (Domain 5).

5.2.27 There is no evidence of a survival benefit for those undergoing contra-lateral risk reducing mastectomy[34, 35] – this should not be offered as routine, except for women with BRCA mutations, and when performed should only be done so based on a full discussion of the risks and benefits and with appropriate psychological support[36] (Domain 5).

5.2.28 After primary surgery the absolute benefit of systemic therapies should be discussed at the MDT meeting (see also 5.2.37).

RADIOTHERAPY [37]

5.2.29 Adjuvant radiotherapy based on standard guidelines should be available within 31 days of decision to treat in patients with early breast cancer[38], or within 31 days of completing adjuvant chemotherapy, which should be given before radiotherapy if indicated. If radiotherapy needs to be delayed e.g. because of post-operative seroma or wound infection, the reason should be recorded and the earliest clinically acceptable date (ECAD) should be set when radiotherapy planning commences.

5.2.30 Specifically, adjuvant radiotherapy is indicated for the great majority of patients treated with breast-conserving surgery. If the MDT decision is not to give this, then the reasons (e.g. co-morbidities, low risk, clinical trial) must be specifically recorded.

5.2.31 All patients should have access to intensity modulated radiotherapy and/or heart sparing techniques such as deep inspiration breath hold if required (Domain 5).

5.2.32 Micrometastases or isolated tumour cells on sentinel node biopsy do not require further axillary treatment. One or two sentinel node macrometastases

in patients who are postmenopausal, receiving breast conservation and whole breast radiotherapy, are having systemic endocrine or chemotherapy, and who are also T1, G1/2 and ER positive do not require mandatory further axillary treatment (Domain 5).

5.2.33 Axillary radiotherapy is a reasonable alternative to axillary node clearance following sentinel node biopsy for non-bulky axillary nodal metastases (i.e. negative on axillary imaging) in patients with early breast cancer and may have less morbidity than axillary surgery[39]. The total number of involved axillary nodes is not usually required for decision-making as regards systemic therapies in early breast cancer (Domain 5) but can influence the need for locoregional nodal RT.

ADJUVANT ENDOCRINE THERAPY

5.2.34 Adjuvant endocrine therapy should be offered to all patients with invasive ER positive disease, except for those with a very low risk where there is a no more than 1% 10 year survival gain based on standard risk prediction tools (e.g. NHS PREDICT). In these circumstances this should be documented in the notes (Domain 1).

5.2.35 Adjuvant tamoxifen should be offered to pre-and peri-menopausal patients with invasive ER positive disease (Domain 1 & 5).

5.2.36 Recent data report that the addition of ovarian suppression to tamoxifen further decreases the risk of recurrence in higher risk pre-menopausal women who have had adjuvant chemotherapy, and that substituting an aromatase inhibitor (AI) for tamoxifen further enhances this effect[40]. However this has to be balanced against the risk of a significantly worse quality of life for 2 years or more. The pros and cons of these results need to be discussed with appropriate patients.

5.2.37 An AI should be offered to post-menopausal women with invasive ER positive disease in whom endocrine therapy is appropriate. Tamoxifen can be substituted if persisting significant side effects occur with an AI[41] (Domain 1 & 5).

5.2.38 Patients who have undergone premature ovarian suppression or are on an AI should have a bone density scan and bone health management as per national guidelines[42] (Domain 5).

5.2.39 The standard duration of endocrine therapy after 5 years of tamoxifen has extended from 5 to 10 years for patients with moderate to high risk disease (including the option of switching to an AI for patients who are post-menopausal). Where treatment is stopped after 5 years (e.g. because of low risk or treatment-related morbidity) the reasons should be recorded in the notes[43, 44] (Domain 1).

5.2.40 Recent evidence suggests that more than 5 years of an AI without preceding tamoxifen has only very minor further outcome improvement and is not recommended except in patients with initial high risk disease. In contrast, an AI after around 5 years of tamoxifen does have significant further clinical benefit except for patients at low initial risk[45].

ADJUVANT CHEMOTHERAPY

5.2.41 Adjuvant chemotherapy reduces the risk of metastatic disease, but the actual benefit to any individual patient is dependent on their baseline risk of developing metastatic disease as predicted by standard prognostic factors at diagnosis. All patients with early breast cancer should have their risk of recurrence assessed and benefits of systemic therapies discussed in the MDT meeting following primary surgery as per section 5.2.28. The final plan of systemic therapy should be made in the oncology clinic using this and other patient information and taking into account their views (Domain 5).

