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1.	SH	Society and College of Radiographers	General	General	The fact the disease is significantly less common in men is acknowledged within the scope of this draft guideline. There are perceived differences in the early diagnosis of this disease in men so the Society and College of Radiographers would like to highlight the appropriate inclusion of men within the evidence gathering process.	Thank you for your comment – we agree.
2.	SH	Association for Palliative Medicine of Great Britain and Ireland	General	General	Patients are usually referred to palliative care services when they have an incurable illness. However, referral to palliative care service should be needs-based and it is possible that patients with invasive adenocarcinoma or locally advanced breast cancer may have a significant symptom burden and would benefit from palliative care input. Not all patients with invasive adenocarcinoma or locally advanced breast cancer will need referral to specialist palliative care services.	Thank you for your comment. The scope is not addressing palliative care. This is covered by the NICE guideline on Improving supportive and palliative care for adults with cancer
3.	SH	HQT Diagnostics	General	General	Many cancer patients choose to add complementary therapies to conventional treatments. These may not only temper the adverse side effects of conventional cancer therapy, but also improve its effectiveness via independent anti-cancer effects. Review Complementary and Alternative Medicine options http://www.lifeextension.com/Protocols/Cancer/Alternative-Cancer-Therapies/ https://is.gd/nicebc2	Thank you for your comment. We will be reviewing lifestyle within the guideline. However, we are not including complementary and alternative medicines specifically in this guideline.
4.	SH	HQT Diagnostics	General	General	Some cancer patients have had to fight battles between conventional doctors and complementary therapists Review the ways in which these groups can work together for the benefit of the patient	Thank you for your comment. We will be reviewing lifestyle within the guideline. However, we are not including complementary and alternative medicines specifically in

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					http://healthinsightuk.org/2015/10/08/the-cancer-whisperer-how-to-broker-a-peace-deal-in-the-war-on-cancer/ Book: The Cancer Whisperer, By Sophie Sabbage	this guideline.
5.	SH	HQT Diagnostics	General	General	Is cancer a nuclear genetic disease or a mitochondrial metabolic disease? Books: Cancer as a Metabolic Disease, by Professor Thomas Seyfried Tripping over the Truth, by Travis Christofferson Talk: https://www.youtube.com/watch?v=SEE-oU8_NSU	Thank you for your comment. We will not be reviewing causes of cancer in this guideline.
6.	SH	Breast Cancer Care	General	General	Breast Cancer Care welcomes this draft scope, which we feel is a promising step forward. However, there are elements we feel are lacking/require further clarification in the draft scope. We have detailed these in the subsequent comments.	Thank you for your comment. We have addressed your subsequent comments.
7.	SH	Association of Breast Surgery	General	General	The document is not currently commenting on breast reconstruction but this is a major issue and it alludes to one of the problems in Section 9. Is there room to reconsider the scope to include the timing of reconstruction if radiotherapy is required?	Thank you for your comment. This is being covered in section 1.5, point 9, post-mastectomy radiotherapy, question 9.2.

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8.	SH	Breast Cancer Now	General	General	**Access for younger women with breast cancer to fertility preservation services** There is still significant variation in (younger) women with breast cancer being able to discuss their fertility options and being referred to relevant services before treatment commences. Recent research by Breast Cancer Care showed that just over half (53%) of younger women diagnosed with breast cancer have no discussion with healthcare professionals about fertility preservation options. This is despite the NICE Fertility guideline recommending that women of reproductive age are offered fertility preservation before starting breast cancer treatment. There is no mention of fertility preservation in the current Early and Locally Advanced Breast Cancer guideline. We feel that it would be very helpful to have a very clear cross-reference to the Fertility guideline from the part of the Early and Locally Advanced guideline that is most relevant to this part of the pathway.	Thank you for your comment. We will include a reference to the Fertility problems: assessment and treatment guideline in the scope. However, we are not covering fertility issues in the guideline.
9.	SH	Breast Cancer Now	General	General	**Managing the consequences of treatment** **Cross-referencing to NICE Menopause guideline** As mentioned above, the menopause section in the current guideline does not mention referral to a specialist menopause clinic ie it doesn't go as far as the more recent Menopause guideline. Therefore, we believe there should be a clear cross-reference and link from the Early and Locally Advanced Breast Cancer guideline to the breast cancer section in the Menopause guideline.	Thank you for your comment. Evidence on interventions for menopausal symptoms in women with breast cancer or a history of breast cancer have been systematically reviewed by the Menopause: diagnosis and management guideline that was

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					The relevant section in the NICE Menopause guideline says: Offer menopausal women with, or at high risk of, breast cancer: ○ information on all available treatment options ○ information that the SSRIs paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen ○ referral to a healthcare professional with expertise in menopause. **Reviewing evidence for progestogens as a treatment for hot flushes** The current guideline specifically prohibits progestogens: "1.13.11 Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer." We would like to see the evidence to support this statement reviewed as part of the guideline review, taking into account in particular the following: • Bines, J. et al (2014): "Activity of megestrol acetate in postmenopausal women with advanced breast cancer after nonsteroidal aromatase inhibitor failure: a phase II trial", *Annals of Oncology* **25,** 831–836. • Mohammed, H. et al (2015): "Progesterone receptor modulates estrogen receptor-α action in breast cancer", *Nature* **523** (7560), 313–317. • Goodwin, J.W. et al (2008): "Phase III Randomized Placebo-Controlled Trial of Two Doses of Megestrol Acetate as Treatment for Menopausal Symptoms in Women With Breast Cancer: Southwest	published in 2015. We will include a cross-reference to the NICE Menopause: diagnosis and management Guideline. Therefore, we are not covering menopause issues in the guideline update.

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					Oncology Group Study 9626", *Journal of Clinical Oncology* **26,**1650-1656. **Roll-out of the Recovery Package** The English Cancer Strategy *Achieving World Class Cancer Outcomes 2015-2020* outlines how we should transform our approach to support people living with and beyond cancer.	
10.	SH	Breast Cancer Now	General	General	It recommends **"**accelerating the roll-out of stratified follow up pathways and the Recovery Package", with the aim that "by 2020 every person with cancer will have access to elements of the Recovery Package, and stratified pathways of follow-up care will be in place for the common cancers". The Recovery Package is a combination of different interventions, which when delivered together, can greatly improve the outcomes and coordination of care, including better and earlier identification of consequences of treatment. It has been developed and tested through the National Cancer Survivorship Initiative to assist people living with a diagnosis of cancer to prepare for the future, identify their individual needs and support them to live well after treatment. We firmly support this approach to supporting people living with and beyond cancer, as it is a key element of our vision to see breast cancer turned into a chronic disease so that by 2050 no-one dies of breast cancer. We strongly recommend that this recommendation of the Independent Cancer Taskforce is fully explored when developing the clinical follow-up	Thank you for your comment. We have cross referenced this in section 3.3. The guideline is not looking at follow-up as part of the update.

