Australian Government

Cancer Australia

Guidance for the management of early breast cancer

Methods

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Locked Bag 3 Strawberry Hills NSW 2012 Australia
Tel: +61 2 9357 9400 Fax: +61 2 9357 9477
canceraustralia.gov.au

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1 Background

1.1 Breast cancer in Australia

In Australia, breast cancer is the most common cancer in women, affecting one in seven women by the age of 80.*,† Breast cancer is also the most commonly diagnosed cancer for female Indigenous Australians.[1] While less common, breast cancer also occurs in men. Surgery, chemotherapy, radiation therapy and endocrine therapy are the main treatment options. Breast cancer treatment is an evolving area of research with ongoing advances in various modes of therapy.

1.2 Current Australian guidelines related to early breast cancer

The National Breast and Ovarian Cancer Centre (amalgamated with Cancer Australia in 2010) published the second edition of the *Clinical Practice Guidelines for the management of early breast cancer* in 2001. The guidelines covered all aspects of the management of early breast cancer, except screening. Since then, Cancer Australia has continued to develop evidence-based guidelines on specific topics relating to early breast cancer care, including: *the use of aromatase inhibitors, taxanes, and bisphosphonates*, *the role of sentinel lymph node biopsy*, *management of the axilla, management in women with a high risk gene mutations*, *the use of hypofractionated radiation therapy*, *the management of menopausal symptoms*, and *recommendations for follow-up care*. Cancer Australia has also published the *Cancer Australia Statement: influencing best practice in breast cancer* which identifies 12 key appropriate and inappropriate practices which represent agreed priority areas in breast cancer practice, from diagnosis to palliative care.

Details of Cancer Australia guidelines and Statements across the continuum of breast cancer care are provided in Appendix A . In addition, Cancer Australia has published evidence-based guidelines on topics of relevance to all cancer types including breast cancer, such as on 'fear of recurrence', and 'best practice in survivorship care'.

1.3 Challenges with updating of national guidelines

There is a recognised need for up-to-date, national guidance across all aspects of early breast cancer care. However, typical processes to develop or update clinical practice guidelines (CPGs) are resource-intensive and time-consuming, involving multiple systematic reviews and subsequent evidence-to-recommendation methods to formulate the recommendations.

* Australian Institute of Health and Welfare. Cancer in Australia 2019: AIHW, 2019.

† Australian Institute of Health and Welfare. Breast cancer in Australia: An overview. Cancer series no. 71. Cat. no. CAN 6. Canberra: AIHW, 2012.

The management of breast cancer is a high-intensity research area with a very high volume of publications and covers a large scope. The challenge, therefore, was how to update the 2001 clinical guidance using rigorous, transparent methods that accounted for the scope and volume of relevant evidence published since 2001, but that were less resource-intensive and time-consuming than traditional CPG development methods.

Pragmatic approaches, provided that all decisions are transparent and well-documented, are possible to create a trustworthy guideline with limited resources (Browman et al 2015; NHMRC 2017). As such, to expedite the development of up-to-date, evidence-based guidance, a 'meta-guideline' approach was selected to develop the current guidance for the management of early breast cancer. In this context, a meta-guideline is defined as a set of recommendations and practice points that are developed through the analysis, synthesis, and expansion of 'source recommendations' from current evidence-based guidelines.

The meta-guideline approach differs from a traditional CPG approach in that the foundational units of the new guidance are the evidence-based recommendations of other developers, whereas the foundational units in a standard CPG are systematic reviews. Practice points are developed in both approaches and are informed largely by expert opinion. In the current meta-guideline approach, practice points have been informed by source recommendations and/or developed by experts through a consensus process.

2 Purpose and scope

2.1 Purpose

The purpose of the *Guidance for the Management of Early Breast Cancer* (*'the Guidance'*) is to provide health professionals with up-to-date evidence-based guidance that is relevant to the Australian health care setting for the management of patients with early breast cancer. The Guidance is intended for all health professionals caring for any patient with early breast cancer, including general practitioners, specialists, nurses, and allied health professionals. Secondary audiences include service providers and policy makers. It is intended that the Guidance will assist health professionals and patients in shared decision-making regarding the management of early breast cancer. A separate resource is currently being developed for consumers by the Breast Cancer Network Australia (BCNA), with support from Cancer Australia.

2.2 Scope

Early breast cancer is considered in the current context to be: '*invasive breast cancer that is contained in the breast and may or may not have spread to lymph nodes in the breast or armpit. Some cancer cells may have spread outside the breast and armpit area but cannot be detected*'. This excludes ductal carcinoma in situ (DCIS), which is non-invasive, and advanced or metastatic cancer which is known to have spread outside the breast and armpit area.

The scope of *the Guidance* encompasses the management of early breast cancer in women and men. It considers management of early breast cancer in pregnant or breastfeeding women and, where appropriate, distinguishes between premenopausal and postmenopausal women, and specifies age where this was a key inclusion/exclusion criterion in the underlying evidence base.

'Management' in the current context includes: treatment-planning, information and support (e.g. pathology and imaging for treatment planning); treatment (e.g. surgery, systemic therapies, radiation therapy, psychological therapy, physical therapy); and, follow-up and survivorship care (e.g. follow-up schedules, managing risk of recurrence, managing lymphoedema), for patients diagnosed with early breast cancer. Management in the current context excludes screening or initial detection of breast cancer. Consideration has been given to the general principles of care, including psychosocial and supportive care, to warranted variations for specific patient groups, and to cultural appropriateness, in development of *the Guidance*.

3 Development

3.1 Governance

A multidisciplinary Steering Group and a multidisciplinary Expert Working Group were appointed to oversee development of *the Guidance*. Membership of the Steering Group comprised representatives of relevant professional colleges, professional organisations, and specialist groups, and consumers. Membership of the Expert Working Group comprised members of professional colleges and organisations with clinical, academic, and community knowledge and experience of managing breast cancer, and breast cancer consumers. Memberships for the Steering Group and the Expert Working Group are provided in Appendices B and C, respectively.

The Steering Group provided strategic, high-level input and advice regarding the scope of the guidance, the overall approach to its development, and agreed on final wording of the recommendations and practice points‡. The Expert Working Group provided detailed input to the selection of source recommendations, the adaptation of recommendations, and development of practice points. Additional technical experts provided input on specific topics, as detailed in Appendix D.

During the appointment process all members were required to disclose any potential conflict(s) of interests. Declaration of conflicts of interest was also declared at start of each meeting of the groups. These declarations are recorded. The content of *the Guidance* is not influenced by any external funding body.

3.2 Methods

3.2.1 The meta-guideline approach§

The term 'meta-guideline' was used by Stahl et al (2013) in development of a 'guideline of guidelines' for the treatment of schizophrenia, which involved reconciling a number of existing guidelines to create 'a comprehensive yet concise set of guidelines that reflects all of the current evidence'. The meta-guideline approach used for development of *the Guidance* is informed by established methods for adopting and adapting existing evidence-based guidance (e.g. Darzi et al 2017; Schünemann et al 2017).

‡ While members of both governance groups agreed on the final wording of the recommendations and practice points for the version that was sent out for stakeholder consultation, some minor changes were made to the guidance points after stakeholder consultation. These changes were made by Cancer Australia, informed by more recently published evidence-based guidelines and evidence, and with input and advice from the experts where possible (cf. section 3.2.9).

§ The meta-guideline approach used in the development of the Guidance was substantively informed by Health Research Consulting (hereco).

A very similar approach to the one used to develop *the Guidance* has been used by many authors nationally (e.g. Australian Adult Cancer Pain Management Guideline Working Party) and internationally (e.g. Remington et al 2017).

3.2.2 Identification of relevant guidelines

The first step in development of the Guidance involved identification and quality appraisal of existing CPGs on the management of early breast cancer from the point of diagnosis forward. Electronic databases and websites of peak cancer authorities were searched for potentially relevant national and international guidelines, as detailed in Table E.1, Appendix E. The searches were conducted in late November and early December 2017. Only CPGs that were underpinned by an evidence review were included for consideration. CPGs published prior to 2007 were excluded on the basis that they were unlikely to reflect current practice.

A total of 84 individual CPGs were identified by the search. Forty-seven individual CPGs were considered relevant for inclusion into the Guidance. Most of the CPGs were from North America (13 from the US, eight from Canada, and one from both the US and Canada); nine CPGs were from Australia (with eight of these developed by Cancer Australia), and one was from New Zealand. Two CPGs were from the UK (both from the National Institute for Health and Care Excellence [NICE]), and there was one each from Scotland and Ireland. Five CPGs were 'European' while there were also CPGs for specific European countries or regions. There were two CPGs from Japan. The CPG from NICE was updated in July 2018, and the update was included at that time.