5.2.42 A number of online tools are available to assist e.g. NHS PREDICT, and for those with ER positive disease a number of molecular tests can give further refinement of the likely benefit from chemotherapy e.g. Oncotype DX, IHC4 and EndoPredict. NICE now recommends the use of Oncotype DX in in ER positive, HER2-ve, node negative patients where the benefit of adjuvant chemotherapy is uncertain. A proportion of patients who might otherwise have had adjuvant chemotherapy can avoid this on the basis of these further tests[46] (Domain 5).

5.2.43 Anthracyclines should be avoided if there is a significant history of cardiac disease and used with caution in those over 60 or with significant hypertension, with a pre-treatment left ventricular ejection fraction carried out (Domain 1 & 5).

5.2.44 Treatment should be with a standard schedule of which there are several (as covered by Chemotherapy CRG: https://www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b15/).

ANTI-HER2 THERAPY

5.2.45 All patients with invasive HER2 positive disease 1cm or greater should be offered adjuvant trastuzumab for 1 year along with adjuvant chemotherapy. The benefit of such treatment for HER2 positive cancers <1cm is less certain and the decision should be left to the oncologist in charge (Domain 1 & 5).

5.2.46 Single agent paclitaxel with trastuzumab appears as effective as standard chemotherapy for small node-negative cancers (2cm or less) and is a lot less toxic and expensive[47]. It should also be encouraged where there is a contra-indication to standard chemotherapy e.g. because of age or co-morbidity (Domain 1 & 4).

5.2.47 Cardiac monitoring should be carried out based on standard guidelines[48].

5.2.48 Recently, the addition of 4-6 courses of neoadjuvant pertuzumab to trastuzumab and chemotherapy has been shown to improve significantly both pathological complete remission rates and 5 year survival outcome, and this is recommended for patients with higher risk cancers. In contrast, the evidence from the APHINITY trial does not suggest a clinically worthwhile benefit for yearlong adjuvant pertuzumab, despite the trial statistically meeting its primary endpoint[49].

ADJUVANT BISPHOSPHONATES

5.2.49 Based on strong evidence, adjuvant bisphosphonate therapy with zoledronate 4mg by IV infusion 6 monthly or oral ibandronate 50mg daily, for a minimum of 3 years, should be offered to postmenopausal women with early breast cancer to reduce the risk of bone recurrence and fractures, and improve breast cancer survival[50]. For lower risk patients, however, the absolute benefit is likely to be very small and may be outweighed by the potential side effects (in particular a 1% risk of osteonecrosis of the jaw). This is being reviewed by NICE. Note that switching between zoledronate and ibandronate is an option (appendix 4; Domain 1; Cancer Strategy Recommendation 47).

ADJUVANT LIFESTYLE MEASURES

5.2.50 Evidence shows that patients who maintain a healthy weight and take regular exercise can reduce the risk of recurrence in breast cancer, sometimes to the same degree as with adjuvant medical treatment[51]. It is therefore mandatory that all patients are given advice on weight control and regular moderate exercise, and this must be recorded in the notes (Domain 1,2 & 3; Cancer Strategy recommendation 8).

RECURRENT/METASTATIC BREAST CANCER

5.2.51 Patients with recurrent/metastatic disease should be re-discussed at a dedicated metastatic MDT slot if they develop local and/or metastatic disease. A record of this discussion must be filed in the notes and relevant fields in the COSD completed (Cancer Strategy recommendation 46).

5.2.52 It is particularly important that all patients with recurrent or metastatic breast cancer have access to a clinical nurse specialist with specialist knowledge of secondary disease[52]. They should be available to give information and psychological support to patients and their families[53] (Domain 2 & 4).

5.2.53 Re-biopsy with re-assessment of ER and HER2 markers on disease recurrence is strongly recommended. This is to confirm histology and determine whether markers (ER, HER2) have changed, altering treatment options (Domain 1).

5.2.54 There is no single 'best treatment' for patients with recurrent/metastatic breast cancer. All appropriate options should be discussed with the patient who should be involved in choice of therapy[54]. The availability and importance of clinical trials should also be discussed.