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					section of the early and locally advanced breast cancer pathway. In fact, we believe this should be considered more as a standard part of the treatment pathway, rather than as a 'clinical follow-up' addendum. Independent Cancer Taskforce (2015): "Achieving World Class Cancer Outcomes: A Strategy for England, 2015-2020". See in particular pp54-58. http://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf	
11.	SH	Breast Cancer Now	General	General	**Identifying people in primary care with suspected recurrence** There is no NICE guidance for health professionals on spotting the signs of breast cancer recurrence and referring appropriately. We believe that the appropriate place for this is the Early and Locally Advanced Breast Cancer guideline, for instance in what is currently called the 'Clinical follow-up' section. It is not covered by any of the other NICE breast cancer guidelines, or the NICE Suspected Cancer guideline. We know from talking to people living with metastatic breast cancer that healthcare practitioners, particularly GPs, do not always recognise potential symptoms of metastatic disease. We have heard from patients with metastatic breast cancer who have been repeatedly prescribed indigestion medication when presenting to GPs with stomach pains or have been referred to osteopaths and chiropractors for bone pain. We feel strongly that healthcare practitioners would benefit significantly from additional support recognising these signs and symptoms and that it cannot be left to clinical	Thank you for your comment. The guideline is not looking at follow-up as part of the update. However, we will include information on the signs and symptoms that need to be recognised for breast cancer recurrence within the guideline.

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					judgement alone.	
12.	SH	Breast Cancer Now	General	General	**BRCA testing for all women diagnosed under 50** The English Cancer Strategy *Achieving World Class Cancer Outcomes 2015-2020* recommends that "NHS commissioners should ensure that all women under the age of 50 diagnosed with breast cancer are offered testing for BRCA1/BRCA2 at the point of diagnosis". This is important because it enables any family members at high risk to be identified and active surveillance programmes put in place. Where applicable, positive tests can also guide decisions on the most clinically and cost-effective treatments. We suggest that the appropriate place to reflect this recommendation would be in the Early and Locally Advanced guideline, section 1: *Referral, diagnosis and preoperative assessment.* As it relates to women being identified in the mainstream breast cancer pathway (as opposed to a familial breast cancer pathway), we feel that it needs to be flagged to clinicians in the Early and Locally Advanced breast cancer guideline rather than the Familial breast cancer guideline. Independent Cancer Taskforce (2015): "Achieving World Class Cancer Outcomes: A Strategy for England, 2015-2020". http://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf	Thank you for your comment. Genetic testing for a person with breast cancer is covered in the Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer, NICE guideline, and will not be covered in this update

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13.	SH	Breast Cancer Now	General	General	Q1 (as outlined in the introduction of this comments form) **Which interventions or forms of practice might result in cost saving recommendations if included in the guideline?** In **Comment 1** we have outlined the financial value of increasing adherence to adjuvant endocrine therapy: McCowan et al (2013) showed that patients with low adherence to their adjuvant medication have shorter time to recurrence, increased medical costs and worse quality of life. They concluded that interventions that encourage patients to continue taking their treatment on a daily basis for the recommended 5-year period may be highly cost-effective. Indeed, they estimated the expected value of changing a patient from low to high adherence as £33,897 (95% CI: £28,322–£39,652). **Comment 5** has similar implications to comment 1, in that if we can support patients to better cope with the consequences of treatment, they are more likely to be able to adhere to treatment that can prevent them from developing secondary breast cancer which is a huge financial burden on the NHS. In **Comment 2**, we have outlined the estimated cost-savings from implementing adjuvant bisphosphonates routinely: The total cost of administering this treatment in the UK to the annual patient population of 35,700 would be £16,917,783 per year. This cost is offset in the short term by savings from no longer needing to take DEXA bone scans in	Thank you for your comment and the information. Cost-effectiveness is taken into account when producing NICE guidelines.

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					this patient population – a saving of £6,835,122 per year, and in the long term by 1,178 less people developing secondary breast cancer per year – a saving of at least £14,725,000 per year.* This means that there would be a net saving of at least £4.64m per year, which amounts to £3,941 saved for every life saved. These figures are also available by UK nation – please get in touch if you would like to see these. In **Comment 3**, we have highlighted that there is now clear evidence to show that patients who maintain a healthy weight and take the recommended exercise can reduce the risk of breast cancer recurrence, sometimes to the same degree as adjuvant medical treatment (a reduction in risk of approximately 30 per cent). Therefore, there is potential to notably reduce incidence of secondary breast cancer if this recommendation was implemented, with associated cost-savings. The cost of secondary breast cancer is modelled in comment 2.	
14.	SH	RCGP	General	General	The scope seems appropriate. Will the lifestyle section cover survivorship following treatment?	Thank you for your comment. Lifestyle issues pertinent to survivorship will be covered.
15.	Individual	Michelle Leech	Current Guideline	1.14 Follow-up	Surveillance of ispalateral soft tissues after mastectomy is not recommended within current guideline due to insufficient evidence of survival benefit. If this group were kept within the National Mammogram Program would there	Thank you for your comment. The issues you raise are not covered within the scope of this guideline. We will be looking at surgical

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					be cost savings? Detection of recurrence at an earlier stage would mean less extensive treatment; and potentially less risk of loss of life Are there groups of women who should receive a mammogram to ispalateral tissues after mastectomy? For e.g. Those with superficially located breast tissue Those with extensive and/or high grade DCIS Those with an involved/positive margins Is there evidence of higher levels of recurrence in some groups beginning to emerge in research studies: Prof Bundred of The University of Manchester spoke at SABCS 2015 about a retrospective study comparing local recurrence rates after simple mastectomy or skin-sparing mastectomy for ductal carcinoma in situ (DCIS). Script from his presentation to follow: Traditionally DCIS has been treated by simple mastectomy. This is associated with a low (<1%) rate of local breast cancer recurrence The Sloan Study), but there have been recent data suggesting that local recurrence	margins and will provide evidence of recurrence rates relating to this topic.

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					rates are increasing. Skin-sparing mastectomy has emerged as an alternative as it results in a better cosmetic outcome, but there are few data looking at local recurrence. Local recurrence at 10-years was 0% in women who had a simple mastectomy and 5.6% in those who had skin-sparing mastectomy. Should the surveillance after mastectomy recommendation be reviewed? Recurrence rates of disease may be increasing as the uptake of breast reconstruction and therefore the supporting skin sparing mastectomy is on the increase. At least women should be informed as part of the decision making process around breast reconstruction that surveillance on any reconstructed breast will most likely end. Most women are likely to accept a modest increase in risk of recurrence but current lack of surveillance after mastectomy is not well shared.	