Each identified CPG was allocated a unique identified (the 'CPG ID'; comprised of the name of the authoring organisation and the year of publication), and the following characteristics for each CPG were then extracted:

- First author (if there was no authoring organisation)
- Country or countries covered
- Title of CPG
- Source of evidence – systematic literature review or non-systematic literature review (and literature search dates)
- Methods used to link evidence to recommendations – e.g. GRADE, SIGN, NHMRC
- Breast cancer subtype(s) – early breast cancer, inflammatory breast cancer, Paget's disease, patients at high-risk of breast cancer, patients BRCA1/2 positive
- Main aspect(s) of care covered (referred to during development as 'topics') – e.g. surgery, radiotherapy, systemic therapy, follow up, survivorship care, etc.

Key characteristics of all initially identified CPGs are provided in Appendix F.

3.2.3 Selection of guidelines

Thirty-eight of the 84 identified CPGs were based on systematic review of the evidence, and nine of the 84 identified guidelines were based on a non-systematic review of the evidence. Guidelines that were not clearly based on a review of the evidence were excluded from

further consideration. The 47 evidence-based guidelines were quality appraised using a modified AGREE-II (Appraisal of Guidelines for Research & Evaluation version II) assessment (full details of AGREE-II are available at https://www.agreetrust.org/agree-ii/). A modified version of AGREE-II was used to provide a focus on quality of the methods used by guideline developers to gather and synthesise evidence, and methods to translate that evidence into clinical guidance. The AGREE-II domains that were included in the quality assessment were: 1 (scope and purpose), 3 (rigour of development), and 6 (editorial independence); and the AGREE-II domains not included were: 2 (stakeholder engagement), 4 (clarity of presentation), and 5 (applicability), as these were considered of 'lower value' in the current context.

Guidelines were classified, based on the modified AGREE II scores, as 'good', 'fair' or 'poor' in quality. The spread of classifications of the 47 guidelines that were quality appraised are shown in Table 3.1, below.

Table 3 1 Quality rating of included CPGs according to modified AGREE II

Quality rating	***Modified AGREE II score (%)***	***Number of CPGs***
CPGs based on a systematic review of the evidence		
Good	*65-100*	*27*
Fair	*45-64*	*11*
Poor	*<45*	*0*
CPGs based on a non-systematic review of the evidence		
Good	*65-100*	*0*
Fair	*45-65*	*2*
Poor	*<45*	*7*

Abbreviations: AGREE, Appraisal of Guidelines for Research and Evaluation; CPG, clinical practice guideline.

As shown in Appendix F, 26 out of the 47 evidence-based guidelines contained recommendations that informed recommendations or practice points included in the Guidance.

3.2.4 Extraction of recommendations from evidence-based guidelines

All recommendations that addressed topics within scope were extracted from the final 47 evidence-based guidelines and grouped by topic and sub-topic. Sub-topics were specific aspect(s) of care within a main topic, for example, surgery sub-topics included 'breast-conserving surgery or mastectomy', 'breast reconstruction techniques', 'sentinel lymph node biopsy', and 'timing of surgery and radiation therapy'. A full list of all original topics and sub-topics into which the extracted recommendations were sorted is provided in Appendix G.

Within a sub-topic, recommendations and associated key characteristics of the relevant guideline were organised in reverse chronological order according to the date of the corresponding evidence review.

The full set of sub-topics was reviewed by the Steering Group and aspects of care not addressed by any of the extracted recommendations were listed as possible 'gap' topics.

The definitions of early breast cancer used in the various guidelines are listed in Appendix H. All definitions exclude distant metastases. Where CPGs had a broader scope, e.g. early and

advanced breast cancer, recommendations specifically relating to metastatic breast cancer were not extracted.

3.2.5 Selection of source recommendations

A structured process was used to assess the extracted recommendations across a total of 73 sub-topics. For each sub-topic, the Expert Working Group or the nominated external experts selected source recommendations from the list of extracted recommendations. This advice was documented and was based on the following criteria:

- Currency (of the potential source recommendation, and the evidence review underpinning it)
- Transparency in the decision-making process by CPG developers (e.g. a focus on grading, levels of evidence, and declarations of interest noted in source guidelines)
- Consistency of recommendations across existing guidelines
- Generalisability (i.e. how well the recommendations match the population being targeted by this Guidance)
- Applicability (i.e. whether the recommendations were considered relevant to the Australian healthcare context in terms of health services, delivery of care and cultural factors).

If the extracted list of recommendations on a specific sub-topic were considered to be not sufficiently current, then these sub-topics were identified as requiring a *de novo* systematic review to develop up-to-date evidence-based recommendations. Currency of the recommendations was often questioned for sub-topics where there was known to be a high intensity of research activity and a rapidly evolving evidence base. Topics considered to require a *de novo* systematic review were outside of the scope of the meta-guideline approach.

In the final guidance that was prepared for stakeholder consultation, recommendations were developed from 25 of the 47 potentially relevant CPGs (shaded in grey in Appendix F). Details of the grading systems for the final source guidelines are included in Appendix I.

3.2.6 Adoption and adaptation of source recommendations

Each source recommendation was further considered by relevant experts within the Expert Working Group, and additional experts as appropriate, to determine whether it should be adopted or adapted. Expert Working Group considered the criteria that were used to select each source recommendation and used a deliberative process to share their different perspectives and reach agreement on how the recommendations in *the Guidance* would be informed by the source recommendations.

The following scenarios gave rise to an adopted recommendation:

- Wording of the source recommendation was accepted with no changes; or

- Wording of the source recommendation was rearranged with no change to the meaning or tone of the recommendation (i.e. the changes were stylistic only – there were no changes to the population, intervention, comparator or outcomes (for intervention questions) to the population, prognostic factors, or outcomes (for prognostic questions), or to the population, intervention, reference standard (for diagnostic questions)).

The following scenarios gave rise to an adapted recommendation:

- details for an aspect of care were removed but the remaining information was unchanged (e.g. removal of the dosage regimen for a named pharmaceutical while retaining the name of the pharmaceutical)
- the patient population was expanded in the source recommendation to reflect the target population for the guidance point (e.g. from 'women' to 'patients' [i.e. considered to be appropriate care for men with breast cancer] or from 'young women' to 'premenopausal women' [as young women is variously described in guidelines but often is younger than 35 or 40 years])
- the recommendation was changed to reflect a broader or narrower range of interventions than the source recommendation (e.g. from a listed of specific breast reconstruction techniques to 'all breast reconstruction options')
- the tone of the recommendation was changed by using more, or less, directive verbs (see text below for further details), or by adding a verb where there was none in the source recommendation (i.e. the source recommendation is an evidence statement)
- the recommendation was simplified and/or source recommendations were merged to make the resulting guidance clearer.

The strength of the source recommendations was always considered during the adoption/adaptation step and in the choice of wording for the final recommendations. As a guiding principle, it was agreed that a *clear sequencing* of guidance within a topic using *active* verb forms should be used across *the Guidance*, namely 'discuss', 'consider', 'offer', and 'do not use'. Changes in the tone of a source recommendation were typically made to comply with this guiding principle. 'Discuss' recommendations or practice points were placed first within an aspect of care to encourage patient-centred care. Strong source recommendations tended to give rise to 'offer' or 'do not use' recommendations in the Guidance, whereas conditional source recommendations tended to give rise to 'consider' recommendations. Changes in tone were also made to align a source recommendation with the Australian health care context.

Across the subtopics, consideration was given to the benefits and harms associated with investigative tests and therapies. Consideration of benefits and harms has occurred at two levels – by the authors of the source recommendations, and by the Expert Working Group and external experts who contributed to *the Guidance*. In some instances, the harms associated with an investigative procedure or a therapy were explicitly included within a recommendation (e.g. radiation therapy for pregnant woman), in other instances they formed an entire subtopic (e.g. lymphoedema, cardiotoxicity, pain management).

For each point of guidance, the nature and rationale for any changes to the source recommendation(s) are documented in accompanying text entitled 'How this guidance was developed'. The Expert Working Group also provided advice on relevant resources and weblinks for health professionals and patients.

3.2.7 Development of practice points

Practice points were developed for aspects of care that were deemed clinically important by the Steering Group and Expert Working Group but for which there were no (or no appropriate) recommendations from the included evidence-based guidelines (termed 'gap topics'). Practice points were developed using a consensus process. In some instances, targeted evidence reviews were undertaken to inform the development of practice points by the Expert Working Group where it was likely that such a review would yield useful information. In all instances, the Expert Working Group relied on their clinical expertise, and that of additional external experts where required, to develop practice points to address gap topics.

The following scenarios gave rise to a practice point:

- a major re-wording of the source recommendation was made that changed the tone and meaning of the recommendation (sometimes to the extent that the source recommendation may have been effectively rejected).
- The source recommendation had been explicitly graded by the guideline authors as 'Expert opinion' (or equivalent). Even when the wording of a such a recommendation was adopted or adapted it was still labelled as a practice point because the source recommendation was not evidence-based.
- There was no source recommendation for an aspect of care deemed to be clinically important and relevant to the Australian health care context (and which was considered to not require a *de novo* systematic review).