5.2.55 Treatment should be selected based on the following principles (Domain 1 & 4):

- Endocrine therapy should be used prior to chemotherapy for invasive ER positive disease except for immediately life-threatening disease
- Single agent palliative chemotherapy is as effective as combination treatment and generally less toxic
- No one type of chemotherapy has been shown superior to others, and selection should be based on previous treatments, toxicity, co-morbidities and patient choice (e.g. preference for oral therapy or wish to avoid alopecia).

5.2.56 All patients should be offered a Holistic Needs Assessment (HNA) at diagnosis of recurrent and/or metastatic disease. A formal care plan should be developed. It should be ensured that the results of patients' HNAs are taken into account at MDT decision making and that patients are offered referral to other services as appropriate (Domain 2, 3 & 4).

5.2.57 Patients with metastatic breast cancer should be referred to a palliative care team at any point where symptoms require this, and when the patient or medical team decide that further active treatment is inappropriate.

CLINICAL TRIALS

5.2.58 The availability and importance of clinical trials should be discussed with all patients for both early and advanced disease at appropriate time points.

FOLLOW UP

5.2.59 All patients should have an end of primary treatment consultation, a summary of treatment given, advice on signs and symptoms of which to be aware, access to a health and wellbeing event or programme and a plan for follow-up. These interventions, when delivered together with a HNA, form The Recovery Package[55] (Domain 2 & 3; Cancer Strategy Recommendation 65).

5.2.60 There is no evidence of benefit for routine clinical follow up, despite this being widespread current practice. Stratified Open Access Follow Up including self-management and supported self-management should be strongly considered for patients with early breast cancer, on the basis of established patient satisfaction and resource savings. This should not, however, jeopardise appropriate follow up of patients in clinical trials (appendix 5; Domain 2, 3 & 4; Cancer Strategy Recommendation 67).

5.2.61 There is evidence that regular surveillance with mammography conveys a survival benefit and is most likely to be considered cost-effective if performed on an annual basis. The optimum frequency and duration has yet to be determined, whilst randomised and other trial data (such as Mammo-50) are awaited[56, 57].

RISK REDUCTION

5.2.62 Chemoprevention with (tamoxifen or raloxifene for 5 years) should be discussed with women at an estimated moderate or high risk of developing breast cancer, based on NICE guidelines[58 59] (Domain 1; Cancer Strategy Recommendation 6).

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6 Appendices

Appendix 1: NHS Outcomes Framework Domains

Available from:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf

NHS Outcomes Framework Domains		Relevant sections
Domain 1	Preventing people from dying prematurely	5.2.2; 5.2.4; 5.2.7; 5.2.15; 5.2.18; 5.2.23; 5.2.34; 5.2.35; 5.2.37; 5.2.39; 5.2.43; 5.2.45; 5.2.46; 5.2.49; 5.2.50; 5.2.53; 5.2.55; 5.2.58; 5.2.62
Domain 2	Enhancing quality of life for people with long term conditions	5.2.9; 5.2.10; 5.2.11; 5.2.12; 5.2.14; 5.2.25; 5.2.46; 5.2.48; 5.2.50; 5.2.52; 5.2.55; 5.2.56; 5.5.59; 5.2.60
Domain 3	Helping people to recover from episodes of ill health or following injury	5.2.10; 5.2.11; 5.2.12; 5.2.13; 5.2.14; 5.2.24; 5.2.25; 5.2.46; 5.2.50; 5.2.52; 5.2.55; 5.2.56; 5.5.59; 5.2.60
Domain 4	Ensuring people have a positive experience of care	5.2.1; 5.2.2; 5.2.4; 5.2.9; 5.2.10; 5.2.11; 5.2.12; 5.2.14; 5.2.15; 5.2.21; 5.2.24; 5.2.46; 5.2.52; 5.2.55; 5.2.56; 5.2.60
Domain 5	Treating and caring for people in a safe environment and protecting them from avoidable harm	5.2.1; 5.2.2; 5.2.4; 5.2.6; 5.2.21; 5.2.23; 5.2.24; 5.2.26; 5.2.27; 5.2.31; 5.2.32; 5.2.33; 5.2.35; 5.2.37; 5.2.38; 5.2.39; 5.2.41; 5.2.42; 5.2.43; 5.2.45;