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16.	NICE	NICE MPP	1	13	What about providers of services who may not be healthcare professionals but managers who oversee service provision and compliance to contracts set by their commissioner. To include providers of breast cancer services as an additional bullet point?	Thank you for your comment. We have included NHS managers involved in the provision of multidisciplinary care of people with early and locally advanced breast cancer in the scope.
17.	SH	Society and College of Radiographers	1	14	The Society and College of Radiographers strongly supports a patent centric approach to multi-disciplinary care. The profession is also striving for a workforce to be based upon the need to provide a patient-centred, holistic approach across the entire radiotherapy pathway of care including the provision of patient information and psychological support. It will be need to be streamlined care, sensitive and responsive to patients' needs, and not based upon professional roles and /or historical practices	Thank you for your comment. We agree that the workforce in this field is evolving.
18.	SH	Society and College of Radiographers	1	16	The Society and College of Radiographers supports the inclusion of all stakeholders as key to the patient pathway. There are Therapeutic Radiographer advanced and consultant level practitioner-led planning services including on-treatment review, supplementary and independent prescribing addressing the need to ensure access to a key worker for all patients in a high quality, modern service	Thank you for your comment. We recognised the important role that the therapeutic radiographer play and we will be including one on the group.
19.	Individual	Michelle Leech	2	47	The draft currently scope excludes women with locally recurrent breast cancer or DCIS. Where is treatment for this group covered? Or is treatment on a 'case by case' basis? After BCS + RT the ispalateral recurrence rate is stated between 10-20%	Thank you for your comment. We recognise that there is a gap in the guidance. However, due to the complexity of the topic it is not possible to include it within the

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					and after mastectomy between 2-8% across the larger scale studies. Women who have had a previous diagnosis of BC also have a slightly greater risk of BC in the contralateral breast. Unfortunately the size of the group who experience a local recurrence is likely to be considerable in size (I guess?) and growing. Where is the guidance for women with local recurrence but without evidence of metastases (so not covered by CG80 or CG81 Advanced Breast Cancer) should they be included within this guideline? Treatment of locally recurrent disease would, I guess, follow the same pathway as first diagnoses unless there was evidence of metastases.	update of EBC. But we will flag the gap to NICE surveillance programme.
20.	Individual	Michelle Leech	2	48	This draft scope excludes women with lobular carcinoma in situ. LCIS is a known risk factor for being at higher risk of developing breast cancer in the future in either breast but management of it is very variable. It is a diagnosis that can cause anxiety because of the lack of clear practice guidelines. Pleomorphic LCIS is currently recommended to be treated as DCIS and complete removal is recommended. Should this group be noted within current surveillance recommendations of CG80 or within the guideline for those people at increased risk of breast cancer?	Thank you for your comment. LCIS is not within the scope of either CG80 nor the familial breast cancer guidelines. The Association of Breast Surgery issues guidelines which include the management of LCIS.
21.	SH	Guy's and St Thomas' NHS Foundation Trust	2	49	The draft scope currently excludes adults who have an increased risk of breast cancer due to their family history. We appreciate that for unaffected women guidance is provided by NICE CG164. However for women affected by breast cancer who have a strong family history or carry a pathogenic mutation in a high-risk breast cancer	Thank you for your comment. This group of women are covered by CG164 and are therefore are correctly excluded from the scope.

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					gene, neither NICE CG164 nor the Early and Locally Advanced Breast Cancer guidance currently provide guidance about their management. The management options for high-risk women affected by breast cancer differ from other women, for example risk-reducing mastectomy for contralateral breast cancer risk, platinum-based chemotherapy or PARP inhibitor trials for BRCA1/2 gene mutation carriers. At present there is inconsistency and a lack of clarity about the management of this group of patients across the UK. We believe that the remit for guidance on the management of these women should reside with the Early and Locally Advanced Breast Cancer guidance.	
22.	SH	Society and College of Radiographers	3	53/54	As well as the 68 NHS centres that provide radiotherapy services there is a growing independent /private sector so this is of key consideration in order to provide continuity of care centred on the patient.	Thank you for your comment. This guideline covers all settings in which NHS care is provided.
23.	SH	Breast Cancer Care	3	59	**Key areas that will be covered** The draft scope does not state whether the section in the current guideline, **1.14 Follow-up**, will be included and updated in the updated guideline. We feel that this section should be included in the scope and be updated. The current version of the guideline refers to giving patients information on '*signs and symptoms to look out for and seek advice on'* within a written care plan.	Thank you for your comment. The guideline is not looking at follow-up as this topic area was not identified as a priority topic as part of the update.

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					As the scope is unclear as to whether this section is to be included/ updated, we emphasise the need for the guideline to include clearer guidance on informing patients specifically about signs and symptoms which could be indicative of secondary (metastatic) breast cancer. Breast Cancer Care hears from many people with a secondary breast cancer diagnosis who say they were unaware of the signs and symptoms of secondary disease Guidance on informing patients of symptoms which could be indicative of secondary (metastatic) breast cancer is not currently covered in any other guidance, including Clinical Guideline 81, *Advanced Breast Cancer: Diagnosis and Treatment*, or NICE Guideline 12, *Suspected Cancer: Recognition and Referral.* ---	
24.	SH	Breast Cancer Care	3	70	**Section - Areas that will be covered** We welcome the inclusion of *lifestyle* into the scope for the updated guideline. We would welcome clarity on whether this section will reflect the Recovery Package.	Thank you for your comment. We are addressing lifestyle within the scope of the guideline and the final question of what to include will be made at the first GC meeting. We will systematically search and review evidence according to the NICE guidelines manual.

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					It may also be helpful when developing the guideline to consider breast cancer specific services which look at lifestyle, such as Breast Cancer Care's Moving Forward course. Run in partnership with NHS hospitals in various locations across the UK, Moving Forward courses usually take place over half a day for three or four weeks. Delivered by a range of expert speakers, they aim to provide information, support and professional guidance on how to cope with and adjust to life after breast cancer treatment. Topics covered include: healthy eating and exercise, as well as managing menopausal symptoms, lymphoedema, cancer fatigue, and intimacy and relationships. The course is open to people who have had a primary breast cancer diagnosis and have finished their hospital-based treatment.	
25.	SH	Cambridge University Hospitals Foundation Trust	4	87	The Draft Scope for the CG80 update currently excludes menopausal symptom management from this review. This topic should definitely be reviewed. One of the most effective treatments for hot flushes in breast cancer survivors is progesterone, but NICE CG80 states that progesterone should not be used. Since 2009 there have been significant advances in our understanding of progesterone effects in breast cancer, and the current NICE recommendation (which states that progestogens should not be used for menopausal symptoms (1.13.11)) is **now out of date**. Megace is a cheap and effective treatment for disabling hot flushes, and there is mounting	Thank you for your comment. Evidence on interventions for menopausal symptoms in women with breast cancer or a history of breast cancer have been systematically reviewed by the Menopause: diagnosis and management guideline that was published in 2015. We will include a