During the development of practice points, Expert Working Group members also discussed potentially relevant evidence published since the most recent guideline search date, and any other information they considered might be relevant to the applicability and generalisability of the source recommendation(s) (e.g. local optimal care pathways, local protocols for pathology and imaging reporting).

As the structure and content of the Guidance was finalised, some recommendations and practice points were merged or deleted to remove inadvertent duplication of guidance and/or to provide greater clarity within the guidance. Additional practice points were also developed at this step if it became apparent that some important clinical scenarios had not been accounted for by the previously drafted recommendations and practice points.

Following finalisation of the draft Guidance by the Expert Working Group, the Steering Group reviewed the draft in totality. In particular, the Steering Group reviewed consistency or duplication across the guidance points. The Steering Group feedback was addressed using a systematic approach to incorporate revisions that improved the clarity and/or precision of the guidance points. As part of this review process, the Steering Group highlighted a series of guidance points which they considered applied more broadly across early breast cancer

care. These guidance points were subsequently removed as recommendations or practice points and instead included as overarching principles of care at the start of the Guidance**.

Final wording and consistency checks were completed by Cancer Australia prior to targeted external stakeholder consultation.

3.2.8 External consultation and finalisation of the guidance points

A wide range of relevant stakeholders were identified for external consultation on the draft Guidance. Stakeholder consultation was held from 03 March to 06 April 2020, subsequently extended to 20 April 2020. Stakeholder feedback was considered by Cancer Australia and appropriate minor changes made based on more recently published guidelines and/or more recent evidence for some of the guidance points. These changes were made in consultation with experts from the two governance groups or the additional experts, where appropriate and possible within timeframes. More recently published guidelines were only consulted for verification of any suggested changes from the stakeholder feedback, therefore not all relevant recently published guidance will have been assessed. The quality of these more recent guidelines was not explicitly assessed. In some instances, this more recent guidance is provided in support of the initially drafted guidance.

3.2.9 Documentation of guidance point development

As part of the transparent and robust process used in development of *the Guidance*, for each point of guidance, details of [where applicable] the source recommendation, the strength of the source recommendation and the evidence-to-recommendation method where reported, a link to the source guidelines, and text describing the nature and rationale for any changes to the source recommendation, is included in accompanying text entitled 'How this guidance was developed'.

The importance of this citing of the developers of the source guideline to acknowledge the work used to create the adapted recommendations and describe the changes made is highlighted by NHMRC (2017) in the 'Adopt, Adapt, Start from scratch' module, and is noted to be important regardless of the method used to develop clinical guidance.

The Expert Working Group and Steering Group members also provided advice on relevant resources and weblinks for health professionals and for patients. Additional useful links were added by Cancer Australia where appropriate.

3.2.10 Final guidance

The final guidance is published by Cancer Australia on a dedicated website to support accessibility by users.

** These were subsequently considered to be optimally represented by the key *Principles of the Optimal Care Pathway for patients with breast cancer*

Inevitably there are aspects of management and care that have not been included within the current guidance, especially as some of these aspects of care would have required time-consuming systematic reviews of the evidence. It is as comprehensive as possible to ensure that it is published while the underlying evidence base and source guidelines remain current.

Appendix A: Cancer Australia guidance on breast cancer

Table A 1 Breast cancer guidelines and position statements published by Cancer Australia since 2001

Guideline or Position Statement Title	Topic	Date
Cancer Australia Statement – Influencing best practice in metastatic breast cancer	*Metastatic breast cancer*	*2019*
Cancer Australia Statement – Influencing best practice in breast cancer	*Breast cancer*	*2017*
Management of menopausal symptoms in women with a history of breast cancer	*Early breast cancer*	*2016*
Clinical guidance for the management of lobular carcinoma in situ	*In situ breast cancer*	*2016*
Hypofractionated radiotherapy for early (operable) breast cancer	*Early breast cancer*	*2015 (2011)*
CNS metastases in women with secondary breast cancer	*Advanced breast cancer*	*2014*
Recommendations for the management of early breast cancer in women with an identified BRCA1 or BRCA2 gene mutation or at high risk of a gene mutation	*Early breast cancer*	*2014*
Recommendations for use of bisphosphonates in early breast cancer	*Early breast cancer*	*2011*
Recommendations for staging and managing the axilla in early (operable) breast cancer	*Early breast cancer*	*2011*
Recommendations for use of bisphosphonates for advanced breast cancer	*Advanced breast cancer*	*2011*
Recommendations for use of chemotherapy for the treatment of advanced breast cancer	*Advanced breast cancer*	*2010*
Recommendations for follow-up of women with early breast cancer	*Early breast cancer*	*2010*
Recommendations for use of Sentinel node biopsy in early (operable) breast cancer	*Early breast cancer*	*2008*
Recommendations for use of endocrine therapy for the treatment of hormone receptor-positive advanced breast cancer	*Advanced breast cancer*	*2008*
Recommendations for use of Taxane-containing chemotherapy regimens for the treatment of early (operable) breast cancer	*Early breast cancer*	*2008*
Recommendations for use of Trastuzumab (Herceptin®) for the treatment of HER2-positive breast cancer	*Advanced breast cancer*	*2007*
Recommendations for Aromatase inhibitors as adjuvant endocrine therapy for post-menopausal women with hormone receptor-positive early breast cancer	*Early breast cancer*	*2006*

Appendix B: Steering Group membership

Cancer Australia wishes to acknowledge the members of the Steering Group who have generously contributed their time and expertise to this work.

Table B 1 Members of the Steering Group

Name	Role/Affiliation	College/Organisation represented
Professor Fran Boyle *(Chair)*	*Professor of Oncology, University of Sydney and Medical Oncologist, Mater Hospital, North Sydney*	*Medical Oncology Group of Australia (MOGA)*
Ms Leanne Carlson	*Consumer Representative*	*Breast Cancer Network Australia (BCNA)*
Professor Bogda Koczwara	*Senior staff specialist, Medical Oncology, The Flinders Centre for Innovation in Cancer*	*Medical Oncology Group of Australia (MOGA)*
Dr Christine Lai	*Senior Staff Specialist, Breast and Endocrine Surgical Unit, CALHN, The Queen Elizabeth Hospital*	*Royal Australian College of Surgeons (RACS)*
Dr Gillian Lamoury	*Radiation Oncologist Northern Sydney Cancer Centre, Royal North Shore Hospital*	*Royal Australian and New Zealand College of Radiologists (RANZCR)*
Professor Danielle Mazza	*Professor and Head, Department of General Practice, Monash University*	*Royal Australian College of General Practitioners (RACGP)*
Ms Carmel O'Kane	*Nurse Practitioner and Member of Board, CNSA*	*Cancer Nurses Society of Australia (CNSA)*
Professor Sandra O'Toole	*Senior Staff Specialist Pathologist, Dept of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital*	*Royal College of Pathologists of Australasia (RCPA)*
Dr Michelle Reintals	*Clinical Radiologist, I-Med Radiology*	*Royal Australian and New Zealand College of Radiologists (RANZCR)*

Appendix C: Expert Working Group membership

Cancer Australia wishes to acknowledge the members of the Expert Working Group who have generously contributed their time and expertise to this work.

Table C 1 Members of the Expert Working Group

Name	Role/Affiliation
Associate Professor Philip Beale (Co-Chair)	*Medical Oncologist, Clinical Director, Cancer Services SLHD and Concord Clinical School, University of Sydney*
Professor Christobel Saunders (Co-Chair)	*Surgical Oncologist, The University of Western Australia*
Dr Siddhartha Baxi	*Radiation Oncologist, GenesisCare Gold Coast*
Associate Professor Martin Borg (member until 30 September 2019)	*Radiation Oncologist, GenesisCare Adelaide*
Associate Professor Meagan Brennan	*Breast Physician, University of Sydney*
Dr Helen Frazer	*Radiologist, St Vincent's BreastScreen, Melbourne*
Megan James	*Consumer representative, BCNA*
Dr Alia Kaderbhai	*General Practitioner, Lalor Plaza Medical Centre*
Dr Narayan Karanth	*Medical Oncologist, Royal Darwin Hospital*
Elizabeth Kochman	*Consumer representative, Cancer Voices NSW*
Professor Sherene Loi	*Medical Oncologist, Peter MacCallum Cancer Centre*
Associate Professor Paul Mckenzie	*Pathologist, Royal Prince Alfred Hospital*
Associate Professor Nicholas Pachter	*Clinical Geneticist, Genetic Services of WA, King Edward Memorial Hospital*
Kerry Patford	*Breast Nurse, Chair, Breast Oncology Specialist Practice Network*
Associate Professor Chris Pyke	*Breast and Endocrine Surgeon, Mater Hospital*
Dr Kylie Snook	*Breast Surgeon, University of Sydney*
Professor Jane Turner	*Psycho-Oncologist, University of Queensland*

Appendix D: Additional experts

Cancer Australia wishes to acknowledge the additional subject-matter experts who have generously contributed their time and expertise to this work (Table D 1).