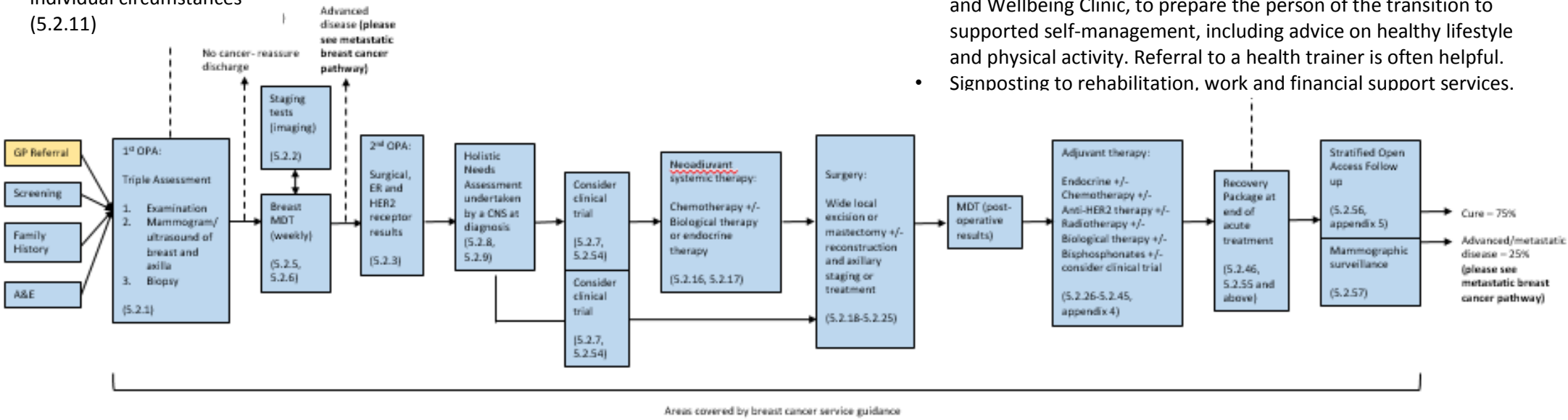
Appendix 2: Example breast pathways

Early and locally advanced breast cancer

NB numbers in brackets denote relevant paragraphs in the Clinical Advice for the Provision of Breast Cancer Services.

Written information:

- Each point of the pathway should be supported by quality mark accredited written information tailored to the patients' individual circumstances (5.2.11)



Key:

= Primary care

= Secondary care

Abbreviations:

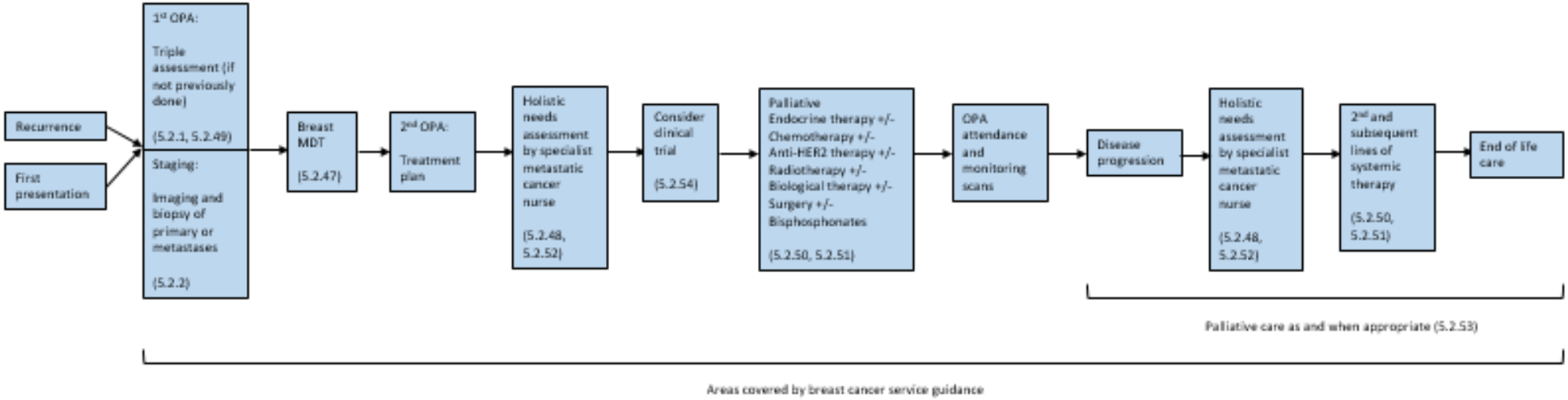
A&E – Accident and Emergency
CNS – Clinical Nurse Specialist
ER – Oestrogen Receptor
GP – General Practitioner
HER2 – Human Epithelial Growth Factor receptor
OPA = Outpatient Appointment
MDT – Multidisciplinary team