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					evidence that it beneficial effects in breast cancer activity. This recent evidence should be reviewed. Unless it is endorsed as a treatment option for menopausal symptoms by the updated guideline, it will continue to be inaccessible to NHS patients.	cross-reference to the NICE Menopause: diagnosis and management Guideline. Therefore, we are not covering menopause issues in the guideline update.
26.	SH	BASO~The Association for Cancer Surgery	4	103	Change 'tissue margin in people' to 'tissue margin in patient'	Thank you for your comment. The use of people is correct here.
27.	SH	Association of Breast Surgery	4	103	Margins are not relevant for mastectomy. Please see the ABS guidelines for conservation, which are attached and awaiting publication in the EJSO	Thank you for your comment. We will be looking at the evidence regarding the relevance of margins.
28.	Individual	Michelle Leech	4	103	Question would require amendment to: What is the optimal tumour-free tissue margin (s) in people with invasive breast cancer ***and/or ductal carcinoma in situ (DCIS)*** treated with breast conserving surgery or mastectomy? Above amendment needed because the aim of first-line DCIS treatment is identical to the treatment of invasive breast cancer; to attempt to remove all present disease with surgery and with a clear, 'acceptable' 'safe' margin. (DCIS is thought to develop into invasive cancer in up to 70% of women where it is found. Higher the grade of DCIS the higher the likelihood of this step.) DCIS is often more extensive and multi-focal than other types of BC. Finally, If DCIS does recur there is an around 50% chance it will be as invasive breast cancer. So margins are important here too.	Thank you for your comment. We agree and have amended the question 1.1 in section 1.5, point 1. However, these are still draft questions and will be finalised at the first GC meeting.

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					I believe there are 6 possible margins after a mastectomy; which are important to success of excision other than just the deep/ chest wall margin? Anterior, skin side Therefore there may there need to be a different recommendation for size of margins after surgery for invasive or for non-invasive disease?	
29.	SH	Association of Breast Surgery	4	106	Please see the ABS Guidelines on the axilla: http://www.associationofbreastsurgery.org.uk/media/50934/axilla_abs_consensus_statement_16_3_15.pdf. It is not clear if you mean SLNB or US guided axillary node biopsy of both.	Thank you for your comment. We meant both.
30.	SH	Association of Breast Surgery	4	108	2.2 is not a clear question. Do you mean, "What are the indications for AXILLARY nodal radiotherapy after a positive axillary node biopsy" or "What are the indications for REGIONAL (axilla/ SCF/ IMC) nodal radiotherapy after a positive axillary node biopsy. The RCR are drafting guidelines on this currently.	Thank you for your comment. We feel that the question is clear, however they will be finalised at the first GC meeting. We are aware the RCR are drafting guidelines and we are hoping to recruit a member of this committee to the GC.
31.	SH	Breast Cancer Care	4	84 & 87	**Fertility issues** Breast Cancer Care is concerned to see that the current areas on Providing information and psychological support (section 1.2) and Complications of local treatment and menopausal symptoms (section 1.13) are not included in	Thank you for your comment. We will include a reference to the Fertility problems: assessment and treatment guideline in the scope. However, we are not covering

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					the scope for update. There is a need for the updated guideline to include reference to fertility issues. This is likely to fall into one of the above areas. Breast Cancer Care is aware that people diagnosed with breast cancer are often not having discussions with their healthcare professionals about options to preserve their fertility. Recent research* by Breast Cancer Care found that 52.5% of women with breast cancer said that their healthcare professionals did not discuss fertility preservation options with them. This is despite recommendations in NICE clinical guideline 156: *Fertility Problems: Assessment and Treatment* that, '*At diagnosis, the impact of the cancer and its treatment on future fertility should be discussed between the person diagnosed with cancer and their cancer team'.* Breast Cancer Care would like to see recommendations in the updated guideline along the lines of: 1. People diagnosed with breast cancer are able to discuss the possible effects of treatment on their fertility and future pregnancies, and how likely this is, before treatment starts. 2. People diagnosed with breast cancer are offered a prompt referral to a fertility specialist, whether they have a partner or not, to discuss options for trying to preserve fertility before starting chemotherapy or	fertility issues in the guideline

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					hormone treatment. At the very least, the updated guideline should signpost healthcare professionals to the NICE guideline *Fertility Problems: Assessment and Treatment* (clinical guideline 156). ---- *Survey undertaken online between Monday 25 January and Tuesday 9 February 2016. Total sample size: 556 women.	
32.	SH	Breast Cancer Now	5	134-135	**Adjuvant bisphosphonates** **New indication** A meta-analysis of 26 randomised controlled trials involving nearly 19,000 women around the world with primary breast cancer, more than 11,000 of whom were post-menopausal, concluded that giving a bisphosphonate to post-menopausal women with primary breast cancer could improve the following outcomes: • Reduced risk of breast cancer spreading to the bones within 10 years by 28% (reduction in absolute risk from 8.8% to 6.6%) • Reduced risk of death from breast cancer within 10 years by 18% (reduction in absolute risk from 18.0% to 14.7%) No benefits or harms were seen in pre-menopausal women. The benefits of bisphosphonates were similar irrespective of histological type of breast cancer and the use of other treatments such as chemotherapy.	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.

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					Although the percentage of absolute benefit appears small, the treatment is estimated to save 1,178 lives every year in the UK if given routinely to the entire eligible population (around 35,700), and it is about the same absolute benefit seen from some types of chemotherapy. This meta-analysis was conducted by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) and was published in the *Lancet* in July 2015. **Clinical consensus** The NHS England Breast Cancer Clinical Reference Group has developed breast cancer service guidance, which is in final draft form. This guidance will recommend that this treatment is offered routinely for postmenopausal women with primary breast cancer, and that both IV (to be delivered in the Oncology Unit) and oral tablet (to be initiated in secondary care but continued in primary care) options are available to patients, and that switching between the two is an option. The results of the meta-analysis were discussed at a meeting of the UK Breast Cancer Group in November 2015, a forum made up exclusively of breast oncologists. There was unanimous agreement that the data from the paper was sufficient to support implementation and also that there was a moral duty to do so. Some oncologists have started providing the treatment using local funding arrangements; others are attempting to do so, but with many pending funding approval; some have expressed their desire to wait for some kind of national guidance or protocol.	

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					In addition, European consensus guidance was published in the *Annals of Oncology* in January 2016. The panel recommended that "bisphosphonates (either intravenous zoledronic acid or oral clodronate) should be used as part of routine clinical practice in the prevention of metastases in patients with low levels of female sex hormones - age 55 and over and/or postmenopausal. **Clinical pathway** The NHS England Breast Cancer Clinical Reference Group draft guidance recommends a treatment regime of: • IV zoledronate/ zoledronic acid (4mgs every 6 months for 3 years) • Oral ibandronate (50mg daily for 3 years) It also notes that switching between the IV zoledronate and oral ibandronate is an option. For IV zoledronate, patients should be treated in the Oncology Units with monitoring and input by Oncology teams. For oral ibandronate, this should be initiated in secondary care but continued in primary care. The guidance includes advice as to the monitoring of renal function, calcium and vitamin D as well as dental health, owing to the increased risk of osteonecrosis of the jaw (ONJ). The increased risk of ONJ may influence the patient's risk/ benefit decision. However, the leading specialist in this area, Professor Rob Coleman, found a low incidence of ONJ and considers the risk in this indication to be very	