Cancer Australia wishes to acknowledge the significant contribution of Health Research Consulting (hereco) to this work.

Table D 1 Additional subject-matter experts consulted during guidance development

Name	Role/Affiliation	Topic/s consulted on
Professor Phyllis Butow	*Health Psychologist, The University of Sydney*	*Psychosocial support*
Professor Susan Davis	*Endocrinologist, Cabrini Medical Centre and Head, Women's Specialist Clinic (The Alfred Hospital Melbourne)*	*Assessment of Bone Health*
Professor Paul Glare	*Chair in Pain Medicine, Director of the Pain Management Research Institute (PMRI), University of Sydney*	*Pain management*
Professor Sandi Hayes	*Exercise Physiologist, Institute of Health and Biomedical Innovation, Queensland University of Technology*	*Role of exercise physiology in managing Lymphoedema*
Professor Martha Hickey	*Professor of Obstetrics and Gynaecology, University of Melbourne, The Royal Women's Hospital*	*Management of menopausal symptoms during and after primary treatment*
Dr Louise Koelmeyer	*Occupational therapist, Macquarie University Health Sciences Centre*	*Lymphoedema management*
Professor Len Kritharides	*Senior Staff Specialist, Head of the Department of Cardiology at Concord Repatriation General Hospital (CRGH) Sydney*	*Management and surveillance of cardiotoxicity associated with treatment of breast cancer*
Professor Kazuaki Negishi	*Cardiologist, Head of Discipline of Medicine at Sydney Medical School Nepean, University of Sydney*	*Management and surveillance of cardiotoxicity associated with treatment of breast cancer*
Associate Professor Kate Stern	*Fertility specialist, Melbourne IVF and The Women's Hospital*	*Reproductive and sexual health prior to, during and after breast cancer treatment*
Dr Aaron Sverdlov	*Clinical Lead, Heart Failure & Cardio-oncology, Hunter New England Local Health District & University of Newcastle*	*Management and surveillance of cardiotoxicity associated with treatment of breast cancer*
Professor Janette Vardy	*Medical oncologist, Concord Clinical School, University of Sydney*	*Psychosocial support and identification and management of cognitive impairment*

Appendix E: Details of searches for existing CPGs

Table E 1 Search strategy for clinical practice guidelines and position statements

Source of information	Database/website	Search terms and restrictions
Clinical practice guideline databases	*Australian Clinical Practice Guidelines Portal (https://www.clinicalguidelines.gov.au/)* *AHRQ's National Guideline Clearinghouse (https://guideline.gov/)* *Guidelines International Network (http://www.g-i-n.net/library/international-guidelines-library)* *SIGN (http://sign.ac.uk/search.html)* *NICE (https://www.nice.org.uk/)* *New Zealand Guidelines Group (https://www.health.govt.nz/publications?f%5B0%5D=im_field_publication_type%3A26&f%5B1%5D=im_field_category%3A36#find-by-region)* *Canadian Medical Association CPG Database (https://www.cma.ca/En/Pages/clinical-practice-guidelines.aspx)*	*Breast cancer search terms* *Published from 2007 onwards*
Electronic databases	*Medline (PubMed)*	*(Breast neoplasm[tiab] OR breast cancer[tiab] OR ((cancer* OR neoplasm* OR tumour* OR tumor* OR carcinoma*) AND (breast OR mammar*))) AND (guideline* OR recommendation*)* *Published from 2007 onwards*
Peak cancer authorities	*American Cancer Society (https://www.cancer.org/)* *ASCO (http://www.asco.org/)* *Cancer Australia (https://canceraustralia.gov.au)* *Cancer Care Ontario (https://www.cancercare.on.ca/)* *Cancer Research UK (https://www.cancerresearchuk.org/)* *EORTC (http://www.eortc.org/)* *ESMO (http://www.esmo.org/)* *IARC (http://www.iarc.fr/)* *NCCN (https://www.nccn.org/)* *NCI (https://www.cancer.gov/)* *Society of Gynecologic Oncology (https://www.sgo.org/)*	*Breast cancer search terms* *Published from 2007 onwards*

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; ASCO, American Society of Clinical Oncology; CPG, clinical practice guideline; EORTC, European Organization for Research and Treatment of Cancer; ESMO, European Society for Medical Oncology; NICE, National Institute for Health and Care Excellence; IARC, International Agency for Research on Cancer; NCCN, National Comprehensive Cancer Network; NCI, National Cancer Institute; SIGN, Scottish Intercollegiate Guidelines Network.

Appendix F: Details of originally identified guidelines

Table F 1 Characteristics of the identified CPGs[††]

Organisation/ Abb	Author (year)	Country/ region	Title	Method used to identify evidence base (search date)	Method used to assess the level/quality/ certainty of the evidence base	Method used to link evidence to recommendation	Quality of CPG
NICE 2018	NICE 2018	UK	Early and locally advanced breast cancer: diagnosis and management	SR (Sep 2017)	GRADE - current	GRADE - adapted	Good
ASCO 2017	Lyman 2017	US	Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update	SR (Jul 2016)	ASCO	ASCO	Fair
ASCO 2017b	Armenian 2017	US	Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline	SR (Feb 2016)	ASCO	ASCO	Good
CCO/ASCO 2017	Dhesy-Thind 2017	US/Canada	Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: A Cancer Care Ontario and American Society of Clinical Oncology Clinical Practice Guideline	SR (Jun 2016)	NR	NR	Good
AOIM 2017	Lambertini 2017	Italy	Temporary ovarian suppression during chemotherapy to preserve ovarian function and fertility in breast cancer patients: A GRADE approach for evidence evaluation and recommendations by the Italian Association of Medical Oncology	SR (Jan 2016)	GRADE - current	GRADE - current	Good
ASCO 2017	Krop 2017	US	Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women with Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update	SR (Sep 2015)	ASCO	ASCO	Good
CCO	Sussman 2017	Ontario, Canada	Models of Care for Cancer Survivorship	SR (Apr 2012)	NR	NR	Good

[††] CPGs that gave rise to recommendations that were used in the guidance are shaded in light grey.

RACP 2016	Alexander 2016	Australia	Timely initiation of chemotherapy: a systematic literature review of six priority cancers – results and recommendations for clinical practice	SR (Apr 2014)	NHMRC	NHMRC/FORM	Good
ASCO 2016	Burnstein 2016	US	Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update on Ovarian Suppression	SR (Jun 2015)	ASCO	ASCO	Good
CA 2016	CA 2016	Australia	Management of menopausal symptoms in women with a history of breast cancer	SR (Jan 2014)	NHMRC	NHMRC/FORM	Good
ASTRO 2016	Correa 2016	US	Accelerated Partial Breast Irradiation: Executive summary for the update of an ASTRO Evidence-Based Consensus Statement	SR (Mar 2016)	ACP	ACP	Good
ASCO 2016a	Denduluri 2016	US	Selection of optimal adjuvant chemotherapy regimens for human epidermal growth factor receptor 2 (HER2)-negative and adjuvant targeted therapy for HER2-positive breast cancers: an American Society of Clinical Oncology guideline adaptation of the Cancer Care Ontario clinical practice guideline.	SR (July 2015)	NR	NR	Good
ASCO/SSO 2016	Recht 2016	US	Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update	SR (Jul 2015)	ASCO	ASCO	Good
ASCO 2016b	Runowicz 2016	US	American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline	SR (Apr 2015)	Runowicz	NR	Good
CCO 2016	Zhong 2016	Ontario, Canada	Breast cancer reconstruction surgery (immediate and delayed) across Ontario: Patient indications and appropriate surgical options	SR (Sep 2013)	NR	NR	Good
AHS 2015c	AHS 2015c	Alberta, Canada	Follow-up care for early-stage breast cancer	SR (Apr 2013)	NR	NR	Fair
CA 2015	CA 2015	Australia	Hypofractionated radiotherapy for early (operable) breast cancer	SR (Nov 2013)	NHMRC	NHMRC/FORM	Good
NCCP 2015	NCCP 2015	Ireland	Diagnosis, staging and treatment of patients with breast cancer	SR (Sep 2014)	SIGN	SIGN	Good
CA 2014	CA 2014	Australia	Recommendations for the management of early breast cancer in women with an identified BRCA1 or BRCA2 gene mutation or at high risk of a gene mutation	SR (Apr 2012)	NHMRC	NHMRC/FORM	Good