Recovery Package:

- Holistic needs assessment (HNA).
- A treatment summary (including surveillance programme) sent to the patient and their GP.
- Information on likely side-effects of treatment and how best to manage these.
- Information on potential symptoms of recurrence/secondary cancers and what to do in these occurrences.
- Key contact point for rapid re-entry if symptoms of recurrence are experienced or if serious side effects become apparent.
- Access to a patient education and support event, such as a Health and Wellbeing Clinic, to prepare the person of the transition to supported self-management, including advice on healthy lifestyle and physical activity. Referral to a health trainer is often helpful.
- Signposting to rehabilitation, work and financial support services.

Metastatic breast cancer

NB numbers in brackets denote relevant paragraphs in the Clinical Advice for the Provision of Breast Cancer Services.



Key:

= Secondary care

Abbreviations:
OPA = Outpatient Appointment
MDT – Multidisciplinary team

Appendix 3: Underpinning documents

- Advanced Breast Cancer (update): Diagnosis and Treatment (CG81), NICE (2014)
- Best Practice Diagnostic Guidelines for Patients Presenting with Breast Symptoms (2010)
- Breast Cancer Quality Standard (QS12), NICE (2011, last updated June 2016)
- Early and Locally Advanced Breast Cancer (CG80), NICE (2009, last updated March 2017)
- Familial Breast Cancer (CG164), NICE (2013, last updated March 2017)
- Living With and Beyond Cancer: Taking Action to Improve Outcomes, Department of Health, NHS Improvement and Macmillan Cancer Support (2013)
- Oncoplastic Breast Reconstruction – Guidelines for Best Practice, Association of Breast Surgery and British Association of Plastic Reconstructive and Aesthetic Surgeons (2012)
- Royal College of Radiologists, Postoperative radiotherapy for breast cancer: UK consensus statements (2016).
- Report of the Independent Cancer Taskforce, *Achieving world-class cancer outcomes: A strategy for England 2015-2020*
- NHS England, Delivering World-Class Cancer Outcomes: Guidance for Cancer Alliances and the National Cancer Vanguard (2016).

Appendix 4: Adjuvant bisphosphonates – guidelines for implementation

Evidence for use

Until recently the results of adjuvant bisphosphonate breast cancer trials had not provided evidence of consistent benefit across all patient groups and study-level meta-analyses of these studies had also provided conflicting results.

There is now, however, a patient-level meta-analysis of data from all unconfounded trials in early breast cancer that randomized between bisphosphonate and control. Data was received on 18766 women of which 97% were of studies of between 2 and 5 years of bisphosphonate therapy. Median follow up was 5.6 woman-years. This meta-analysis has been published in the Lancet by the Early Breast Cancer Trialists Collaborative Group (EBCTCG) (on-line open access July 23rd 2015; http://press.thelancet.com/EBCTCG2.pdf) following presentation by Rob Coleman at the 2013 San Antonio Breast Cancer Symposium (SABCS: abstract S4-07, 2013) and has provided important results, which are considered to be practice changing.

The primary outcomes of the study were time to recurrence, distant recurrence, and breast cancer mortality. Primary planned subgroup analyses were site of first distant recurrence (bone or other) menopausal status, and bisphosphonate class.