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					small. Given this, we believe that the indication should be offered to all post-menopausal women in line with the European consensus guidance, and that patients must be given the option to make the risk-benefit decision themselves. It is crucial to note that the indication that most oncologists are currently using (first dose given only through chemotherapy to high risk patients only) is not the indication indicated by the meta-analysis but is largely due to the challenges of implementing; the first dose given at the time of chemotherapy is more or less cost-neutral because it incurs drug costs only and not consultant time. Of the consultants we have spoken to about this, they are pursuing this route as a stop gap whilst waiting for approval to use beyond the first dose, and with a wider group of patients. **Variable access** Despite the clinical consensus, a UK-wide survey by the UK Breast Cancer Group in March 2016 showed that access is highly variable, and currently only 24% of respondents are routinely offering it. The survey represented at least 125 breast cancer oncologists across approximately 56 hospitals in the UK. This is estimated to be 50-60% of the total UK population of breast cancer oncologists. A common theme from the survey is a perceived requirement to wait for, or a desire to have, national endorsement/ guidance. What is most concerning is that some oncologists are waiting for a national funding decision, or believe that one is underway – though we're not aware that any is planned in any of	

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					the nations. **Need for national commissioning guidance** The survey showed that the vast majority of those trying to implement it were currently experiencing blockages in funding and commissioning (rather than for clinical reasons). Indeed the blockage for this indication seems to be that oncologists lack a robust business case to persuade hospital management and/or local commissioners. Although the treatment is cheap, it is not cost-neutral (best estimate is about £474 per patient for the whole course when you factor in calcium and renal monitoring and consultant time), and a common complaint is the need for a national appraisal which includes a business case/ some element of cost-effectiveness analysis and/or a national commissioning policy. **Potential savings for the NHS** A lay summary of the financial modelling of adjuvant bisphosphonates has been developed by Breast Cancer Now in collaboration with Professor Rob Coleman. This is based upon cost of treatment and of potential savings outlined in the business case and financial modelling undertaken by South Yorkshire Cancer Strategy Group in February 2016. This is also included as an attachment. The total cost of administering this treatment in the UK to the annual patient population of 35,700 would be £16,917,783 per year. This cost is offset in the short term by savings from no longer needing to take DEXA bone scans in this patient population – a saving of £6,835,122 per year, and in the long	

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					term by 1,178 less people developing secondary breast cancer per year – a saving of at least £14,725,000 per year.* This means that there would be a net saving of at least £4.64m per year, which amounts to £3,941 saved for every life saved. *There is no comprehensive up-to-date estimate of the total cost of a secondary breast cancer patient to the NHS. The best estimate currently available is £12,500 and this, from 2004, is likely to be a gross underestimate. So in reality, the savings are anticipated to be notably higher. Remak, E; Brazil, L (2004): Cost of managing women presenting with stage IV breast cancer in the UK, E Remak and L Brazil, *British Journal of Cancer* **91**, 77-83. Early Breast Cancer Trialists' Collaborative Group (2015): "Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials", *The Lancet* **386** (10001), 1353–1361. Hadji, P; Coleman, R (2016): "Adjuvant bisphosphonates in early breast cancer: Consensus guidance for clinical practice from a European Panel" *Annals of Oncology* **27** (3), 379-390. Final draft guidance from NHS England Breast Cancer Clinical Reference Group, "Appendix 4: Adjuvant bisphosphonates – guidelines for implementation".	

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33.	SH	Breast Cancer Now	5	122-123	**<u>Endocrine therapy for invasive disease</u>** The guideline could say more about managing the side effects of endocrine therapy and encouraging adherence. Section 1.7.7 goes some way to acknowledging this but we believe there should be a statement dedicated to encouraging patient understanding of the value of adherence to adjuvant endocrine therapy and support for managing side effects. This issue is likely to become even more pertinent if the optimal duration of endocrine therapy is extended from 5 to 10 years. **The value of increasing adherence** McCowan et al (2013) showed that patients with low adherence to their adjuvant medication have shorter time to recurrence, increased medical costs and worse quality of life. They concluded that interventions that encourage patients to continue taking their treatment on a daily basis for the recommended 5-year period may be highly cost-effective. Indeed, they estimated the expected value of changing a patient from low to high adherence as £33,897 (95% CI: £28,322–£39,652). **Supporting patients to cope with side effects and adhere to their adjuvant treatment regime** The menopausal side effects of breast cancer treatment can be severe and can have a significant impact upon quality of life. In some cases, they can be severe enough to cause people to discontinue or disrupt their treatment for breast cancer, thus compromising their survival.	Thank you for your comment. The focus of the question will be finalised within the GC meetings. Adherence to treatment could be an outcome when looking at the evidence. Evidence on interventions for menopausal symptoms in women with breast cancer or a history of breast cancer have been systematically reviewed by the

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					Treatment options are available to help people to manage the menopausal side effects of breast cancer treatment but more often than not, people are not made aware of these and/or are not referred to the appropriate specialist. It has become clear that patients with early invasive breast cancer need support and information to help them to continue to adhere to their adjuvant treatment plan, and therefore have better survival outcomes. **Support with managing side effects could play an important role in encouraging adherence** Makubate et al (2013) showed that many women do not take the medication as directed and they stop treatment before completing the standard 5-year duration. The researchers commented that they were unable to examine reasons for non-adherence, but a case note review of the women with an incidence of breast cancer between 1998 and 2007 had 382 women who discontinued medication, reporting they did so owing to side effects (the study comprised 3361 women in total). Over half of the women whose notes were reviewed, reported side effects due to endocrine therapy. **Include a clear link to the NICE Menopause guideline** The menopause section in the current guideline does not mention referral to a specialist menopause clinic ie it doesn't go as far as the more recent Menopause guideline. Therefore, we believe there should be a clear cross-reference and link from the Early and Locally Advanced Breast Cancer guideline to the breast cancer section in the Menopause guideline.	Menopause: diagnosis and management guideline that was published in 2015. We will include a cross-reference to the NICE Menopause: diagnosis and management Guideline. Therefore, we are not covering menopause issues in the guideline update..

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					The relevant section in the NICE Menopause guideline says: Offer menopausal women with, or at high risk of, breast cancer: ○ information on all available treatment options ○ information that the SSRIs paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen ○ referral to a healthcare professional with expertise in menopause. Makubate et al (2013): "Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality" *British Journal of Cancer* **108**, 1515–1524. McCowan et al (2013): *"*The value of high adherence to tamoxifen in women with breast cancer: a community-based cohort study", *British Journal of Cancer* **109**, 1172–1180.	A link to the Menopause: diagnosis and management. NICE guideline has been included in the scope. Evidence on interventions for menopausal symptoms in women with breast cancer or a history of breast cancer have been systematically reviewed by the Menopause: diagnosis and management guideline that was published in 2015. We will include a cross-reference to the NICE Menopause: diagnosis and management Guideline. Therefore, we are not covering menopause issues in the guideline update.
34.	SH	British Lymphology Society	5	111/112	BLS feel that there are variations in the care of patients with and at risk of developing lymphoedema following breast cancer treatment around the UK and there is uncertainty regarding recommended best practice. There have been multiple systematic reviews in recent years but largely these conclude that there is limited available evidence for the effectiveness of the different elements of treatment. The current NICE guidance does not reflect the evidence that is available in these systematic reviews regarding the range of available treatments and need for early treatment. Also, there	Thank you for your comment. We are not covering management of lymphoedema within the update of the guideline. Early identification of lymphoedema will be covered in section 1.5, point 2, question 2.3.