CCO 2014a	CCO 2014a	Ontario, Canada	Optimal Systemic Therapy for Early Female Breast Cancer	SR (Mar 2012)	NR	NR	Good
SSO-ASRO 2014	Moran 2014	US	Society of Surgical Oncology-American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer	SR (May 2010)	Descriptive	NR	Good
CCA 2014	Shea-Budgell 2014	Alberta, Canada	Breast reconstruction following prophylactic or therapeutic mastectomy for breast cancer: Recommendations from an evidence-based provincial guideline	SR (Apr 2013)	Shea-Budgell	NR	Fair
KCE 2013	KCE 2013	Belgium	Breast cancer in women: diagnosis, treatment and follow-up	SR (Jan 2010/ Nov 2012)	GRADE – current or GRADE - early	GRADE – current	Good
ASCO 2013	Khatcheressian 2013	US	Breast Cancer Follow-Up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update	SR (Mar 2012)	NR	NR	Fair
Paterson 2013	Paterson 2013	Canada	Bone Health in Patients with Breast Cancer: Recommendations from an Evidence-Based Canadian Guideline	SR (Jul 2012)	NR	NR	Fair
SIGN 2013	SIGN 2013	Scotland	Treatment of primary breast cancer	SR (Dec 2011)	SIGN	GRADE - current	Good
AHS 2012a	AHS 2012a	Alberta, Canada	Sentinel lymph node biopsy and axillary node dissection in early stage breast cancer	SR (Mar 2011)	AHS	NR	Fair
AHS 2012b	AHS 2012b	Alberta, Canada	Magnetic Resonance Imaging for Breast Cancer Screening, Pre-operative Assessment, and Follow-up	SR (Jul 2010)	AHS	NR	Fair
ASPS 2012	ASPS 2012	US	Evidence-based clinical practice guideline: breast reconstruction with expanders and implants	SR (Dec 2011)	ASPS	ASPS	Good
SIOG/EUSOMA 2012	Biganzoli 2012	Europe	Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)	SR (Jun 2010)	NR	NR	Fair
CA 2011a	CA 2011a	Australia	Recommendations for use of bisphosphonates	SR (Aug 2010)	NHMRC	NR	Good
CA 2011b	CA 2011b	Australia	Recommendations for staging and managing the axilla in early (operable) breast cancer	SR (Aug 2007)	NHMRC	NR	Fair
CA 2010	CA 2010	Australia	Recommendations for follow-up of women with early breast cancer	SR (Jan 2008)	NHMRC	NR	Good

GEC-ESTRO 2010	Polgar 2010	Europe	Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009)	SR (Jul 2009)	NR	NR	Fair
NZGG 2009	NZGG 2009	NZ	Management of Early Breast Cancer	SR (Unknown)‡‡	NZGG	NZGG	Good
NICE 2009	NICE 2009	UK	Early and locally advanced breast cancer: diagnosis and treatment	SR (Jul 2008)	SIGN	NR	Good
CA 2008a	CA 2008a	Australia	Recommendations for use of sentinel node biopsy in early (operable) breast cancer	SR (Jul 2007)	NHMRC	NR	Good
CA 2008b	CA 2008b	Australia	Recommendations for use of Taxane-containing chemotherapy regimens for the treatment of early (operable) breast cancer	SR (Mar 2007)	NHMRC	NR	Good
ASBrS 2017	McLaughlin 2017	US	Considerations for Clinicians in the Diagnosis, Prevention, and Treatment of Breast Cancer-Related Lymphedema, Recommendations from an Expert Panel: Part 2: Preventive and Therapeutic Options	NR	NR	NR	Poor
ESO-ESMO 2017	Paluch-Shimon 2017	Europe	ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3)	NR	ACCP	ACCP	Poor
FertiPROTEKT 2017	Schuring 2017	Germany, Austria, Switzerland	Practical recommendations for fertility preservation in women by the FertiPROTEKT network. Part I: Indications for fertility preservation	LR (NR)	NR	NR	Poor
JBCS 2016	Aihara 2016	Japan	The Japanese Breast Cancer Society Clinical Practice Guideline for systemic treatment of breast cancer, 2015 edition	LR (NR)	JBCS	JBCS	Poor
JBCS 2016b	Yamauchi 2016	Japan	The Japanese Breast Cancer Society Clinical Practice Guideline for radiation treatment of breast cancer, 2015 edition	LR (NR)	JBCS	JBCS	Poor
ACOG 2012	ACOG 2012	US	Management of Gynecologic Issues in Women with Breast Cancer	LR (Nov 2011)	USPSTF	USPSTF	Fair

‡‡ Documentation regarding the search strategy are contained within a separate document that is no longer available.

EUSOMA 2012	Cardoso 2012	Europe	The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer	NR	AHRQ	NR	Poor
ACSM 2010	ACSM 2010	US	American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors	NR	NR	NR	Poor
Amant 2010	Amant 2010	Europe	Breast cancer in pregnancy: Recommendations of an international consensus meeting	LR (NR)	NR	NR	Poor

Appendix G: Initial mapping of recommendations

Table G 1 Initial mapping of recommendations from identified CPGs into topics and sub-topics

Topic	Sub-topics
General	1.1 Multidisciplinary care
	1.2 Elderly women
	1.3 Breast care nurses
	1.4 Psychosocial support
	1.5 Clinical trials
	1.6 Cardiac risk assessment and monitoring
	1.7 Reproductive and sexual health prior to or during treatment
	1.8 Fertility preservation
	1.9 Complementary medicine
Surgery	2.1 Breast-conserving surgery versus mastectomy
	2.2 Breast-conserving surgery versus mastectomy in Paget's disease
	2.3 Surgical margins
	2.4 Breast reconstruction
	2.5 Timing of breast reconstruction
	2.6 Breast reconstruction techniques
	2.7 Management of the axilla
	2.8 Sentinel lymph node biopsy – indications
	2.9 Sentinel lymph node biopsy – indications (inflammatory breast cancer)
	2.10 Sentinel lymph node biopsy – technical considerations
	2.11 Axillary lymph node dissection
	2.12 Risk-reducing surgery
Systemic therapy – planning	3.1 Neoadjuvant systemic therapy planning
	3.2 Adjuvant systemic therapy planning
Systemic therapy – chemotherapy	4.1 Indications for adjuvant chemotherapy
	4.2 Timing of chemotherapy
	4.3 Anthracycline-taxane use
	4.4 Taxane use
	4.5 Anthracycline use
	4.6 Capecitabine use
	4.7 Cyclophosphamide-methotrexate-fluorouracil (CMF) use
	4.8 Chemotherapy protocols
	4.9 Neoadjuvant chemotherapy
Systemic therapy – endocrine therapy	5.1 Indications for adjuvant endocrine therapy
	5.2 Tamoxifen/SERM use
	5.3 Aromatase inhibitor use
	5.4 Ovarian function suppression
	5.5 Neoadjuvant endocrine therapy
Systemic therapy – biological therapy	6.1 Trastuzumab indications
	6.2 Trastuzumab and chemotherapy
	6.3 Trastuzumab- cardiotoxicity

Topic	Sub-topics
Systemic therapy – bisphosphonates	7.1 Adjuvant bisphosphonates
Radiotherapy	8.1 Timing of radiotherapy
	8.2 Radiotherapy after breast-conserving surgery
	8.3 Partial breast irradiation
	8.4 Postmastectomy radiotherapy
	8.5 Radiotherapy after neoadjuvant chemotherapy
	8.6 Radiotherapy after neoadjuvant chemotherapy - inflammatory breast cancer
	8.7 Radiotherapy of the axilla
	8.8 Boost radiotherapy
	8.9 Fractionation of radiotherapy
	8.10 Adverse events
Complications of local treatment	9.1 Lymphoedema
	9.2 Physical therapy
	9.3 Management of menopausal symptoms during primary treatment
Follow up	10.1 Continuity of care
	10.2 Mammography with or without ultrasound
	10.3 MRI (and other imaging)
	10.4 Clinical follow up
	10.5 Cardiac surveillance
	10.6 Gynaecological assessment
	10.7 Other diagnostics
	10.8 Genetic counselling
	10.9 Patient education
	10.10 Surveillance post breast reconstruction
	10.11 Assessment of bone health
	10.12 Bone health - bisphosphonate use
Survivorship	11.1 Management of menopausal symptoms after primary treatment
	11.2 Lifestyle
	11.3 Physical activity
	11.4 Psychosocial support and cognitive impairment
	11.5 Post treatment reproductive and sexual health
	11.6 Fatigue and sleep disorders
	11.7 Pain

Abbreviations: MRI, magnetic resonance imaging; SERM, selective oestrogen receptor modulator.