There was definite benefit ***only*** in ***postmenopausal*** women (11767), with highly significant reductions in:

1] recurrence (RR 0.86, 95% CI 0.78-0.94; 2p=0.002)

2] distant recurrence (bone or otherwise, RR 0.82, 95% CI 0.74-0.92; 2p=0.003)

3] bone recurrence (RR 0.72, 0.60-0.86; 2p=0.002)

4] breast cancer mortality (RR 0.82, 95% CI 0.73-0.93; 2p=0.02)

The absolute gain from treatment at 10 years was 3.3% for breast cancer mortality (95% CI 0.8-5.7) and 2.2% for bone recurrence (95% CI 0.6-3.8)

With regards to reductions in bone recurrence and breast cancer mortality, these did not depend significantly on patient or clinicopathological primary tumour characteristics, including oestrogen receptor status, nodal status, tumour grade or concomitant chemotherapy. Analysing bone recurrence, the most reliable end-point for the sub-group analyses, there was no significant effect from the class or duration of bisphosphonate but pamidronate showed no benefit. Early data presented at ASCO 2015 indicated no obvious benefit of one bisphosphonate over another in the adjuvant setting (Gralow et al, Study S0307 J Clin Oncol 33, 2015 suppl; abstr 503).

Another important effect was the significant reduction in bone fractures (RR 0.85,95%CI 0.75-0.97; 2p=0.02).

These data are compelling and the benefits of adjuvant bisphosphonates in postmenopausal women are as large if not larger than a number of adjuvant interventions used routinely in early breast cancer.

Implementation guidelines

The following have been constructed using input from clinicians involved in UKBCM group (UK Breast Cancer Meeting) and members of the Breast and Chemotherapy CRGs. They are intended as guidance and local protocols should be developed with CCGs and providers.

Registered indication

Bisphosphonates are not licensed in this indication and since all of them are off-patent they are unlikely to be licensed in this setting.

Patient selection

The evidence clearly indicates benefit in postmenopausal women (both natural and induced). The evidence does not support starting bisphosphonate therapy in patients who are beyond the stage of initial diagnosis and no specific risk group is identified. A risk/benefit discussion should be undertaken with each patient on an individual basis as per standard practice with adjuvant treatments.

Choice, dose and duration of bisphosphonate.

From the data above and recent presentation at ASCO (Gralow et al Study S0307, J Clin Oncol 33, 2015 suppl; abstr 503) oral bisphosphonates and/or IV bisphosphonate could be considered depending on factors eg ability to comply with oral medication, GI tract disturbance.

Recommendations are given below.

- IV Zoledronate (4mgs every 6 months for 3 years)
- Oral Ibandronate (50mg daily for 3 years)

Note that switching between the IV Zoledronate and Oral Ibandronate is also an option.

Where?

- For IV Zoledronate, patients should be treated in the Oncology Units with monitoring and input by Oncology teams. Tariffs need to reflect this as an additional adjuvant oncology treatment and not just ‘within baseline’ as currently exists for this IV drug.
- For oral Ibandronate, this should be initiated in secondary care but continued in primary care.

Monitoring of renal function & Calcium

- Baseline renal function and calcium, vitamin D3 level
- Repeat prior each infusion ie 6/12 but may need earlier depending on baseline

Calcium and Vitamin D supplementation

- Patients should be replete in both calcium and vitamin D before commencing treatment and replacement schedules should be followed as per local protocols
- Once replete daily supplementation should be followed as per local guidance eg Adcal D3

Oral/Dental Health

Incidence on osteonecrosis of the jaw (ONJ) was not possible to assess in the above meta-analysis but ONJ appears to be predominantly associated with 'intensive' dosing of zoledronate (as in the AZURE trial, Coleman et al N Engl J Med2011; 31: 1396-405) and is likely to be less of a problem with 6 monthly zoledronate or oral bisphosphonates with the estimated rate of 1% (Paterson et al, Lancet Oncol 2012;13:734-42, von Minckwitz et al, J Clin Oncol 2013; 31: 3531-39, Gnant et al, Ann Oncol 2014; 26: 313-20.)

A cautious approach at this stage would be appropriate and thus the following guidance is suggested;

- Baseline assessment of dental health. If seen dentist in last 6/12 with no concerns can commence infusion.
- If no dental review in last 6/12 to attend dentist and complete any required treatment before commencing first infusion.
- General guidance on dental hygiene as per individual local guidelines as per treatment in advanced disease and should follow general principles of company information sheets.

Potential cost savings over time

Many patients will be on aromatase inhibitors which may induce bone loss. This regimen will improve bone loss related to these drugs and should reduce the need for DEXA scans. The regimen is also sufficient to treat osteopenia and some levels of osteoporosis (after discussion with bone expert) thus simplifying the management of these patients.

Appendix 5: Open Access Follow Up

Open Access Follow Up is appropriate for most breast cancer survivors with supportive self-management and open access back to the specialist service as required.

Several studies have shown most cases of recurrence are detected by the patient or mammographically and the resources released by the conventional model of routine clinical follow up would be better directed towards general support.

The supportive elements are through implementation of the 'recovery package' including holistic needs assessment and care planning, treatment summary and GP cancer care review, together with a health and well-being programme to better inform and educate survivors about healthy life style interventions (especially diet and physical exercise) and what to look out for in terms of early warning of further problems relating to recurrence or metastatic disease or due to the late effects of treatments - and who to contact.

The supportive and educational components of survivorship, together with some specialist services for the management of consequences of treatment do have resource implications, which will need commissioning support - with funding partly from resources released from changes in follow up (with no routine medical follow ups).

There will need to be robust 'remote' surveillance systems to ensure five years of annual mammographic surveillance (NICE guidance) with results shared with patients and their GPs or recall for further assessment by the symptomatic service managed in a similar way to the NHS Breast Screening Programme.

7 Glossary

Adjuvant treatment – treatment given in addition to other treatment e.g. chemotherapy given after surgery

Advanced breast cancer – breast cancer that has involved the whole breast or has spread (see metastasis)

Anthracyclines – type of chemotherapy drugs, includes doxorubicin and epirubicin

Anti-HER2 therapy – treatment with drugs that target the HER2 receptor e.g. trastuzumab

Aromatase inhibitors – type of hormone treatment used to treat breast cancer by blocking the production of oestrogen in the body

Axilla – the medical term for the armpit

Axillary node sampling – removal of a few lymph nodes from the armpit

Bilateral – both sides of the body e.g. a bilateral mastectomy is the removal of both breasts

Biopsy – removal of tissue for examination under a microscope

Bisphosphonate - a class of drugs used to strengthen bone e.g. zoledronate. Bisphosphonates are used to treat osteoporosis and the bone pain from diseases such as metastatic breast cancer

Breast conserving surgery – surgery that removes a tumour and surrounding tissue but not the whole breast. Also known as lumpectomy or wide local excision

Breast reconstruction – surgery to rebuild a breast after a tumour is removed

Chemoprevention - the use of drugs or other agents to try to reduce the risk of, or delay the development or recurrence of, cancer

Chemotherapy – drug treatment that aims to destroy cancer cells, usually injected into the bloodstream, but can also be injected into muscle or given as a tablet

Core biopsy - removal of tissue using a needle to check for cancer cells

DCIS (Ductal Carcinoma in Situ) – a pre-cancerous breast condition where the cancerous cells remain in the duct and have not spread to the surrounding area in the breast. DCIS may or may not become cancerous in time

Deep inspiration breath hold – an effective method of limiting radiation exposure to the heart and lungs used in radiotherapy treatment

Early breast cancer – cancer in the breast that has not spread beyond the breast and axillary lymph nodes

Endocrine therapy – see hormone therapy

Fine needle aspiration (FNA) – biopsy using a thin needle to extract cells to see if they are cancerous

Holistic Needs Assessment (HNA) – a process of gathering and discussing information with the patient and/or carer in order to develop an understanding of what the person living with and beyond cancer knows, understands and needs. This holistic assessment is focused on the whole person and their entire well-being is discussed – physical, emotional, spiritual, mental, social, and environmental. The process culminates when the assessment results are used to inform a care plan

Hormone/hormonal/endocrine therapy – drug treatment used to stop the hormones oestrogen and progesterone from helping breast cancer cells to grow e.g. tamoxifen

Intensity modulated radiotherapy – an advanced form of radiation therapy using advanced technology to manipulate beams of radiation to conform to the shape of a tumor

Invasive breast cancer - cancer that has spread from where it began in the breast to surrounding normal tissue. The most common type of invasive breast cancer is invasive ductal carcinoma

Isotopic bone scan - a way of imaging bones, organs and other parts of the body by using a small dose of a radioactive chemical

Locally advanced breast cancer – cancer cells have extensively spread to lymph nodes and/or other tissue in the area of the breast, but not to distant sites in the body

Lumpectomy – see breast conserving surgery

Lymph node – a gland which is part of the immune system; it filters lymph fluid, fights infection and forms white blood cells

Lymphoedema – long-term swelling in the tissues, which can occur in the arm or upper body after breast cancer surgery or radiotherapy. It is caused by a build-up of excess fluid in the tissues

Mammography – an x-ray of the breast using very low doses of radiation

Mastectomy – surgery to remove the breast

Metastasis/metastases/metastatic – cancer cells that have spread to another part of the body, also called secondary or advanced cancer

MRI (magnetic resonance imaging) – a type of scan using radio waves and a magnetic field to create images of the body

MDT (multidisciplinary team) – a team of health professionals with a variety of roles and specialisms, who work together to provide treatment and care

Neoadjuvant therapy – treatment given before surgery e.g. the use of chemotherapy before surgery to shrink a large tumour so surgery can be performed

Nodes – glands that are part of the lymphatic system. When breast cancer spreads, lymph nodes in and around the armpit are some of the first places it travels, and surgeons often remove some of these nodes to determine whether the cancer has spread

Oestrogen receptor (ER) test – test to discover if a tumour is sensitive to the hormone oestrogen

Oncologist – a doctor specialising in the treatment of cancer, known as a clinical or medical oncologist

Oncoplastic conservation – surgery involving lumpectomy and cosmetic surgery, sometimes to both breasts to even their appearance (known as contra-lateral symmetrisation surgery)

Ovarian suppression – completely blocking the release of hormones by the ovaries either by surgery, radiotherapy to the ovaries, or treatments with drugs

Paclitaxel – a chemotherapy drug (see taxanes)

Primary breast cancer - see early breast cancer

Raloxifene – a drug that blocks the effects of the hormone oestrogen in the breast and increases the amount of calcium in bone. It is a type of selective oestrogen receptor modulator (SERM)

Receptor status - a test that tells you whether or not the breast cancer cells have certain receptors e.g. for the hormones oestrogen and progesterone

Recovery Package - a combination of different interventions, which when delivered together, will greatly improve the outcomes and coordination of care for people living with and beyond cancer.

Recurrence - when breast cancer returns in the chest/breast area, or in the skin near the original site or scar, this is called a local recurrence. Regional recurrence is breast cancer which has come back following treatment and has spread to lymph nodes (glands) around the breast.

Radiotherapy – the use of high energy x-rays to destroy cancer

Secondary cancer – see metastasis

Sentinel node biopsy – a way of checking to see whether cancer has spread to the lymph nodes in the armpit; sentinel nodes are the first nodes in the armpit that cancer could spread to

Seroma – swollen area of tissue filled with blood serum

Staging – the process to determine the extent to which a cancer has grown and spread

Stratified Open Access Follow Up – see appendix 5

Systemic treatment – treatment that affects the whole body, such as chemotherapy and hormone therapy

Tamoxifen – a drug used in the treatment of breast cancer that blocks the effects of oestrogen

Taxanes – group of chemotherapy drugs e.g. Taxotere

Trastuzumab (Herceptin) – a targeted treatment for breast cancer used to treat approximately 1 in 5 breast cancers known as HER2 positive

Triple negative breast cancer – triple negative breast cancer ie tumours which are oestrogen receptor negative, progesterone receptor negative and HER2 receptor negative

TNM (tumour, nodes, metastases) – a way of describing the cancer and whether it has spread

Triple assessment – initial testing for breast cancer, carried out in a breast clinic, which includes physical examination, imaging of the breast and biopsy

Ultrasound imaging – technique for taking pictures inside the body using sound waves

Wide local excision – see breast conserving surgery

8 Abbreviations

AI – Aromatase inhibitor

BRCA 1 or 2 – two genes that, if inherited in a mutated form, may predispose some carriers to develop breast or ovarian cancer

COSD – Cancer Outcomes Services Dataset

CT – Computed tomography

DCIS – Ductal Carcinoma in Situ

ECAD – Earliest clinically acceptable date

ER – Oestrogen receptor

FNA – Fine needle aspiration

HER2 – Human epidermal growth factor receptor 2

HNA – Holistic Needs Assessment

IMRT – Intensity Modulated Radiotherapy

MDT – Multidisciplinary team

MRI – Magnetic resonance imaging

NHSBSP – NHS Breast Screening Programme

PET-CT – Positron emission tomography – computed tomography

TNM – Tumour, nodes, metastases

T3 – Part of staging. Indicates the size/extent of the primary tumour

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