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					are differences in the recommendations provided in the 2 NICE breast cancer guidance documents; specifically there is updated guidance for CG81 (Advanced breast cancer, July 2014) which is not reflected in this guidance CG80 for early breast cancer. What measures can be implemented to ensure that lymphoedema is promptly identified to enable prudent and effective management?	
35.	SH	Association of Breast Surgery	5	111	Unnecessary axillary clearance should always be avoided where possible.	Thank you for your comment. We agree.
36.	SH	Genomic Health	5	118	My colleague Andrew Paramore and I attended the scoping meeting on the 3rd May and found it to be a very productive discussion. We particularly welcomed the interesting discussion about adjuvant systemic therapy planning. We would like to express our support for question 3.3 ('What is the role of gene profiling in determining the need for adjuvant systemic therapy') being incorporated and addressed in the updated CG80 guidance. We acknowledge that the NICE Diagnostics Assessment Programme was responsible for publishing the relevant guidance (DG10) related to this question. That being said, we believe it is important for NICE to align their guidance, leading to better uptake of their recommendations. We would like to emphasise the important role of gene profiling in allowing more equitable access to adjuvant chemotherapy across the country. This is such an important topic and is now embedded in breast cancer clinical practice that it should be reflected in the overarching NICE clinical guidance (CG80) in	Thank you for your comment. The question on the role of gene profiling has been removed from the scope of this guideline. The update of DG10 will be undertaken by the Diagnostic Assessment Programme at NICE.

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					addition to the more niche diagnostics guidance. We propose that the role of gene profiling to inform adjuvant systemic therapy should be described directly in the CG80 guidance, rather than merely referencing the DG10 guidance. The recommendation in the current CG80 guidance is to 'consider using Adjuvant! Online to support estimations of individual prognosis and the absolute benefit of adjuvant treatment for patients with early invasive breast cancer'. This recommendation is now outdated and I would suggest that no update to this recommendation could be complete without describing the role of gene profiling. We were very pleased that NICE has recently prioritised this specific topic in the updated Breast Cancer Quality Standards. This is a very positive step towards more consistent use of gene profiling to inform adjuvant chemotherapy use. Given this acknowledgement of the topic as being a key area for quality improvement, it would therefore seem to make sense to also incorporate the topic in the CG80 guidance. Furthermore, you call for views on which forms of practice might result in cost saving recommendations if included in the guideline. Oncotype DX breast cancer testing has been directly shown to result in important savings by avoiding unnecessary adjuvant chemotherapy use. Indeed Oncotype DX testing is expected to be net cost-saving to the NHS, as supported by a large body of real-world decision impact evidence. Finally, I would also like to propose that this important topic be incorporated into the NICE Pathway for early and locally advanced breast cancer. This	

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					would provide an important overview of the point at which gene profiling for adjuvant systemic therapy planning fits into the broader patient pathway.	
37.	Individual	Michelle Leech	5	121	Should the question statement be Endocrine Therapy for Breast Cancer The guideline currently excludes women with oestrogen-positive DCIS, strong evidence exists that endocrine therapy offers protective benefit against recurrence in both breasts. What is the benefit of prevention in this scenario? What is the benefit versus side-effects of endocrine therapy? Are there groups for whom adjuvant endocrine therapy may not add any disease free survival benefit or survival benefit. Older women with low-grade invasive cancer? Ovarian suppression is not well covered by many of the Breast Cancer support websites for patients such as Breast Cancer Care and Cancer Research. Is there research which shows the levels of breast cancer patient awareness of this option? the benefits and risks and how it fits into wider treatment.	Thank you for your comment. Older women with low-grade invasive cancer and ovarian suppression is included in the scope of the guideline, section 1.5, point 4.

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38.	SH	HQT Diagnostics	5	122	There is very good evidence that adjusting Vitamin D levels of 25(OH)D to 100-150 nmol/L helps to prevent and treat breast cancer Some doctors recommend aiming for 200 nmol/L during the treatment phase Vitamin D has a half-life in the body of 30-60 days, so dosage is required at least every 7-30 days. Vitamin D is fat soluble, so the dosage needs to be adjusted according to weight of the patient. Source: http://www.vitamindwiki.com/Cancer+-+After+diagnosis http://www.vitamindcouncil.org/health-conditions/breast-cancer/ http://grassrootshealth.net/ http://ar.iiarjournals.org/content/34/3/1163.full http://www.tandfonline.com/doi/pdf/10.4161/derm.1.1.7388 http://www.greenvits.eu/blogs/news/31767747-how-much-vitamin-d-do-i-need	Thank you for your comment. We are not covering vitamin D in the scope of this guideline.
39.	SH	HQT Diagnostics	5	122	There is very good evidence that adjusting Omega-3 and Omega-6 levels helps to prevent and treat breast cancer **Key Indicators**……**Target**…**Comments** **Omega-3 Index**…..>8%.....Is the Omega-3 level high enough ? **Omega-6/3 Ratio** <3:1……Is the Inflammation low enough ?	Thank you for your comment. We are not covering Omega-3 and Omega-6 levels within the scope of the guideline.

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					Increasing Omega-3 may need 2-5 grams of Omega-3 per day. Reducing Omega-6 needs advice about diet and lifestyle from a Dietitian or Nutritional Therapist Source: http://www.expertomega3.com/omega-3-studies/oncology http://analysis.hqt-diagnostics.com/Products/HQT-Analysis http://www.greenvits.eu/collections/omega-3 http://preventcancer.aicr.org/site/News2?page=NewsArticle&id=7629&news_iv_ctrl=0&abbr=pub_ http://www.ncbi.nlm.nih.gov/pubmed/26714774	
40.	SH	HQT Diagnostics	5	122	Review the effect of Vitamin C on prevention and treatment of breast cancer. This can be Intravenous (Riordan Protocol) or Liposomal or normal capsules, powder and tablets. Sources: http://vitamincfoundation.org/vitcancer.php http://www.cancer.gov/about-cancer/treatment/cam/patient/vitamin-c-pdq Book: Vitamin C: The Real Story, by Steve Hickey & Andrew Saul	Thank you for your comment. We are not covering vitamin C in the scope of this guideline.
41.	SH	HQT Diagnostics	5	122	Review the effect of Vitamin K2 on prevention and treatment of breast cancer and Ductal Carcinoma (DCIS) Source: http://www.ncbi.nlm.nih.gov/pubmed/18374196	Thank you for your comment. We are not covering vitamin K2 in the scope of this guideline.