Appendix H: Definitions of early breast cancer

Table H 1 Definitions of early breast cancer in CPGs used to develop the guidance

Guideline	Population	*Definition*
NICE 2018	Early and locally advanced breast cancer	*Adults (18 and over) with newly diagnosed invasive adenocarcinoma of the breast of any size (T1–T4), with or without spread to locoregional lymph nodes (N0–N3) and with no distant metastases (M0).* *Adults (18 and over) with newly diagnosed ductal carcinoma in situ (DCIS)* *Adults (18 and over) with Paget's disease of the breast.*
Lyman 2017	Early-stage breast cancer	*No definition given*
Krop 2017	Early-stage invasive breast cancer	*No definition given*
AHS 2015c	Early-stage breast cancer	*No definition given*
CA 2015	Early (operable)breast cancer	*Early breast cancer is defined as tumours not more than five centimetres in diameter, with either impalpable lymph nodes or palpable but freely moveable lymph nodes, and with no evidence of distant metastases*
NCCP 2015	Early and locally advanced breast cancer	*Adults (18 years or older) with newly diagnosed early and locally advanced breast cancer. The scope of this guideline does not include patients with metastatic disease or breast cancer recurrence.*
CA 2014	Early breast cancer in women with an identified BRCA1 or BRCA2 gene mutation or at high risk of a gene mutation	*Non-metastatic breast cancer (early breast cancer, or potentially curable locally advanced breast cancer)*
CCO 2014a	Early-stage invasive breast cancer	*The preferred definition of early breast cancer in this guideline is invasive cancers Stage I–IIA (T1N0−1, T2N0). Studies with cancer described as operable (no other description of stage) and some studies with both Stage I–IIA and operable Stage IIB–IIIA (sometimes considered locally advanced) are included.*
SIGN 2013	Operable early breast cancer	*No definition given but includes DCIS and invasive breast cancer and excludes management of patients with metastatic disease*
AHS 2012a	Newly diagnosed, early stage breast cancer	*No definition given*
CA 2011b	Early (operable) breast cancer	*Early (operable) breast cancer is defined as the presence of tumour/s not more than five centimetres in diameter, with lymph nodes (either impalpable or palpable) that are not fixed, and with no evidence of distant metastases*
CA 2010	Early breast cancer	*Early breast cancer is defined as tumours of not more than five centimetres diameter, with either impalpable or palpable but not fixed lymph nodes and with no evidence of distant metastases.*
NZGG 2009	Early breast cancer	*No definition given*
NICE 2009	Early and locally advanced breast cancer	*Early breast cancer is sub-divided into two major categories, in situ disease in the form of ductal carcinoma in situ (DCIS), or invasive cancer.*
CA 2008a	Early (operable) breast cancer	*Early (operable) breast cancer is defined as tumours not more than five centimetres in diameter, with either impalpable or palpable, but not fixed, lymph nodes and with no evidence of distant metastases*
CA 2008b	Early (operable) breast cancer	*Early (operable) breast cancer is defined as tumours not more than five centimetres in diameter, with either impalpable or palpable, but not fixed, lymph nodes and with no evidence of distant metastases*

Appendix I: Grading systems used across source guidelines

Table I 1 Details of 'levels of evidence' and 'strength of recommendation' grading systems used in source guidelines (where available)

Guideline (abb.)	Guideline	Review method Evidence to recommendation method	Level of evidence	Grading of recommendation
ABS/BSBR (2019) Association of Breast Surgery / British Society of Breast Radiology	Axillary surgery following neoadjuvant chemotherapy – Multidisciplinary guidance from the Association of Breast Surgery, Faculty of Clinical Oncology of the Royal College of Radiologists, UK Breast Cancer Group, National Coordinating Committee for Breast Pathology and British Society of Breast Radiology	Review of published evidence. A writing group representing all disciplines quorate within a breast cancer multidisciplinary meeting prepared the guidelines.	NR	NR
ACOG (2012) American College of Obstetricians and Gynecologists	Management of gynecologic issues in women with breast cancer	Review of evidence. Based in the highest level of evidence found in the data. USPSTF methods.	I Evidence obtained from at least one properly designed randomised controlled trial. II-1 Evidence obtained from well-designed controlled Trials without randomization. II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one centre or research group. II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence. III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	Level A: Recommendations are based on good and consistent scientific evidence. Level B: Recommendations are based on limited or inconsistent scientific evidence. Level C: Recommendations are based primarily on consensus and expert opinion.

ACS/ASCO (2016) (Runowicz et al) American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care	American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline	Systematic review. The methods used to develop this guideline reflect an evolving process that was influenced by ACS screening and survivorship guidelines. Where appropriate, this guideline builds upon the recently published ASCO symptom-based guidelines for adult cancer survivors.	I Meta-analyses of RCTs IA RCT of breast cancer survivors IB RCT based on cancer survivors across multiple cancer sites IC RCT not based on cancer survivors but on general population experiencing a specific long-term or late effect (e.g. managing menopausal symptoms, sexual dysfunction, etc) IIA Non-RCTs based on breast cancer survivors IIB Non-RCTs based on cancer survivors across multiple sites IIC Non-RCTs not based on cancer survivors but on general population experiencing a specific long-term or late effect III Case-control study or prospective cohort study 0 Expert opinion, observational study (excluding case-control and prospective cohort studies), clinical practice, literature review, or pilot study 2A NCCN* Clinical Practice Guidelines in Oncology	
AHS (2015) Alberta Health Services	Follow-up care for early-stage breast cancer	Systematic review. Adapted from the Infectious Diseases Society of America and the European Society for Medical Oncology (ESMO).	<u>Level I</u> • evidence from at least one large randomized controlled trial (RCT) of good methodological quality with low potential for bias • meta-analyses of RCTs without heterogeneity <u>Level II</u> • small RCTs • phase II RCTs • large RCTs with potential bias or meta-analyses including such trials RCTs with	A Strongly recommended: strong evidence for efficacy with a substantial clinical benefit. B Generally recommended: strong or moderate evidence for efficacy but with a limited clinical benefit. C Optional: insufficient evidence for efficacy or benefit does not outweigh the risks/disadvantages. D Generally not recommended:

			heterogeneity Level III • prospective cohort studies • post-hoc and ad-hoc analyses of RCTs Level IV • retrospective cohort studies • case-control studies • instrument validation studies (note: could be level III, based on size of population, methods) Level V • studies without a control group • case reports • expert opinions • review articles or narrative reviews • Delphi studies • cross-sectional studies (interviews, focus groups, surveys)	moderate evidence against efficacy or for adverse outcomes. E Never recommended: strong evidence against efficacy or for adverse outcomes.
AIOM (2017) Italian Association of Medical Oncology	Temporary ovarian suppression during chemotherapy to preserve ovarian function and fertility in breast cancer patients: A GRADE approach for evidence evaluation and recommendations by the Italian Association of Medical Oncology	Systematic review. GRADE methods.	High We are very confident that the true effect lies close to that of the estimate of the effect Moderate We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect Very low We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Strong The desirable effects of an intervention clearly outweigh the undesirable effects (the intervention is to be put into practice), or the undesirable effects of an intervention clearly outweigh the desirable effects (the intervention is not to be put into practice) Weak/ Conditional The desirable effects of an intervention probably outweigh the undesirable effects (the intervention probably is to be put into practice), or the undesirable effects of an intervention probably outweigh the desirable effects (the intervention probably is not to be put into practice)
ASCO (2016) (Denduluri et al) American Society of Clinical Oncology	Selection of Optimal Adjuvant Chemotherapy Regimens for Human Epidermal Growth Factor Receptor 2 (HER2)–Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers:	Guideline adaptation informed by the ADAPTE methodology, with updated evidence review.	NR	NR

	An American Society of Clinical Oncology Guideline Adaptation of the Cancer Care Ontario Clinical Practice Guideline			
ASCO (2017) (Armenian et al) American Society of Clinical Oncology	Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline	Systematic review. ASCO methods.	<u>High</u> High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits v harms) and that further research is very unlikely to change either the magnitude or direction of this net effect. <u>Intermediate</u> Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect. <u>Low</u> Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect. <u>Insufficient</u> Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.	<u>Strong</u> There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g. benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation. <u>Moderate</u> There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g. benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation. <u>Weak</u> There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g. benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.
ASCO (2018) (Burstein et al) American Society of Clinical Oncology	Adjuvant endocrine therapy for women with hormone receptor–positive breast cancer: ASCO clinical practice guideline focused update	Systematic review. ASCO methods.		
ASCO/CAP 2019 American Society of Clinical Oncology/College of American Pathologists	Estrogen and progesterone receptor testing in breast cancer: ASCO/CAP guideline update	Systematic review. ASCO methods		
ASCO 2017 (Lyman et al) American Society of Clinical Oncology	Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update	Systematic review. ASCO methods		

ASTRO 2018 (Smith et al) American Society for Radiation Oncology	Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline	Systematic review. GRADE methods.	As above	As above but also noting: A **strong recommendation** indicated the task force was confident the benefits of the intervention clearly outweighed the harms, or vice versa, and "all or almost all informed people would make the recommended choice." **Conditional recommendations** were made when the risks and benefits were even or uncertain and "most informed people would choose the recommended course of action, but a substantial number would not," suggesting a strong role for **shared decision-making.**
CA 2008a Cancer Australia	Recommendations for use of Sentinel node biopsy in early (operable) breast cancer	Systematic review. NHMRC methods (Level of evidence only).	I A systematic review of level II studies II A randomised controlled trial III-1 A pseudo randomised controlled trial (i.e. alternate allocation or some other method) IIII-2 A comparative study with concurrent controls (non-randomised experimental trial, cohort study, case–control study, interrupted time series with a control group) III-3 A comparative study without concurrent controls (historical control study, two or more single-arm studies, interrupted time series without a parallel control group) IV Case series with either post-test or pre-test/post-test outcomes	NR
CA 2008b Cancer Australia	Recommendations for use of Taxane-containing chemotherapy regimens for the treatment of early (operable) breast cancer	Systematic review. NHMRC methods (Level of evidence only).		NR
CA 2010 Cancer Australia	Recommendations for follow-up of women with early breast cancer	Systematic review. NHMRC methods (Level of evidence only).		NR
CA 2011 Cancer Australia	Recommendations for use of bisphosphonates in early breast cancer	Systematic review. NHMRC methods (Level of evidence only).		NR
CA 2014 Cancer Australia	Recommendations for the management of early breast cancer in women with an identified BRCA1 or BRCA2 gene mutation or at high risk of a gene mutation	Systematic review. NHMRC methods.		A Body of evidence can be trusted to guide practice B Body of evidence can be trusted to guide practice in most situations C Body of evidence provides some support for recommendation(s), but care should be taken in its application D Body of evidence is weak, and recommendation must be applied with caution
CA 2016 Cancer Australia	Management of menopausal symptoms in women with a history of breast cancer	Systematic review. NHMRC methods.		

CCO 2016 Cancer Care Ontario	Breast Cancer Reconstruction Surgery (Immediate and Delayed) Across Ontario: Patient Indications and Appropriate Surgical Options	Systematic review.	NR	NR
CCO/ASCO 2017 (Dhesy-Thind et al) Cancer Care Ontario / American Society of Clinical Oncology	Use of adjuvant bisphosphonates and other bone-modifying agents in breast cancer: A Cancer Care Ontario and American Society of Clinical Oncology clinical practice guideline	Systematic review.	NR	NR
ESA/ANZBMS/AMS/COSA 2018 Endocrine Society of Australia / Australian and New Zealand Bone & Mineral Society / Australasian Menopause Society / Clinical Oncology Society of Australia	Assessment and management of bone health in women with oestrogen receptor-positive breast cancer receiving endocrine therapy: Position statement of the Endocrine Society of Australia, the Australian and New Zealand Bone & Mineral Society, the Australasian Menopause Society and the Clinical Oncology Society of Australia	Systematic review. ADAPTE process.	NR (referred readers to original guidelines as needed)	NR (referred readers to original guidelines as needed)
ESMO 2019 European Society of Medical Oncology	Early Breast Cancer: ESMO Clinical Practice Guidelines	NR ESMO guidelines methodology adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System	I Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity II Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity III Prospective cohort studies IV Retrospective cohort studies or case–control studies V Studies without control group, case reports, expert opinions	A Strong evidence for efficacy with a substantial clinical benefit, strongly recommended B Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended C Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional D Moderate evidence against efficacy or for adverse outcome, generally not recommended E Strong evidence against efficacy or for adverse outcome, never recommended
ESMO 2020	Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations	NR ESMO guidelines methodology adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System		

ESO-ESMO 2017 European School of Oncology and European Society of Medical Oncology Endorsed by the European Society of Breast Specialists (EUSOMA)	ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3)	Literature review. American College of Chest Physicians (ACCP) methods.	<u>High quality evidence</u> RCTs without important limitations or overwhelming evidence from observational studies <u>Moderate quality evidence</u> RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies <u>Low quality evidence</u> Observational studies or case series <u>Expert opinion</u> No evidence	1A Strong recommendation, high quality evidence. Strong recommendation, can apply to most patients in most circumstances without reservation 1B Strong recommendation, moderate quality evidence. Strong recommendation, can apply to most patients in most circumstances without reservation 1C Strong recommendation, low quality evidence. Strong recommendation, but may change when higher quality evidence becomes available 2A Weak recommendation, high quality evidence. Weak recommendation, best action may differ depending on circumstances or patients' or societal values 2B Weak recommendation, moderate quality evidence. Weak recommendation, best action may differ depending on circumstances or patients' or societal values 2C Weak recommendation, low quality evidence. Very weak recommendation, other alternatives may be equally reasonable
ESO-ESMO 2020 European School of Oncology and European Society of Medical Oncology Endorsed by the European Society of Breast Specialists (EUSOMA)	ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3)	Literature review. ESMO guidelines methodology adapted from Adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System	I Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity II Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity III Prospective cohort studies	A Strong evidence for efficacy with a substantial clinical benefit, strongly recommended B Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended C Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs), optional D Moderate evidence against efficacy or for adverse outcome, generally not

			IV Retrospective cohort studies or case-control studies V Studies without control group, case reports, experts' opinions	recommended E Strong evidence against efficacy or for adverse outcome, never recommended
EUSOMA 2012 European Society of Breast Cancer Specialists	The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer	Literature review. AHRQ (US Agency for Healthcare Research and Quality) methods.	I SR, RCTs II Cohort studies III Case-control studies IV Case series V Expert opinion	<u>High</u> We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions. <u>Moderate</u> We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains. <u>Low</u> We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect. <u>Very low</u> We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.
JBCS 2016	The Japanese Breast Cancer Society Clinical Practice Guideline for systemic treatment of breast cancer, 2015 edition	NR	NR	A There is sufficient scientific evidence and it is recommended to be actively performed. B There is scientific evidence and it is

				recommended to be performed. C1 There is not sufficient scientific evidence; however, it may be considered to be performed with utmost attention. C2 There is not sufficient scientific evidence and basically it is not recommended to be performed. D There is scientific evidence that it may be harmful for the patient and it is recommended not to be performed.
KCE 2013 Belgian Health Care Knowledge Centre	Breast cancer in women: diagnosis, treatment, and follow-up	Systematic review. CPG adaptation using GRADE.	High quality: We are very confident that the true effect lies close to that of the estimate of the effect; RCTs without important limitations or overwhelming evidence from observational studies Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies. Low: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; RCTs with very important limitations or observational studies or case series. Very low: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect; RCTs with very important limitations or observational studies or case series.	Strong The desirable effects of an intervention clearly outweigh the undesirable effects (the intervention is to be put into practice), or the undesirable effects of an intervention clearly outweigh the desirable effects (the intervention is not to be put into practice) Weak/ Conditional The desirable effects of an intervention probably outweigh the undesirable effects (the intervention probably is to be put into practice), or the undesirable effects of an intervention probably outweigh the desirable effects (the intervention probably is not to be put into practice)
NAMS 2015 North American Menopause Society	Nonhormonal Management of Menopause-associated Vasomotor Symptoms: 2015 Position Statement of The North American Menopause Society	Evidence review.	Level I—high-quality randomized trials; systematic reviews of level I studies. Level II— lesser-quality randomized, controlled trials (RCTs), systematic reviews of level II studies, or level I studies with inconsistent results. We included trials using	

			poorly validated measures in this category. Level III— uncontrolled trials, case-control studies, systematic reviews of level III studies. Level IV—case series, case-control studies. Level V—expert opinion	
NCCN 2019 National Comprehensive Cancer Network	NCCN Flash Updates: NCCN Guidelines®, NCCN Compendium®, and NCCN Radiation Therapy Compendium™ for Breast Cancer	Evidence-based, consensus-driven recommendations.		Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate
NCCP 2015 Department of Health, Government of Ireland	Diagnosis, Staging and Treatment of Patients with Breast Cancer	Systematic review (only if not in up to date evidence-based guidelines). SIGN	1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. 1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias. 1 Meta-analyses, systematic reviews, or RCTs with a high risk of bias. 2++ High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. 2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal. 2 Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not	A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated a 1+, directly applicable to the target population, and demonstrating overall consistency of results. B A body of evidence including studies rated a 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+. C A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++. D Evidence level 3 or 4; or Extrapolated

			causal. 3 Non-analytic studies (e.g. case reports, case series). 4 Expert opinion.	evidence from studies rated as 2+.
NICE 2018 (NICE 2009) National Institute for Health and Care Excellence	Early and locally advanced breast cancer: diagnosis and management	Systematic review (for topics requiring an update). GRADE.		**Strength (or certainty) of recommendation** The wording used denotes the certainty with which the recommendation is made (the strength of the recommendation). **Interventions that must (or must not) be used** We usually use "must" or "must not" only if there is a legal duty to apply the recommendation. Occasionally, we use "must" (or "must not") if the consequences of not following the recommendation could be extremely serious or potentially life threatening. **Interventions that should (or should not) be used**: a '**strong**' recommendation We use "offer" (and similar words such as "refer" or "advise") when we are confident that, for the vast majority of patients, an intervention will do more good than harm and be cost-effective. **Interventions that could be used** We use "**consider**" when we are confident that an intervention will do more good than harm for most patients, and be cost-effective, but other options may be similarly cost-effective. The choice of an intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation.
NZGG 2009 New Zealand Guidelines Group	Management of Early Breast Cancer: Evidence-based Best Practice Guideline	Systematic review (except 4 topic areas – non-systematic evidence reviews and expert opinion. NZGG.	Grades of recommendations indicate the strength of the supporting evidence rather than the importance of the evidence.	A: The recommendation is supported by good evidence (based on a number of studies that are valid, consistent, applicable and clinically relevant) B: The recommendation is supported by fair evidence (based on studies that are valid, but there are some concerns about the

				volume, consistency, applicability and clinical relevance of the evidence that may cause some uncertainty but are not likely to be overturned by other evidence) C: The recommendation is supported by international expert opinion I: The evidence is insufficient, evidence is lacking, of poor quality or opinions conflicting, the balance of benefits and harms cannot be determined
RACP 2016 Royal Australasian College of Physicians	Guidelines for timely initiation of chemotherapy: a proposed framework for access to medical oncology and haematology cancer clinics and chemotherapy services	Systematic review. NHMRC.	I A systematic review of level II studies II A randomised controlled trial III-1 A pseudo randomised controlled trial (i.e. alternate allocation or some other method) IIII-2 A comparative study with concurrent controls (non-randomised experimental trial, cohort study, case–control study, interrupted time series with a control group) III-3 A comparative study without concurrent controls (historical control study, two or more single-arm studies, interrupted time series without a parallel control group) IV Case series with either post-test or pre-test/post-test outcomes	A Body of evidence can be trusted to guide practice B Body of evidence can be trusted to guide practice in most situations C Body of evidence provides some support for recommendation(s), but care should be taken in its application D Body of evidence is weak, and recommendation must be applied with caution
SIOG/EUSOMA 2012 International Society of Geriatric Oncology / European Society of Breast Cancer Specialists	Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)	A consensus by an expert task force on available evidence and expert opinion. Task force used SIOG 2007 guidelines as a starting document.	NR	NR
Shea-Budgell 2014 Published on behalf of Alberta Breast Reconstruction Working Group	Breast reconstruction following prophylactic or therapeutic mastectomy for breast cancer: Recommendations from an evidence-based provincial guideline	Systematic review.	NR	NR

SIGN 2013 Scottish Intercollegiate Guidelines Network	Treatment of primary breast cancer A national clinical guideline	Systematic review. SIGN (for evidence) and GRADE (for recommendations).	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. 1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias. 1 Meta-analyses, systematic reviews, or RCTs with a high risk of bias. 2++ High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. 2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal. 2 Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal. 3 Non-analytic studies (e.g. case reports, case series). 4 Expert opinion.	Importance difference to other SIGN guidelines is the absence of grades of recommendation. The wording of the recommendation reflects how strongly the guideline development group believes following the recommendation will achieve the expected results. Recommendations will either be: 'unconditional' (strong evidence, no important drawbacks) or 'conditional' (weaker evidence, serious potential drawbacks)

Abbreviations

Abbreviation	Definition
AC	Doxorubicin and cyclophosphamide
AC→TH	Doxorubicin/cyclophosphamide-docetaxel/trastuzumab
ACCP	American College of Chest Physicians
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
ACS	American Cancer Society
ACSM	American College of Sports Medicine
ADM	acellular dermal matrix
AGREE	Appraisal of Guidelines for Research and Evaluation
AHRQ	Agency for Healthcare Research and Quality
AHS	Alberta health services
AI	aromatase inhibitor
ALND	Axillary lymph node dissection
ASBrS	American Society of Breast Surgeons
ASCO	American Society of Clinical Oncology
ASM	areola-sparing mastectomy
ASPS	American Society of Plastic Surgeons
ASTRO	American Society for Radiation Oncology
BCS	breast-conserving surgery
BCT	breast-conserving treatment
BMAs	bone modifying agents
BMD	bone mineral density
BMI	body mass index
BRCA	BReast CAncer gene
BRCA1/2	BReast CAncer genes 1 and 2
CA	Cancer Australia
CA 15-3	cancer antigen 15-3
CA 27.29	cancer antigen 27.29
CAP	College of American Pathologists
CBC	Complete blood count
CCA	CancerControl Alberta (Alberta Breast Tumour Team)
CCO	Cancer Care Ontario
CDT	Complete decongestive therapy
CEA	Carcinoembryonic antigen
CLE	Complete local excision
CMF	Cyclophosphamide-methotrexate- fluorouracil
CPG	Clinical practice guideline
CQ	Clinical question
CT	Chemotherapy

Abbreviation	Definition
CT	Computed tomography
DCIS	Ductal carcinoma in situ
DEXA	Dual-energy x-ray absorptiometry
DIEP	Deep inferior epigastric perforator
EC	Epirubicin-cyclophosphamide
ECG	Electrocardiograph
EORTC	European Organization for Research and Treatment of Cancer
ER	Oestrogen receptor
ESMO	European Society for Medical Oncology
ESO	European School of Oncology
EUSOMA	European Society of Breast Cancer Specialists
FAC	fluorouracil doxorubicin cyclophosphamide
FDG-PET	Fludeoxyglucose - positron emission tomography
FEC	Fluorouracil-epirubicin-cyclophosphamide
FORM NHMRC	NHMRC FORM framework for formulating and grading recommendations
FRAX	The Fracture Risk Assessment Tool
G-CSF	Granulocyte colony-stimulating factor
GnRH	Gonadotrophin-releasing hormone
GP	General practitioner
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HADM	Human acellular dermal matrix
HER2	Human epidermal growth factor receptor 2
HRT	Hormone replacement therapy
IARC	International Agency for Research on Cancer
IBTR	Ipsilateral breast tumour recurrence
IHC	Immunohistochemistry
IOM	Institute of Medicine
IORT	Intra-operative radiotherapy
ISH	In situ hybridisation
JBCS	Japanese Breast Cancer Society
KCE	Belgian Health Care Knowledge Centre
LABC	Locally-advanced breast cancer
LCIS	Lobular carcinoma in situ
LHRH	Luteinising hormone-releasing hormone
LHRHa	Luteinising hormone-releasing hormone agonist
LoE	Level of evidence
LR	Literature review
LRF	Locoregional failure
LVEF	Left ventricular ejection fraction
LVI	Lymphovascular invasion
MRI	Magnetic resonance imaging
MUGA	Multigated acquisition

Abbreviation	Definition
NA	Not applicable
NAC	nipple-areolar complex
NACT	neoadjuvant chemotherapy
NBOCC	National Breast and Ovarian Cancer Centre
NCCN	National Comprehensive Cancer Network
NCCP	National Cancer Control Programme (IRE)
NCI	National Cancer Institute
NHMRC	National Health and Medical Research Council
NHSBSP/BTWSP	NHS Breast Screening Programme or Breast Test Wales Screening Programme
NICE	National Institute for Health and Care Excellence
NR	not reported
NSM	nipple-sparing mastectomy
NZGG	New Zealand Guidelines Group
ONJ	osteonecrosis of the jaw
P	paclitaxel
PBI	partial breast irradiation
PCP	primary care physician
pCR	pathologic complete response
PET	positron emission tomography
PGDC	Practice Guidelines Development Cycle
PMRT	postmastectomy radiotherapy
POI	premature ovarian insufficiency
PR	progesterone receptor
RCT	randomised controlled trial
RT	radiotherapy
SERM	selective oestrogen receptor modulators
SIGN	Scottish Intercollegiate Guidelines Network
SIOG	International Society of Geriatric Oncology
SLNB	sentinel lymph node biopsy
SNB	sentinel node biopsy
SNRIs	serotonin–norepinephrine reuptake inhibitors
SR	systematic review
SSM	skin-sparing mastectomy
SSRIs	selective serotonin re-uptake inhibitors
T	docetaxel (Taxotere)
TAC	docetaxel-doxorubicin- cyclophosphamide
TC	docetaxel/cyclophosphamide
TCH	docetaxel, carboplatin and trastuzumab
TNBC	triple negative breast cancer
TRAM	transverse rectus abdominus muscle
USPSTF	United States Preventive Services Task Force
WBRT	whole breast radiotherapy

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