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					http://www.ncbi.nlm.nih.gov/pubmed/20335553 Book: Vitamin K2 and the Calcium Paradox by Dr Kate Rheaume-Bleue	
42.	SH	HQT Diagnostics	5	122	Review the ability of Curcumin to destroy cancer cells and promote healthy cell function Source: https://is.gd/nicebc6	Thank you for your comment. We are not covering Curcumin in the scope of this guideline.
43.	SH	HQT Diagnostics	5	122	Investigate bio-markers for cancer One example is the CA Profile from American Metabolic Laboratories. This claims to provide 3 tests that can show early signs of cancer up to 10 years before a tumour can be detected. Source: http://americanmetaboliclaboratories.net/CA_Profile_.html Book: Cancer Concerns, by Xandria Williams	Thank you for your comment. We are not covering bio-markers for cancer in the scope of this guideline
44.	SH	NHS England	5	130	Additional suggested question is what is the most appropriate adjuvant chemotherapy for node negative, ER positive, HER-2 negative early breast cancer.	Thank you for your comment. We will be reviewing the optimal chemotherapy as part of the question and have amended the question to reflect this.

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45.	SH	Roche Products Ltd	5	131	The draft scope currently excludes potential dual anti-HER2 targeted adjuvant therapy with pertuzumab and trastuzumab; this will be gated on the results from the APHINITY trial. Given the timelines for CG80 approval, this treatment option may be considered for inclusion	Thank you for your comment. The reference to Pertuzumab and also pertuzumab (with trastuzumab and docetaxel) for the neoadjuvant treatment of HER2-positive breast cancer has been included in the scope.
46.	SH	Elekta	5	136	Given diversity of currently available techniques (External Beam Radiotherapy (EBRT), Intraoperative radiotherapy (IORT), brachytherapy etc), choice of full or partial breast irradiation and different fractionation schemes and the importance of patient choice in breast cancer, I think the question should be phrased "What are the optimal radiotherapy techniques for people with early or locally advanced breast cancer" as I feel that more than one technique/fractionation scheme etc will need to be considered and discussed with benefits/drawbacks etc in the final document.	Thank you for your comment. The question has been amended in-line with your suggestion.
47.	SH	BASO~The Association for Cancer Surgery	5	138	Which subgroup of patients with early breast cancer can be offered intra-operative radiotherapy as an alternative to whole breast radiotherapy?	Thank you for your comment. The question has been amended**.**
48.	Individual	Michelle Leech	5	142	Post Mastectomy Radiotherapy treatment can be given to the whole breast to manage a positive margin to skin (anterior) as well as chest wall radiotherapy. So should questions read: What are the indications for radiotherapy to the chest wall or whole breast radiotherapy following mastectomy for people with early or locally advanced breast cancer.	Thank you for your comment. Radiotherapy to the chest wall includes treating the skin.

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49.	SH	Breast Cancer Now	6	154-155	**Lifestyle** There is now clear evidence to show that patients who maintain a healthy weight and take the recommended exercise can reduce the risk of breast cancer recurrence, sometimes to the same degree as adjuvant medical treatment (a reduction in risk of approximately 30 per cent). See in particular the following review: Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis The following may also be useful: World Cancer Research Fund International/American Institute for Cancer Research Continuous Update Project Report: Diet, Nutrition, Physical Activity, and Breast Cancer Survivors. 2014. The NHS England Breast Cancer Clinical Reference Group (CRG), chaired by Professor Ian Smith, has developed breast cancer service guidance, which is in final draft form. This covers essential services for people with early, recurrent and metastatic breast cancer, and focusses specifically on areas where significant progress is needed to improve breast cancer outcomes and ensure that patients have the best possible experience of care. This guidance will state that "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. It is therefore mandatory that all patients are given advice on	Thank you for your comment. We are addressing lifestyle within the scope of the guideline.

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					weight control and regular moderate exercise". Breast Cancer Now provides the Secretariat to the CRG and would be happy to share a confidential draft of the service guidance with NICE. The 2015 Cancer Strategy for England puts a strong emphasis on lifestyle-based secondary prevention. It states that "with an increasing number of patients surviving their primary cancers, there is a growing need for the health service to tailor preventative approaches to reduce the chance of secondary cancer (metastasis)". It argues that there is strong evidence for physical activity: "regular exercise has been shown through multiple observational studies to reduce the risk of a number of different types of cancer by 10-50% and also to reduce the risk of cancer-specific death. The majority of the evidence is in early breast cancer, but there is also evidence in early colorectal, prostate and ovarian cancers." The strategy recommends that "NHS providers should ensure that all patients treated for cancer are given advice, tailored to their individual circumstances and risk level, on how to improve their lifestyle. This advice should include healthy eating, weight control, physical activity levels, smoking cessation and alcohol consumption, to help prevent secondary cancers." The strategy also highlights research which has shown that people who have had cancer would like more information about how to approach lifestyle changes, and would also welcome support tailored to their individual needs. Breast Cancer Now has a key web-based resource about the role of physical	

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					activity in reducing breast cancer risk, called BRISK which is quality assured by the Information Standard. This is primarily about reducing risk of primary breast cancer, however it could be a useful model for developing evidence-based guidance aimed at people *with* breast cancer. Breast Cancer Now is also funding ongoing research to expand knowledge and understanding in this area. For example, we are currently funding a research project which aims to find the best exercise programme for people with breast cancer, in order to help people with breast cancer reduce their risk of recurrence.	
50.	SH	Association of Breast Surgery	6	144	9.2 will require considerable discussion. There is an increasing trend to give PMRT which would deny many patients the benefits of immediate reconstruction. There is evidence that autologous reconstruction performed simultaneously with mastectomy regardless of the need for PMRT is safe with good aesthetic outcomes. This may not be the same for implant (+/- LD flap) reconstruction.	Thank you for your comment. We agree and will review the evidence and discuss this with the guideline committee before making any recommendations in this area.
51.	SH	Association of Breast Surgery	6	151	Please see the summary of discussions from the ABS MDT Meeting on NACT in 2014: http://www.associationofbreastsurgery.org.uk/media/43866/final_summary_of_discussions.pdf	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual.
52.	SH	HQT Diagnostics	6	153	Refer patient at first presentation to a Dietitian or Nutritional Therapist who can review existing diet and advise changes Dietitians https://www.bda.uk.com/	Thank you for your comment. We are reviewing lifestyle within the scope of the guideline. We will systematically search and review

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					Nutritional Therapists http://bant.org.uk/	evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.
53.	SH	HQT Diagnostics	6	153	Invite submissions about diet and lifestyle from charities that give advice and support to cancer patients http://www.macmillan.org.uk/ http://www.canceractive.com/ http://yestolife.org.uk/ http://breastcancernow.org/ https://www.breastcancercare.org.uk/	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.
54.	SH	HQT Diagnostics	6	153	Review how changes to diet and lifestyle can help prevent, treat and aid recovery from breast cancer Books: Vital Signs for Cancer, by Xandria Williams Cancer Concerns, by Xandria Williams TRANSCEND, by Ray Kurzweil & Dr Terry Grossman The Cancer Revolution, by Patricia Peat The Rainbow Diet, by Chris Woollams Say NO to Cancer, by Patrick Holford Knockout, by Suzanne Somers	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.

Early and locally advanced breast cancer (update)

Consultation on draft scope
Stakeholder comments table

26 May 2016 to 24 June 2016

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ID	Type	Stakeholder	Page no.	Line no.	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
55.	SH	HQT Diagnostics	6	153	Exercise during and after cancer treatment is beneficial and should be encouraged Source: http://bjmp.org/files/2014-7-1/bjmp-2014-7-1-a708.pdf	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.
56.	SH	HQT Diagnostics	6	153	Review effects of ketogenic diets on breast cancer Review effect of carbohydrates and sugars on cancer http://www.ketogenic-diet-resource.com/ http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157418/ https://is.gd/nicebc3 https://is.gd/nicebc4 Books: Cancer Concerns, by Xandria Williams Tripping over the Truth, by Travis Christofferson	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.
57.	SH	HQT Diagnostics	6	153	Review the sleep of the patient. 8-10 hours a night of deep sleep is required to help the body repair itself, so advise patients to go to bed at 10:00pm and sleep until at least 6:00am. If sleep is not adequate, suggest a natural sleeping aid such as Natrol or Nutrasleep or Melatonin (Circadin ?). Melatonin is a potent anti-oxidant and is considered a useful adjunct to conventional cancer therapy. The dose needs to be adjusted to provide the	Thank you for your comment. The lifestyle questions will be finalised in the GC meeting. We will then systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.

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					right amount of sleep and avoid drowsiness the next day – this may be between 0.1 and 10 milligrams per night http://www.lifeextension.com/Magazine/2004/1/report_melatonin/Page-01 https://is.gd/nicebc5	
58.	SH	Roche Products Ltd	6	159	Pathological Complete Response (pCR) should also be included as this is an efficacy endpoint evaluated in neoadjuvant breast cancer clinical trials	Thank you for your comment. We will define outcomes on a topic by topic basis.
59.	SH	Roche Products Ltd	6	159	Event-free survival (EFS) or progression-free survival (PFS) should also be included. Both these terms can be interchanged	Thank you for your comment. We will define outcomes on a topic by topic basis.
60.	SH	Roche Products Ltd	6	159	Invasive disease-free survival (iDFS) should also be included as this is also used as an endpoint in some adjuvant breast cancer clinical trials	Thank you for your comment. We will define outcomes on a topic by topic basis.
61.	SH	Roche Products Ltd	6	159	Breast conservation rates should be included, as this is one of the main objectives of neoadjuvant treatment (to downstage the tumour and therefore enable breast conserving surgery)	Thank you for your comment. We will define outcomes on a topic by topic basis.
62.	SH	Society and College of Radiographers	6	167	There were some comments regarding this list indicating PROMs as a priority. This is clearly extremely important but as this list of 7 is not hierarchical there is no comment.	Thank you for your comment.

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63.	NICE	NICE MPP	7	184	To include in the bulleted list - Medicines optimisation (2015) NICE guideline NG5. This guideline offers best practice advice on the care of all people who are using medicines and also those who are receiving suboptimal benefit from medicines. It updates and replaces recommendation 1.4.2 in the NICE guideline on medicines adherence.	Thank you for your comment. This guidance has now been included in the list in section 2.1.
64.	SH	Breast Cancer Care	7	193	**Section – NICE guidance that is closely related to this guideline** We feel that the guideline, *Fertility Problems: Assessment and Treatment (CG156),* should be listed in the section *NICE guidance that is closely related to this guideline*.	Thank you for your comment. We have now included a reference to the Fertility problems: assessment and treatment guideline in the scope. However, we are not covering fertility issues in the guideline.
65.	SH	Elekta	8	220	The 2008 published brachytherapy guideline IPG268 "Brachytherapy as the sole method of adjuvant radiotherapy after breast cancer local excision" is described as being linked to this guideline update, but not as being updated in the process. There have been important brachytherapy data published since 2008 eg.Phase III randomized trial of GEC ESTRO published in the Lancet in January this year (Strnad V et al. Lancet 2016;387:229-38 to be found at pumed link: https://www.ncbi.nlm.nih.gov/pubmed/26494415). It is important in my view to revisit the data around brachytherapy in this process and update this 2008 guideline as well.	Thank you for your comment. We will systematically search and review evidence according to the NICE guidelines manual and make any recommendations based upon this evidence.

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66.	SH	HQT Diagnostics	8	231	Denosumab requires adequate calcium and Vitamin D Source: Email exchange with Professor Michael Holick, Professor of Physiology & Biophysics at Boston University School of Medicine (http://profiles.bu.edu/display/151360) MH: Giving Denosumab is of no value without adequate calcium and vitamin D. RG: Can you point me towards any published papers that can support this ? MH: It is unethical to do this type of study. MH: However there have been other studies showing that people who were vitamin D deficient did not respond well to bisphosphonates	Thank you for your comment. We are not covering Denosumab within the scope of this guideline.
67.	SH	Roche Products Ltd	12	296	HER2-directed therapy should also include trastuzumab with or without pertuzumab, which is now licensed for use as neoadjuvant treatment for HER2-positive early breast cancer.	Thank you for your comment. This is subject to a NICE TA therefore the evidence will not be reviewed as part of the clinical guideline. A reference to the TA's has now been included in the scope.
68.	SH	Society and College of Radiographers	12	307	This strategy highlights the importance of a key worker to support patients. . Therapeutic radiographers may fulfil the role of 'key worker' for individual patients throughout their care pathway, while also utilising their unique knowledge and expertise to ensure evidence-based practice and the safe implementation of innovation for specific patient groups and technical specialities within radiotherapy. Of core consideration are the requirements	Thank you for your comment. We agree.

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					for the delivery of safe and effective patient-centred services.	
69.	SH	Society and College of Radiographers	12	309	There is positive evidence to support the changing nature of care delivery, responsive to patients needs and not based upon professional roles / historical practices in that currently 19 radiotherapy centres (37.25%) have therapeutic radiographers responsible for toxicity monitoring and management of patients after completion of their treatment. This is an increase from 10 centres (23%) in 2012. The percentage of centres with therapeutic radiographers in information and support services roles has increased from 45% to 58% over the same period. The percentage of centres with therapeutic radiographers in on-treatment review clinic roles utilising toxicity assessment scales has increased from 77% in 2012 to 92% in 2015. The NHS Future Forum report and the 2015 Public Health England report, H*ealthy conversations and the Allied Health Professionals* recognise the role therapeutic radiographers already undertake as one of the twelve Allied Health Professionals, in promoting public health and wellbeing through their day to day contact with patients. There are Therapeutic Radiographer advanced and consultant level practitioner-led planning services including on-treatment review, palliative care and supplementary and independent prescribing addressing the need to ensure access to a key worker for all patients in a high quality, modern service	Thank you for your comment. We agree.

None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry'