

check

RACGP CPD solution

Unit 611
May 2024

Breast cancer





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About *check*

check is a CPD learning activity written by expert clinicians and reviewed by subject matter experts. Each unit comprises approximately five clinical cases with answers, followed by 10 multiple-choice questions (MCQs), as well as references and resources.

check aims to keep Australian GPs up to date with the most common and most important clinical conditions. While there are many different ways to keep up to date, it is essential for the RACGP to lead in this space, and provide updated, relevant support to GPs in their clinical practice. *check* seeks to support all GPs, including trainees and those with specific interests, and is a key resource for exam preparation. As such, *check* has a schedule of units that is informed by data on what the most common conditions are in general practice, and is responsive to those parts of general practice that are changing the most rapidly.

How *check* works

There are 11 *check* units each year. Each unit comprises approximately five clinical cases, and the choice of cases covers the broad spectrum of the unit's topic. Each unit is led by a GP with an interest and capability in the topic, and they scope the five different cases for that unit in collaboration with the *check* team.

Members achieve approximately 10 CPD hours (two hours per case) for completing a unit of *check*. Every clinical case included in each unit will follow an agreed standard format, and will carry two CPD hours (one hour of Educational Activities [EA] and one hour of Reviewing Performance [RP]). In addition, each *check* unit will include one or more suggested topics that meet Measuring Outcomes requirements for CPD.

Authors achieve four CPD hours (two hours' EA and two hours' RP) for each case they write. Unit coordinators achieve two hours (one hour EA and one hour RP) in total. Unit coordinators who also write a case achieve six hours (three hours' EA and three hours' RP), based on one written case. Subject matter expert reviewers achieve two CPD hours (one hour EA and one hour RP) for each case they review.

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Breast cancer

Unit 611 May 2024

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The five domains of general practice

- Ⓛ1 Domain 1: Communication skills and the patient–doctor relationship
- Ⓛ2 Domain 2: Applied professional knowledge and skills
- Ⓛ3 Domain 3: Population health and the context of general practice
- Ⓛ4 Domain 4: Professional and ethical role
- Ⓛ5 Domain 5: Organisational and legal dimensions

ACTIVITY ID
767394

Breast cancer



This unit of *check* is approved for 10 hours of CPD Activity (two hours per case). The 10 hours, when completed, including the online questions, comprise five hours' Educational Activities and five hours' Reviewing Performance.

To complete this unit as a CPD Activity, you should carefully read all cases, complete the questions for each case (hard copy or online), answer the linked multiple-choice questions online and score >80%, and complete the evaluation form online.

All doctors also need to do a minimum five hours' Measuring Outcomes CPD each year, and you can do this by completing one Mini-Audit each year. You can do a Mini-Audit based on this unit, or any other unit of *check*, or on any topic that is relevant to your practice.

To do a Mini-Audit on this unit's topic, select the last five relevant patients you managed. Review their records, summarise your management and findings, and indicate in writing (for yourself) where your management and patient outcomes could have been improved, based on what you have learned following your completion of this *check* unit.

You can access all online resources here: <https://mycpd.racgp.org.au>

For any technical issues, including guides and templates for a Mini-Audit, contact us on 1800 284 789. To purchase this unit if you are not an RACGP member, please call 1800 284 789.

About this activity

Breast cancer is the most commonly diagnosed cancer for females in Australia.¹ The estimated number of breast cancer cases diagnosed in females for 2023 was around 20,500 with more than 240,000 Australians living with a history of breast cancer.¹

Breast cancer incidence has increased over the last 20 years. A large portion of this increase occurred around 2013 when breast screening was expanded to include women aged 70–74 years.

While survival rates for breast cancer overall are high, there is substantial variation in survival for different types of breast cancer. The most common type of carcinoma, the infiltrating duct carcinoma (no special type), which accounts for 73% of all breast cancers, had a five-year survival of 93% in the period 2015–2019.

It was estimated that nearly 3300 females would die from breast cancer in 2023. Like many other cancers, the

increasing number of deaths is attributable to increasing population size and the ageing population.

As the first point of health contact for the majority of Australians, general practitioners play a significant role in the prevention, screening, diagnosis and after-treatment care of patients with breast cancer.² General practice can improve the outcomes of cancer diagnosis through early intervention.

This unit of *check* considers the diagnosis, treatment and ongoing management of breast cancers.

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Learning outcomes

At the end of this activity, participants will be able to:

- outline the components of the triple test and its application, including imaging and diagnostic biopsy options
- discuss risk assessment and screening options available to women in the moderate- to high-risk categories for breast cancer
- describe treatment options for breast cancer including surgery, radiotherapy and medical therapies
- discuss the management of risk-reducing medications
- advise on risk-reducing lifestyle changes.

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Abbreviations

BOADICEA breast and ovarian analysis of disease incidence and carrier estimation algorithm

BI-RADS breast imaging reporting and data system

ER-positive/negative oestrogen receptor-positive/negative

HER2-positive/negative human epidermal growth factor receptor 2-positive/negative

PR-positive/negative progesterone receptor-positive/negative

CASE

1 Louise wants to discuss breast screening

Louise, aged 37 years, presents for a review and repeat of her oral contraceptive script. She wants to discuss whether she should start breast screening as her mother Shirley was diagnosed with breast cancer aged 45 years.

Question 1 (D1) (D2)

What questions would you ask Louise to determine her risk for breast cancer, the type of screening she should consider and from what age?

Further information

You decide to complete a rough pedigree with Louise during your consultation (Figure 1).

Louise states that her mother Shirley was diagnosed with breast cancer aged 45 years and is now 68 and that her maternal grandmother Dulcie was diagnosed with breast cancer aged 58 years and died at 85.

Louise's father separated from the family when she was young. Although they have contact, she is uncertain about her paternal history of cancer, but thinks that her paternal aunt Sue may have had breast cancer at a similar age to her mother.

Louise is 174 cm tall and weighs 60 kilograms, giving her a body mass index of 19.8 kilograms/m² (within the healthy range).

She drinks no more than three glasses of alcohol (usually wine) a week, does not smoke and exercises for more than 30 minutes a day.

Her menarche was at age 13 and she has had two children, the first at age 30 years, and breastfed both for six months.

She has been using hormonal forms of birth control since her early 20s and currently uses Zoely for contraception. She is happy with this and has had no significant side effects.

Louise has not had any breast imaging and has not had any concerning breast lumps or breast changes.

You note that use of the oral contraceptive pill is not contraindicated and provide Louise with her script and a family history questionnaire to complete, in case anything has been missed. You ask her to return if there is any significant history to discuss.

Have you any Ashkenazi Jewish ancestors?

Ashkenazi Jewish Other / Unknown

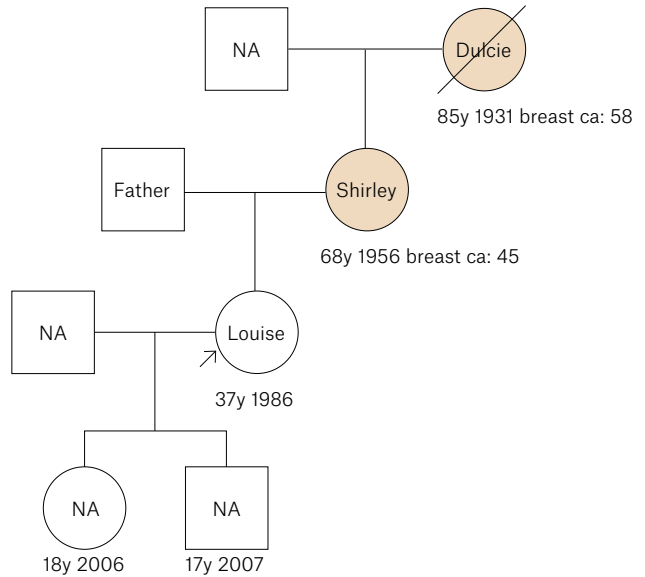


Figure 1. Louise's pedigree created using the CanRisk tool (https://canrisk.org/canrisk_tool).

Question 2 (D1) (D2)

Based on her maternal family history, what is Louise's risk of breast cancer in the short and long term and what would you advise regarding screening?

Further information

Using CanRisk, Louise's maternal history places her at moderate risk over her lifetime (~20%) (Figure 2), but low risk

at present (~1% in the next five years) and screening would not be recommended at her current age (Figure 3).

CanRisk includes the tool BOADICEA, which calculates the likelihood of a high-risk gene variant.

Question 3 (D2) (D4)

Is genetic testing indicated for Louise or her mother Shirley based on this history?

The woman's lifetime risk from age 20 of having breast cancer is 19.4%. According to the National Institute for Health and Care Excellence guidelines¹ the woman would be in the **moderate** risk category.

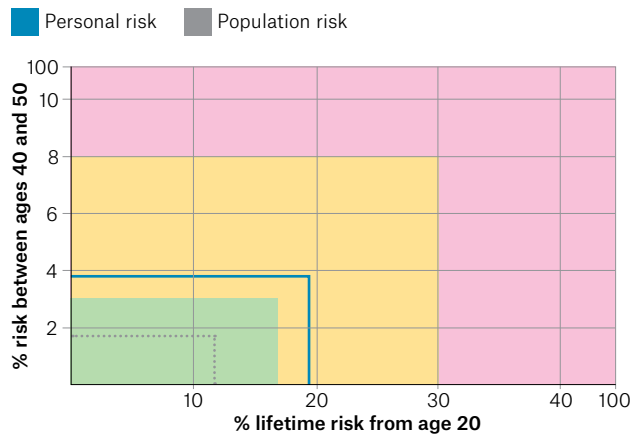


Figure 2. CanRisk estimation of Louise's risk for breast cancer.

Absolute risk of breast cancer from current age

The woman's risk of developing **breast cancer over the next five years is 1.1%**. In other words, about 11 out of 1000 women with these risk factors will develop cancer over the next five-year period.

The woman's risk of developing **breast cancer over the next 10 years is 3%**. In other words, about 30 out of 1000 women with these risk factors will develop cancer over the next 10-year period.

The woman's risk of developing **breast cancer between 37 and 80 is 18.5%**. In other words, about 185 out of 1000 women with these risk factors will develop cancer by the age of 80.

Show table of age-specific risks

Note: for the lifetime risk see the 'Risk Category (NICE)'.

Personal risk of developing breast cancer compared to the population

Personal risk
Population risk

The woman's risk of developing **breast cancer by the age of 80 is 18.5%** compared to the **average population risk of 11.5%**.

In other words, about 185 out of 1000 women with these risk factors will develop breast cancer by the age of 80, compared to an average woman where 115 in 1000 will develop breast cancer.

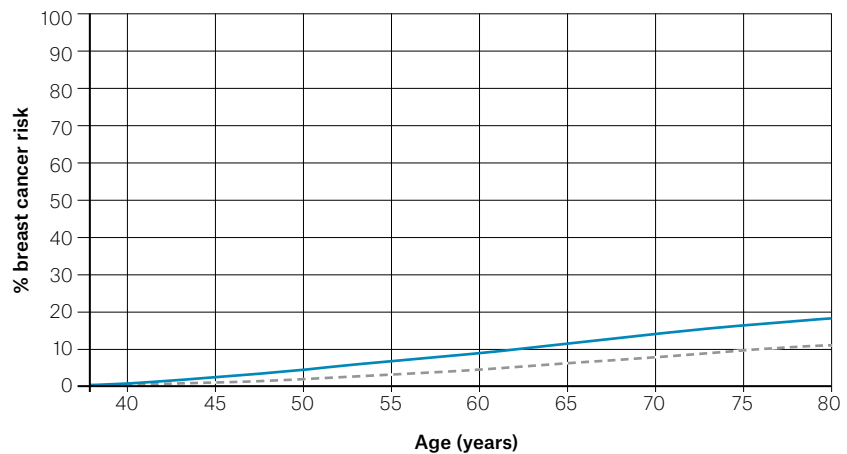


Figure 3. CanRisk calculation of Louise's risk for breast cancer in the next five years, 10 years and to age 80.

Question 4 (D2)

What further information is required?

Further information

Louise returns and confirms that her paternal aunt, Sue, was diagnosed with breast cancer aged 58 years. Her paternal family history is significant; her paternal grandmother, Mabel, was diagnosed with ovarian cancer aged 65 years and died at 67 and a paternal uncle, Peter, was diagnosed with pancreatic cancer aged 58 years and died at 58.

Question 5 (D2)

What would be your next step?

Further information

Louise’s paternal aunt Sue is eligible for Medicare-funded genetic testing.

Question 6 (D1) (D2)

How do you explain this result to Louise?

Further information

Louise tells you that Sue has an appointment with a public family cancer clinic. You agree to wait for the result. As Louise is not symptomatic, you do not organise breast imaging at this time.

When Louise returns she informs you that a pathogenic *PALB2* variant was detected in Sue and that her father John is not interested in having predictive genetic testing.

Question 7 (D1) (D2)

What are Louise’s options and how would you discuss these with her?

Conclusion

Louise returns. She and her siblings have had genetic testing. Her sister Amanda, aged 30 years, carries the familial *PALB2*

variant. She has not yet had children. Amanda has elected MRI breast screening and is currently pursuing preimplantation genetic testing in the setting of in vitro fertilisation to prevent the variant being passed to her children.

Louise and her brother Nathan tested negative. You inform Louise that she should commence breast screening at age 40 and have her eligibility for breast MRI reviewed at that time. Emphasise the importance of lifestyle on cancer risk. Remind her to keep you informed of any changes to her family history.

Louise is happy with this plan and agrees to present promptly if she notices any breast lumps, skin changes or nipple discharge.

CASE 1 Answers

Answer 1

Many factors affect a person's risk for cancer. Broadly, these can be categorised as lifestyle and environmental factors, personal history and family cancer history. Taking a family cancer history is a standard part of a medical assessment and should be revisited even in long-term patients as the family history may change over time.

You could ask Louise questions about her:

- lifestyle (weight, diet, exercise and smoking habits, alcohol consumption)
- age at menarche and menstrual history, birth control, parity and breastfeeding
- breast history, previous imaging and any current symptoms including benign lumps and cysts
- family history including two generations and more distant affected relatives such as first cousins; be sure to ask about paternal history, age at diagnosis, age at death, bilaterality and, if known, subtype
- heritage, specifically if there is any Ashkenazi Jewish heritage (due to known founder variants).

Answer 2

Screening for breast cancer promotes early detection, allowing less aggressive treatment options and better survival.² In Australia women aged 50–75 years are invited to the free BreastScreen service. Women who are asymptomatic and aged 40–49 years or ≥75 years can also access free mammogram screening.³

Patients should be referred to a breast specialist for breast MRI screening if they are aged between 30 and 60 years and have been diagnosed with breast cancer before the age of 50 or have a lifetime risk estimation >30% or a 10-year absolute risk estimation >5% using a clinically relevant risk evaluation algorithm (Medicare Benefits Schedule item 63464).⁴

Risk can be estimated using a variety of validated tools that consider family history and lifestyle factors. Popular models include CanRisk (https://canrisk.org/canrisk_tool), Tyrer-Cuzick (<https://ibis-risk-calculator.magview.com>) and iPrevent, which uses the CanRisk information (<https://iprevent.net.au>).

CanRisk requires registration but has a simple user interface, estimates the likelihood of a pathogenic *BRCA1* or *BRCA2* variant and allows the input data to be saved and edited. All of these tools are free and provide printable risk information, including images.

Answer 3

The likelihood of a germline *BRCA* variant can be estimated using the Manchester Scoring System.⁵ This system tends to overestimate risk in a large, long-lived family and underestimate in a small or male predominant family. It assigns a score to each affected relative, based on age at diagnosis and cancer type. It is quick and simple to use, but not as sophisticated as CanRisk's BOADICEA.

A combined Manchester Score of 15 indicates a 10% likelihood of identifying a pathogenic *BRCA1* or *BRCA2* variant in an affected patient – the threshold required under Medicare Benefits Schedule item 73296.

You calculate Louise's Manchester Score as 6 (for Louise's mother) + 4 (for Louise's maternal grandmother), giving a combined score of 10 for an affected relative. As the score is below the required threshold, genetic testing would not be recommended for an affected relative. (BOADICEA gives the likelihood of a *BRCA1* or *BRCA2* variant in Louise's mother as <2%). Louise is not eligible for testing as she has not had cancer. Self-funded testing could be considered, but would be difficult to justify.

Answer 4

Only half of Louise's genetic risk has been discussed. You need her paternal family history in order to properly assess her risk and to confirm the type of cancer her mother had (eg ER-positive, triple-negative), as this will affect the likelihood of Louise's mother carrying a pathogenic *BRCA* variant and therefore Louise's risk. In addition to a 10% chance via a risk model, Medicare-funded testing (Medicare Benefits Schedule item 73296) is now available for individuals with breast cancer if there is a 10% chance of a pathogenic variant in a gene associated with breast or ovarian cancer. According to the eviQ guidelines, this includes:⁶

- all individuals with triple-negative breast cancer
- all individuals with metastatic breast cancer
- all individuals diagnosed at or before age 40
- all men with breast cancer
- all individuals with breast cancer and Ashkenazi Jewish heritage.

Answer 5

This is a significant family history and Louise’s predicted breast cancer risk has increased (Figure 4). Review the eviQ guidelines with Louise, noting that she, as well as her affected relatives, meet the criteria for referral for genetic assessment.⁷ As you used CanRisk at your earlier consultation, you can reload Louise’s saved file and update the information. The model also allows you to change the proband – the person whose risk you are considering – from Louise to her paternal aunt Sue. The paternal Manchester Score is 4 (Sue) + 10 (Mabel) + 1 (Peter), giving a combined score of 15 and a pathogenic variant probability of ≥10% in an affected relative.

Answer 6

Discuss with Louise that self-funded testing is available for her (with costs ranging from \$450 to \$800 depending on the laboratory used and the number of genes tested), but explain that the best person to test in the first instance would be Sue. Explain that genetic testing should only be performed after genetic counselling to discuss its implications and limitations.

Answer 7

Discuss with Louise that predictive testing is still available for her and her siblings as Sue is a biological relative and that this would be Medicare funded (Medicare Benefits Schedule item 73297). Predictive testing is now funded for ‘genes associated with breast, ovarian, fallopian tube or primary peritoneal cancer’. These genes include *ATM*, *BRIP1*, *BRCA1*, *BRCA2*, *BARD1*, *CDH1*, *CHEK2*, *PALB2*, *PTEN*, *RAD51C*, *RAD51D*, *STK11* and *TP53*.

Discuss the options of testing via a public family cancer clinic or a private specialist.

If you are not familiar with *PALB2*, details can be found on the eviQ website (www.eviq.org.au/cancer-genetics/adult/risk-management/1609-PALB2-risk-management). Print out and review the patient information sheet with Louise.

PALB2 stands for Partner and Localiser of *BRCA2*. It works with *BRCA1* and *BRCA2* to repair errors (double-strand breaks) that occur in the DNA when cells divide. Explain that, if she has inherited the *PALB2* variant, her risk of breast cancer would be ~55% over her lifetime and her risk of ovarian cancer ~5%. The *PALB2* variant also increases her risk of pancreatic cancer to 3% over her lifetime.

Explain that this risk can be managed with funded breast MRI screening (from age 30) and with risk-reducing medications such as tamoxifen (from age 35) or bilateral mastectomies (usually from age 30). Advise Louise that there is no screening for ovarian cancer. Instead, surgery to remove both ovaries and fallopian tubes is strongly recommended by age 50.

If Louise does not carry the familial *PALB2* variant, she still has a maternal history of breast cancer. The CanRisk BOADICEA tool allows you to include the outcome of genetic testing (Figure 5). Louise remains at moderate risk for breast cancer due to her maternal family history.³ From CanRisk, her risk over the next five years is 1%, over the next 10 years 2.7% and to age 80, 18.8%. She is not eligible for breast MRI screening based on her current age in this model.

Starting screening at 10 years younger than the age at which the youngest family member was diagnosed is no longer the

Have you any Ashkenazi Jewish ancestors?

Ashkenazi Jewish Other / Unknown

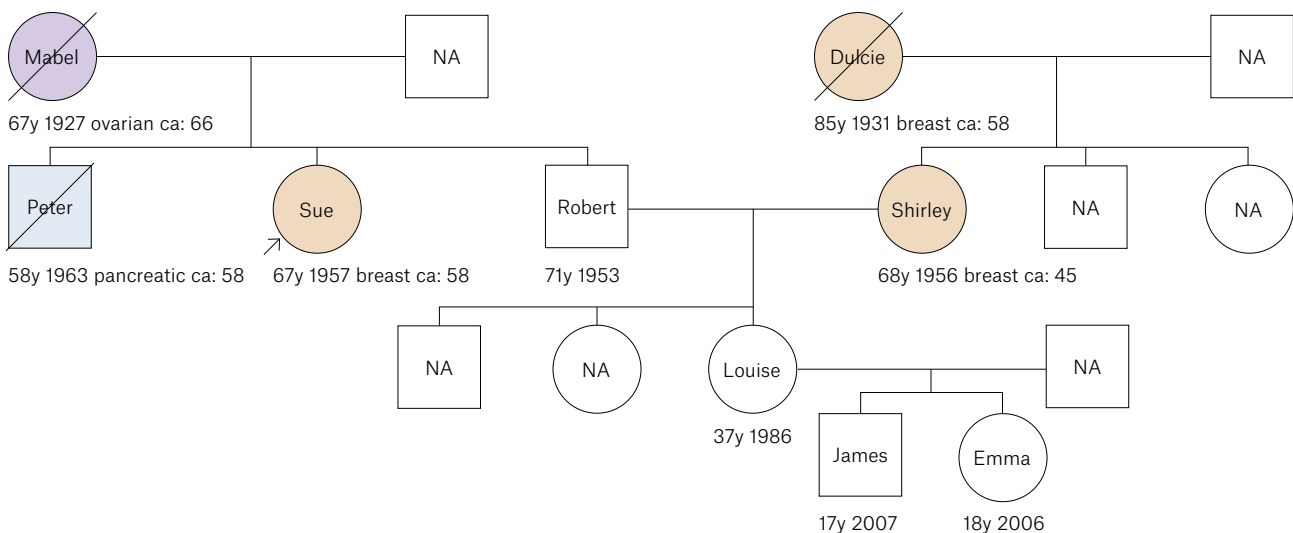


Figure 4. Updated CanRisk pedigree. Louise’s paternal history is consistent with a >10% chance of a pathogenic *BRCA* variant (paternal aunt).

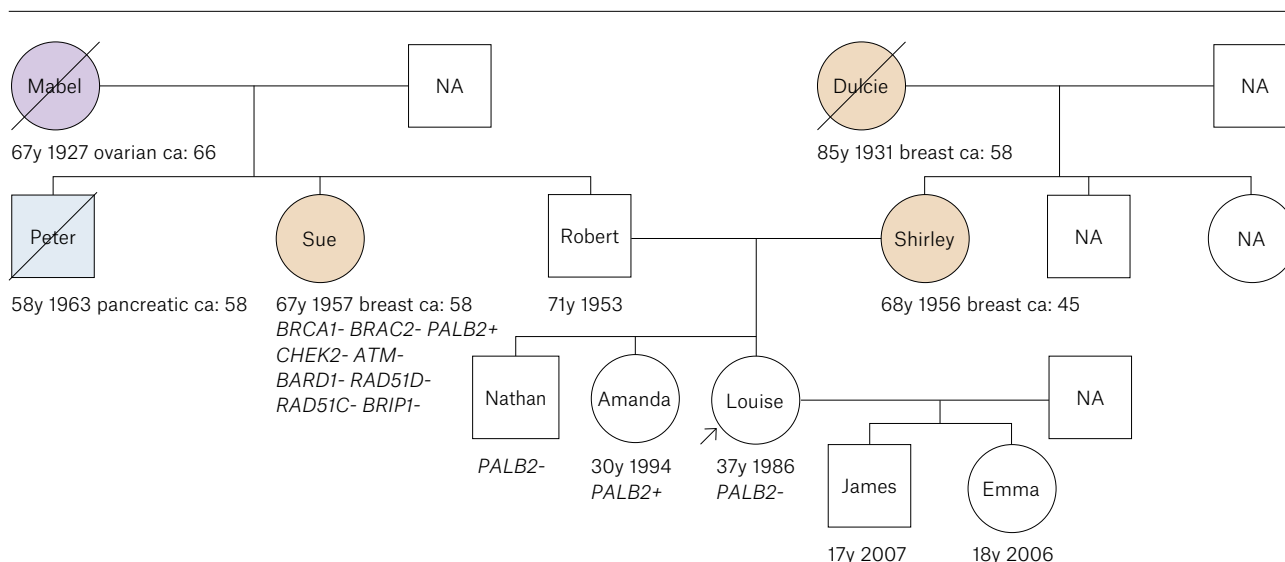


Figure 5. Updated CanRisk pedigree, including the outcome of Louise and her siblings' genetic testing.

rule as the models now used for calculating breast cancer risk and the likelihood of a *BRCA* variant are more sensitive and starting screening too early may be associated with false positives and overdiagnosis.

Resources for patients

- Breast Cancer Network Australia – Information and resources on familial risk for breast cancer, www.bcna.org.au/resource-hub/articles/breast-cancer-in-the-family
- Cancer Australia – Information and resources on familial risk for breast cancer, www.canceraustralia.gov.au/cancer-types/breast-cancer/awareness/family-history
- The Cancer Council – Information and resources on cancer prevention, diagnosis and treatment, www.cancer.org.au/cancer-information

Resources for doctors

- University of Cambridge – CanRisk and BOADICEA risk model, https://canrisk.org/canrisk_tool
- MagView – Tyrer-Cuzick risk model, <https://ibis-risk-calculator.magview.com>
- Peter MacCallum Cancer Centre – iPrevent risk model, <https://iprevent.net.au>
- Cancer Institute NSW – eviQ risk management guidelines for pathogenic gene variants, www.eviq.org.au/cancer-genetics/adult/risk-management
- Cancer Institute NSW – eviQ cancer genetics protocols including referral and testing guidelines, www.eviq.org.au/cancer-genetics

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CASE

2 Marie has a lump in her breast

Marie is a support worker, aged 53 years. She presents to you concerned about a lump in her left breast. Marie found the lump about six weeks ago after having noticed some pain in the same area. She had her second screening mammogram last year, which was reported as showing no sign of cancer, so she was not overly concerned. However, last week, after one of her friends was diagnosed with breast cancer, she thought she would come to see you.

Question 1 (D1) (D2)

What questions would you ask Marie that may be relevant to her history of a breast lump?

Question 2 (D1) (D2)

How would you examine Marie?

Further information

Marie had menarche aged 12 years and her last normal menstrual period was 13 months ago. She has two children, the eldest of whom was born when Marie was aged 31 years. Marie breastfed for a total of four months. She has no family history of breast, ovarian or prostate cancer, nor of melanoma.

Marie has not been diagnosed with any breast conditions previously, nor needed a breast biopsy. She is currently using topical estradiol and progesterone to manage her hot flushes and low libido.

During your assessment of Marie's lifestyle risks, she reports drinking at least one standard drink every night. Her body mass index is 30 kilograms/m².

Marie has a slit-like nipple inversion, unchanged over many years, which can be partially everted. There are no other nipple or areola skin changes. You feel an 18-mm, hard, non-tender, partially mobile mass in Marie's left breast at 2 o'clock, about 50 mm from the nipple. There is no palpable axillary lymphadenopathy.

Marie asks if she has cancer.

Question 3 (D2)

What is your initial diagnostic impression?

Question 4 (D2) (D4)

What steps will you take to confirm the diagnosis?

Table 1. Relevant history of a patient with a breast lump

History of presenting symptom	<ul style="list-style-type: none"> • Site: Is the site constant or changing, unilateral or bilateral? • Duration: When and how was the lump first noticed? • Has there been any subsequent change? • Is there any link with menstrual cycle or exogenous hormones? • Associated symptoms: Breast pain, change in breast size or shape, skin dimpling, nipple changes or nipple discharge
General and personal characteristics	<ul style="list-style-type: none"> • Age • Gender • Mammographic breast density
Family history and genetics	<ul style="list-style-type: none"> • Diagnoses of breast or ovarian cancer on maternal or paternal sides^{1,2} • Number of family members affected • Age at diagnosis in relatives • Whether first- or second-degree relatives • Presence of known breast cancer gene variant in family and who was/is affected
Breast pathology	<ul style="list-style-type: none"> • Number of previous breast biopsies • Previous breast pathology, particularly atypical hyperplasia, ductal or lobular carcinoma in situ • Previous breast surgery, including cosmetic surgery
Endogenous hormones	<ul style="list-style-type: none"> • Age at menarche • Age at first live birth • Number of full-term births • Breastfeeding duration • Age at menopause • Recent pregnancies and breastfeeding
Exogenous hormones	<ul style="list-style-type: none"> • Duration of use of combined oral contraceptive, current or previous • Duration of use of menopausal hormonal therapy, current or previous
Lifestyle factors	<ul style="list-style-type: none"> • Overweight and obesity, including postmenopausal weight gain • Alcohol consumption • Diet • Physical activity
Medical factors	<ul style="list-style-type: none"> • Previous radiation therapy • Previous cancers
Breast imaging	<ul style="list-style-type: none"> • Date of most recent mammogram or ultrasound and whether screening or diagnostic
Recent breast trauma	<ul style="list-style-type: none"> • Details of recent breast trauma(s)

There is now a large body of evidence for a number of risk factors for breast cancer, which can be categorised into the following groups: general factors, personal characteristics, family history and genetics, breast pathology, endogenous hormones, exogenous hormones, lifestyle factors, medical factors, chemical exposures and radiation.³

Answer 2

Ask Marie about the history of the lump. How did she notice it, has it changed, is it tender, has the skin changed, is there nipple discharge?

Conduct a thorough examination of both breasts and axillae.⁴ Aim to identify those features that distinguish malignant from benign lumps.

Ask Marie to remove her clothing from above the waist and sit on the edge of the examination bed with arms by her side, then raised above her head and then pressing on her hips and leaning forward. Clinical breast examination will include inspection and palpation while she is seated and then lying down with the ipsilateral hand behind her head. Use your non-examining hand to immobilise a large breast; a pillow under the shoulder may help with examination of the outer quadrants of a large breast.

Note any lumps, including:

- Site: Position on clock face and distance from nipple
- Size: In millimetres
- Shape: Irregular or round/ovoid
- Surface: Smooth or irregular
- Consistency: Soft, firm or hard
- Tenderness
- Mobility: Is it fixed to the skin or chest wall?

Answer 3

Based on your history-taking and examination, you are suspicious of invasive breast cancer.

Palpable breast masses are common in women and can be divided into benign and malignant masses. While most are benign, 10% of women who present with a palpable breast mass will have a diagnosis of cancer.^{5,6} Up to one in eight Australian women will be diagnosed with breast cancer by the age of 85.^{7,8} Age is the most important risk factor for breast cancer.¹

A number of factors may influence the likelihood of a particular benign or malignant condition (see the table in Cheung and Lam's Approach to a lump in the breast: A regional perspective⁹). There are many non-malignant causes of a discrete breast lump (Table 2); the most common causes in a patient over the age of 50 years include fibroadenoma, fibrocystic change and a cyst.

Answer 4

Based on Marie's history and clinical breast examination you would refer Marie for bilateral mammogram with tomosynthesis (three-dimensional), ultrasound and non-excisional biopsy.⁴

The combination of clinical breast examination, imaging (mammogram and ultrasound) and non-excisional biopsy – the 'triple test' – is more accurate than any modality alone¹²⁻¹⁴ and when performed appropriately, detects more than 99.6% of cancers.

Table 2. Differential diagnosis of benign breast lumps^{10,11}

Cause	Diagnosis
Infectious	<ul style="list-style-type: none"> • Breast abscess and infectious mastitis
Non-infectious	<ul style="list-style-type: none"> • Fibroadenoma • Fibrocystic change • Breast cyst • Hyperplasia • Hamartoma • Intraductal papilloma • Haematoma • Fat necrosis • Sclerosing adenosis • Sarcomas, including phyllodes tumour • Duct ectasia • Lymphadenopathy • Epidermoid cyst • Lobular carcinoma in situ • Idiopathic granulomatous mastitis • Lymphocytic mastopathy • Tubular adenoma • Lactating adenoma • Mucocele • Lymphocytic lobulitis • Pseudo-angiomatous stromal hyperplasia • Lipoma • Seroma • Sarcoidosis • Amyloidosis • Galactocele • Desmoid fibromatosis • Granular cell tumour

MRI is not recommended in the routine investigation of a new breast or nipple symptom, but may be used in conjunction with mammography and ultrasound for the evaluation of lymph nodes and primary occult tumours.¹⁵

Consider organising a referral to a breast surgeon if highly suspicious for breast cancer at the time of examination and there is an expected long delay in accessing diagnostic imaging. BreastScreen is for asymptomatic patients. Women with symptoms are actively discouraged from attending the screening program as they need a diagnostic work-up, not a screening two-dimensional mammogram.¹⁶

Answer 5

Core biopsy is preferred over fine-needle aspiration cytology for suspicious lesions where tumour type, histological grade and the receptor status of cancer is required and because core biopsy is able to differentiate between in situ and invasive cancer.¹⁷ There is still a role for fine-needle aspiration cytology,¹⁸ particularly for the investigation of suspicious lymph nodes or likely benign breast disease.^{19,20}

Answer 6

Using your 'breaking bad news' principles, ensure that Marie has enough time booked in to discuss and process the results. Offer for her to bring along a support person.

Be clear about the diagnosis and information available so far. Explain that she will be given more information as it becomes available. You might say, 'It is not the result we wanted, but the tests confirm that the lump is breast cancer'.

Consider using online resources such as Cancer Australia's guide for women with early breast cancer or Breast Cancer Network Australia's My Journey to guide your conversation. You may be able to say, 'Based on what we can see on imaging, there is no evidence that the cancer is outside the breast or in the lymph nodes'.

Explain the next steps, including referral to a breast surgeon associated with a multidisciplinary team to discuss treatment options. Most women will have the option of either breast-conserving surgery or a mastectomy. You could explain that during the operation at least one axillary lymph node (a sentinel node) will be removed and examined. Further treatment will be planned depending on the surgical results. This may include more surgery, radiotherapy or chemotherapy, and will be determined based on the histology, nodal status and receptor status of the surgical specimens, as well as discussion with a multidisciplinary team and consideration of the individual patient's choice.

Offer Marie a follow-up appointment to discuss any further questions she may have.

Answer 7

Using the available resources, explain that there is a good prognosis for early breast cancer and that it can be treated successfully. Although staging of Marie's cancer will occur after surgery, from the information you have so far you can tell her that the five-year survival rate for small cancers (<20 mm) with no lymph node involvement, treated according to current guidelines, is almost 95%. Most people diagnosed and treated for early breast cancer in Australia will not die from the disease.²¹

Answer 8

If the initial imaging results are not consistent with the clinical findings, further assessment is required to complete the triple test. Other imaging can be considered. Consider referral for contrast-enhanced mammography or MRI. Contrast-enhanced mammography has similar sensitivity to MRI for detecting occult malignancy, but may be slightly more specific.²² Contrast-enhanced mammography can be requested by general practitioners and is cheaper and faster to perform and interpret than MRI. It is often more acceptable to patients and is available in many locations.²³ Contrast-enhanced mammography can reduce the need for ultrasound or MRI. MRI for breast cancer investigation can be requested by any doctor, but will only attract a Medicare rebate if ordered by non-general practitioner specialists.²⁴⁻²⁶

Biopsy is essential for a new discrete solid lump in a woman of this age even when imaging features are benign. Surgical referral is recommended if any *one* component of the triple test is positive, including the clinical examination (whether suspicious or malignant).

Resources for patients and doctors

- Peter MacCallum Cancer Centre – iPrevent breast cancer risk assessment and management tool, www.petermac.org/iprevent
- Cancer Australia – Guide for women with early breast cancer, www.canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/guide-women-early-breast-cancer
- Breast Cancer Network Australia – Peer support information and app, www.bcna.org.au/my-journey/
- McGrath Foundation – Breast care nurse locator, www.mcgrathfoundation.com.au/get-support/find-a-nurse/
- Cancer Council – Guide to best breast cancer care (available in multiple languages), www.cancer.org.au/cancercareguides/breast-cancer

Resources for doctors

- Cancer Australia – Guide to investigating a new breast symptom, www.canceraustralia.gov.au/sites/default/files/publications/investigation-new-breast-symptom-guide-general-practitioners/pdf/investigation-of-a-new-breast-symptom-a-guide-for-general-practitioners.pdf
- Cancer Australia – Review of risk factors for breast cancer, www.canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/risk-factors-breast-cancer-review-evidence-2018
- Cancer Australia – Guidance on management of early breast cancer, www.guidancebreastcancer.gov.au/treatment-planning-information-and-support
- The Royal Australian College of General Practitioners – Preventive health assessment for Aboriginal and Torres Strait Islander people, www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/national-guide/chapter-15-prevention-and-early-detection-of-cancer/prevention-and-early-detection-of-breast-cancer
- The Royal Australian College of General Practitioners – Guidelines for early detection of breast cancer, www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/guidelines-for-preventive-activities-in-general-pr/early-detection-of-cancers/breast-cancer

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You order a core biopsy of the breast lesion. This confirms invasive carcinoma (no special type), grade 3, ER-positive, PR-positive, HER2-positive (triple-positive) breast cancer and Ki-67 expression of 65%. Fine-needle aspiration of the lymph nodes confirms metastasis.

You book Fiona an appointment with the surgeon in two days' time.

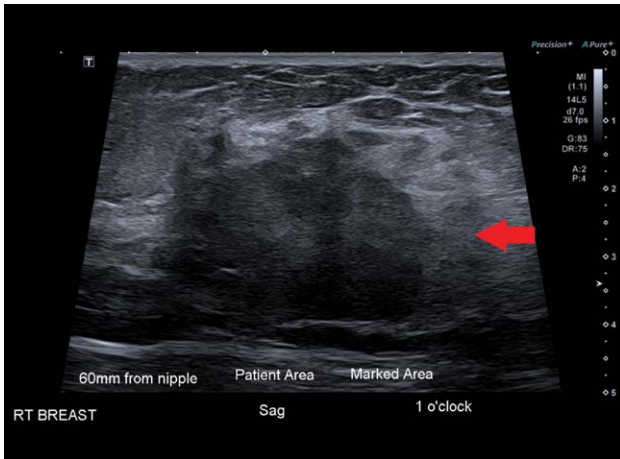


Figure 3. Ultrasound of the right breast at 12.00–1.00 o'clock, 60 mm from the nipple, showing a large hypoechoic lesion.

Question 3 (D1) (D2)

Fiona asks what her treatment options might be. How do you respond?

Question 4 (D2) (D4)

Fiona has been planning to start her family. What other components of her treatment need to be considered?

Further information

Fiona receives TCHP (docetaxel [*taxane*], carboplatin, trastuzumab [*Herceptin*], pertuzumab) chemotherapy and has an excellent response, with complete clinical and radiological resolution (not palpable and not seen radiologically).

Question 5 (D2)

What are the options for surgery, and how has this changed with the advent of neoadjuvant chemotherapy?

Further information

Fiona’s histopathology post wide local excision with targeted axillary dissection has shown a complete pathological response with only fibrosis seen at the site of cancer in both breast and axilla.

for breast cancer (patient history and breast examination, imaging and non-excisional biopsy). If the mass is suspicious clinically but non-diagnostic on either imaging or biopsy, a referral to a surgeon regarding further imaging or diagnostic excisional biopsy of the mass should be made.

As Fiona is young and has dense breasts, contrast-enhanced imaging such as MRI or contrast-enhanced mammography (Table 1) prior to biopsy can be considered (Figures 1–3). There are strict criteria for Medicare-rebatable MRIs, including being referred by a non-general practitioner specialist. An alternative is abbreviated MRI. This has been shown to be equally sensitive in diagnosing breast cancer compared with the traditional 40-minute MRI.¹ An abbreviated MRI does not require referral from a specialist as it is not Medicare-rebatable. It is significantly lower in cost than a full MRI.

Answer 3

Explain that the three main modalities for management of breast cancer include:

- **Surgery:** The only patients who may not be offered surgery are those with non-fungating distant metastatic disease (excluding oligometastasis to the bone) as there is no survival benefit and systemic rather than local treatment is more important in this scenario.
- **Medical oncology:** This includes endocrine therapy, chemotherapy, targeted therapy and immunotherapy.
- **Radiation oncology:** Radiotherapy indications include those undergoing breast-conserving therapy, large tumours (>5 cm) and axillary/supraclavicular lymphadenopathy. Radiotherapy can also be used to treat isolated metastatic disease.

The surgeon will plan the order in which these are performed or required. For screen-detected small tumours, surgery is often the first approach recommended. However, in some circumstances (as with Fiona who has a 49-mm, grade 3, HER2-positive carcinoma with lymph node involvement), neoadjuvant therapy should be considered first.

Neoadjuvant therapy

Neoadjuvant therapy, drug treatment given before surgery, usually refers to intravenous chemotherapy. Depending on the type of breast cancer, chemotherapy may be combined with antibody treatment or immunotherapy. It has several advantages in the treatment of breast cancer including:

- reducing the size of the cancer, which can result in a smaller operation (a lumpectomy rather than mastectomy)
- reducing the disease in the lymph nodes, allowing for less axillary surgery (eg a targeted axillary dissection rather than full axillary lymph node dissection), which reduces the risk of lymphoedema
- learning the treatment response, which allows tailoring or altering adjuvant treatment to improve survival.

Consequently, patients undergoing surgery who will require adjuvant chemotherapy should be considered for neoadjuvant

therapy. Indications for neoadjuvant therapy include the following:

- HER2-positive or triple-negative breast cancer
- inflammatory breast cancer
- luminal B breast cancer with high risk for recurrence – grade 3, a Ki-67 index of more than 20%
- lymph node metastasis.

Neoadjuvant therapy is now the standard of care for two types of breast cancer – triple-negative and HER2-positive – particularly when the primary breast cancer is ≥ 1.5 cm and/or if the axillary lymph nodes are involved. Treatment given before surgery for these two types of breast cancer affects the prognosis and the treatment recommendations after surgery.

If there are no breast cancer cells in the breast or axillary lymph nodes (pathological complete response) after neoadjuvant therapy, we know the patient has an excellent prognosis, with a low chance of the breast cancer recurring. The approach in these patients is to complete the treatment regimen before surgery. If there are still breast cancer cells in the breast and/or axillary lymph nodes after neoadjuvant therapy, the patient has a higher risk of breast cancer returning. As a result, extra treatment is recommended in order to reduce this risk. In HER2-positive breast cancer, instead of completing one year of trastuzumab, patients are given an antibody–drug conjugate called trastuzumab emtansine.² In triple-negative breast cancer, in addition to completing one month of immunotherapy with pembrolizumab, patients receive six months of the oral chemotherapy capecitabine.³

Answer 4

Treatment of young patients with breast cancer is complex and requires the following discussions.

Fertility

Fertility may be affected if chemotherapy is required. Many young women with breast cancer are nulliparous or have not completed their family. Steps to preserve fertility – freezing eggs, ovarian tissue or embryos – should be discussed at the time of diagnosis. If Fiona wants to undertake these steps, she should be referred to a fertility clinic as soon as possible after her diagnosis so that these procedures do not cause an unacceptable delay in starting her treatment. Another strategy to preserve fertility in women having chemotherapy is the use of goserelin. This causes ovarian suppression to help prevent the ovaries from being affected by chemotherapy, so there is more chance of ovarian function recovery after chemotherapy.

Genetics

The criteria for genetic testing in a patient diagnosed with breast cancer include:

- female and aged <40 years
- female and aged between 40 and 50 years with a first- or second-degree relative with breast cancer

- triple-negative breast cancer
- family history assessment that indicates high risk for breast cancer.

Genetic testing is important as patients with a gene variant may wish to undergo mastectomy rather than lumpectomy or contralateral prophylactic mastectomy or, for those with a *BRCA1/2* gene variant who have finished child-bearing, bilateral oophorectomy.

Psychosocial support

Referral to a clinical psychologist is often required.

Other clinical considerations

- Further imaging studies such as staging imaging (positron emission tomography/CT scan or bone scan with chest/abdomen/pelvis CT scan) or MRI to assess the extent of disease may be required.
- If neoadjuvant therapy is required (as in Fiona's case), it is very important that clips are put in at the sites of biopsy in both breast and axilla. Without these, sampling of breast tissue with complete clinical and radiological response would be very difficult.
- For patients with lymph node disease, a baseline L-Dex scan to measure fluid impedance in the arm would be required so that lymphoedema post surgery or radiotherapy can be monitored and treated effectively. Studies have shown that, for patients with more than five lymph nodes removed, three-monthly monitoring for two years (three years for those at high risk) with treatment of subclinical lymphoedema (a change of 10 units in L-Dex score without clinical evidence of arm swelling) can prevent severe lymphoedema occurring.^{4,5}

Answer 5

Surgery for breast cancer includes excision of the cancer from the breast and the lymph nodes.

Excision from the breast

Long-term studies have now confirmed that there is no difference in survival between mastectomy or breast-conserving therapy (lumpectomy with radiotherapy).⁶ In fact, breast-conserving therapy decreases the rate of complications arising from surgery and improves psychosocial wellbeing.⁷ For neoadjuvant patients with good response, we do not need to remove the whole tumour plus a rim of normal tissue (more than 5 cm in Fiona's case), but rather sample the footprint (remove breast tissue around the clip).

Excision from the lymph node

In patients with HER2-positive and triple-negative cancer treated with chemotherapy and targeted therapy or immunotherapy, the pathological response is very high (up to 60%).⁸ Traditionally, any patients with lymph node disease, regardless of treatment response to neoadjuvant

chemotherapy, underwent axillary dissection. However, patients with limited lymph node disease with good response to neoadjuvant chemotherapy often did not have residual disease found on axillary dissection. Furthermore, these patients required axillary radiotherapy. Consequently, as the incidence of lymphoedema increases with lymph node removal, de-escalating surgery in the axilla has been recently investigated. Targeted axillary dissection is the excision of the sentinel lymph nodes as well as the clipped nodes. If treatment response is seen and more than four lymph nodes are sampled, the false negative rate from targeted axillary dissection is low.⁹

Answer 6

Fiona will require the following treatment.

Adjuvant radiotherapy to both breast and axilla

Adjuvant radiotherapy is usually recommended if a patient is undergoing breast-conserving therapy. The exception is for women aged >80 years with low-grade disease (with an accepted increase (double) in local recurrence rate) or who have any contraindications to radiotherapy (pregnancy, prior local radiotherapy, connective tissue disorder, pre-existing lung disease, inability to lie flat and abduct the arm).

Adjuvant radiotherapy involves daily treatment from Monday to Friday, with each treatment appointment taking around 10–15 minutes. Most of the appointment time is for positioning the patient. The actual radiotherapy takes 1–5 minutes. For patients who require only breast radiation, the treatment duration is usually 3–6 weeks while for patients who need breast and axillary radiotherapy, like Fiona, treatment duration will be 5–6 weeks. The most common side effects of radiotherapy are skin burn and lethargy. Very rarely, radiotherapy can cause secondary cancers such as angiosarcoma (0.1%).

Recent studies looking at de-escalation of radiotherapy in breast cancer treatment include a study in patients with low-grade ductal carcinoma in situ. In this cohort, the risk assessment tool DCISionRT can be used to assess the effectiveness of radiotherapy in order to tailor the patient's requirement for it.¹⁰

Adjuvant endocrine therapy

Endocrine therapy refers to treatment that blocks the action of oestrogen (tamoxifen) or stops the formation of oestrogen (aromatase inhibitors) for hormone receptor-positive (ER- and/or PR-positive) breast cancer. In premenopausal women, we also consider adding goserelin, involving a subcutaneous injection, given once per month, that stops the ovaries producing oestrogen. This puts a woman into menopause. These treatments reduce the risk of recurrence of breast cancer by half and reduce the risk of dying of breast cancer by one-third.

Tamoxifen is a well-tolerated oral tablet, taken once per day, that commonly causes hot flushes. In postmenopausal women, there is a small increased risk of deep vein

thrombosis, pulmonary embolism and endometrial cancer. Endometrial cancer is usually picked up early because women present with vaginal bleeding. Endometrial cancer is usually cured with a hysterectomy.

Aromatase inhibitors are taken as an oral tablet, once per day, and commonly cause hot flushes as well as joint and muscle stiffness. They can reduce bone density and cause osteoporosis and osteoporotic fractures. Using goserelin with either tamoxifen or an aromatase inhibitor can cause menopausal side effects (hot flushes, joint and muscle stiffness and a reduction in bone density).

Other side effects of endocrine therapy include vaginal dryness and mood changes, particularly anxiety and depression. There are a number of strategies to treat the side effects of endocrine therapy effectively. Treatment with endocrine therapy is recommended for 5–10 years and is mostly well tolerated.

Answer 7

For a young woman who may have just started her career and/or family, a diagnosis of breast cancer is highly stressful. These women often experience a delay in diagnosis, require extensive systemic treatment and fear recurrence. As a result, they need ongoing psychosocial support. A strong, established relationship with their general practitioner, the medical treatment team, breast care nurse and clinical psychologist can help to alleviate anxiety.

Young women face challenges with hormone receptor-positive breast cancer. This is because the diagnosis may coincide with a time when a woman would like to have children. Chemotherapy for breast cancer can put a premenopausal woman into menopause and in some cases this can be permanent.

Tamoxifen tablets can cause congenital malformations and they must be stopped for three months before any attempt to conceive. There are strong data to support that interrupting endocrine therapy is safe in premenopausal women who want to have a baby. A large prospective trial – the POSITIVE trial – showed that women aged ≤ 42 years, after 18–30 months of endocrine therapy for breast cancer, could interrupt treatment for up to two years to attempt to conceive, have a pregnancy, deliver and breastfeed if they wished.¹¹ They could then resume endocrine therapy to complete the recommended duration of treatment. The babies born to the women in this study were healthy, with the same risk of congenital malformations as women of similar characteristics who did not have breast cancer. Furthermore, these women did not have an increased risk of breast cancer recurrence.

Antidepressants that inhibit cytochrome P450 2D6 should not be prescribed to patients receiving tamoxifen. Prominent examples of such antidepressants include paroxetine, fluoxetine, bupropion and duloxetine. A number of antidepressants have little or no effect on the metabolism of tamoxifen and may be considered safe options, eg venlafaxine, desvenlafaxine, citalopram or escitalopram.

Fiona needs to be aware that, although she may not be having periods while on tamoxifen, this does not mean that she cannot conceive. Therefore, it is very important that counselling regarding contraception during medical treatment is provided as medications such as trastuzumab and tamoxifen can cause congenital malformations. Patients will need to cease tamoxifen at least three months prior to conception. If a patient becomes pregnant while taking trastuzumab, she will require counselling and will need to cease this medication if the pregnancy is ongoing. Fiona should avoid hormonal contraception.

With survival rates of early breast cancer being $>90\%$, survivorship is important, and the effects of surgery and radiotherapy may need to be addressed. These can include (and be addressed by):

- breast asymmetry (contralateral reduction or augmentation)
- breast deformity (lipofilling, or fat grafting, with scar release)
- cording/hardening in axilla or breast because of fibrosis and scarring (physiotherapy)
- lymphoedema (monitoring with L-Dex analysis and treatment with physiotherapy)
- implant contracture (lipofilling, capsulectomy, exchange of implants)
- implant rotation or rupture (implant revision).

Advise Fiona of the recommended schedule for follow-up visits for early breast cancer.¹² Given that Fiona was aged 31 at the time of her diagnosis, she should be advised of her eligibility to have Medicare-funded annual MRI surveillance (if requested by a specialist) until the age of 60. Such surveillance is particularly relevant for Fiona because she has dense breast tissue and had a delay in the diagnosis of her cancer, which was not initially apparent on ultrasound.

Fiona should also be advised to return for assessment if she has any new symptoms, regardless of whether she is due for a scheduled review. Advise her that additional investigations such as positron emission tomography scans, bone scans, tumour marker tests, chest X-rays and CT scans are only clinically indicated if there are concerns about recurrent disease.

Resources for patients

- Breast Cancer Network Australia – Support and information on diagnosis and living with breast cancer, www.bcna.org.au
- Breast Cancer Trials – Online tool for informed treatment decisions, www.breastcancertrials.org.au/breast-cancer-resources/neoadjuvant-patient-decision-aid
- eviQ – Guide to systemic therapies, www.eviq.org.au/medical-oncology/breast/adjuvant-neoadjuvant

Resources for doctors

- ESO–ESMO – International consensus guidelines for breast cancer in young women, [www.annalsofoncology.org/article/S0923-7534\(20\)36363-8/fulltext](http://www.annalsofoncology.org/article/S0923-7534(20)36363-8/fulltext)

- eviQ – Systemic therapies, www.eviq.org.au/medical-oncology/breast/adjvant-neoadjuvant

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In general terms, and to simplify the characteristics of invasive lobular cancer, the two main subtypes are:

- classical: hormone receptor-positive, lower grade
- pleomorphic: more aggressive, higher grade.

Belle has the classical type, which is more indolent and not very chemoresponsive.

Answer 3

Belle has a cancer involving nearly half her breast. Having a wide local excision is not possible without resulting in significant deformity, even using oncoplastic techniques. Having a mastectomy can be confronting. For some people, having a breast removed can lead to psychosocial and sexual issues. For others, it can impact their sense of identity. Indications for mastectomy are dependent on whether disease can be completely excised without causing significant breast deformity. Talking through the different types of mastectomy and reassuring Belle of the reconstructive options will help her grapple with the treatment she has been recommended.

Oncoplastic techniques used to increase the rate of breast-conserving surgery include:²

- For a cancer to breast ratio of 10–20%, oncoplastic level 1 techniques, which include rotating other parts of the breast to fill in the defect.

- For a cancer to breast ratio of 20–40%, oncoplastic level 2 techniques, which include:

- volume displacement: removal of cancer and breast reduction
- volume replacement: removal of cancer and movement of normal subcutaneous tissue from around the breast (lateral chest wall, upper abdomen) to fill in the defect, with no change in breast size.

There are three main types of mastectomy:

- simple mastectomy (flat chest, skin and nipple excised)
- skin sparing mastectomy (skin spared, but nipple with or without the areolar complex excised)
- nipple sparing mastectomy (skin and nipple spared).

Indications for mastectomy type are dependent on the location of the cancer, whether it involves the skin or nipple, and the size and ptosis of the breasts.

Reconstruction can occur during breast removal or be delayed. Skin and nipple sparing mastectomies are usually coupled with immediate reconstruction. Reconstruction options are shown in Figures 4–6, and their advantages and limitations listed in Table 2.

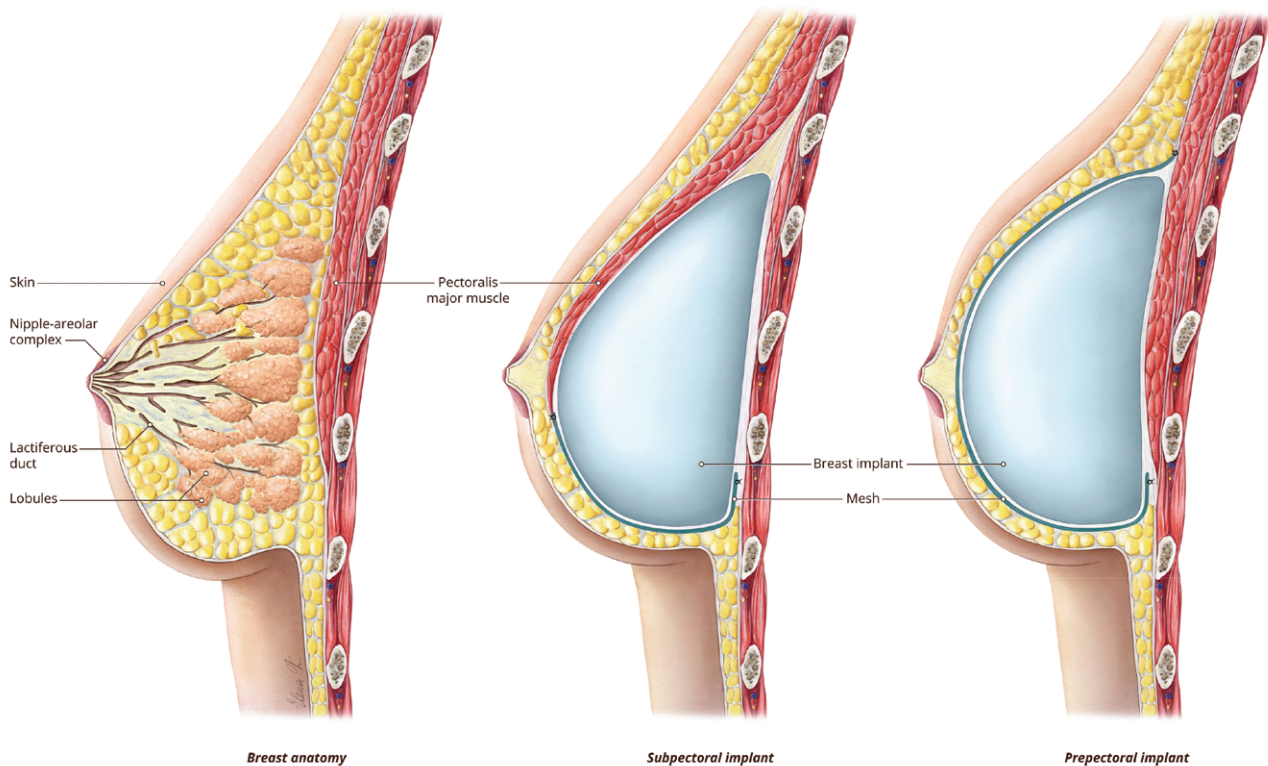


Figure 4. Breast implant reconstruction. In a subpectoral implant reconstruction, the implant is placed behind the pectoralis muscle. In a prepectoral implant reconstruction, the implant is placed in front of the pectoralis muscle.

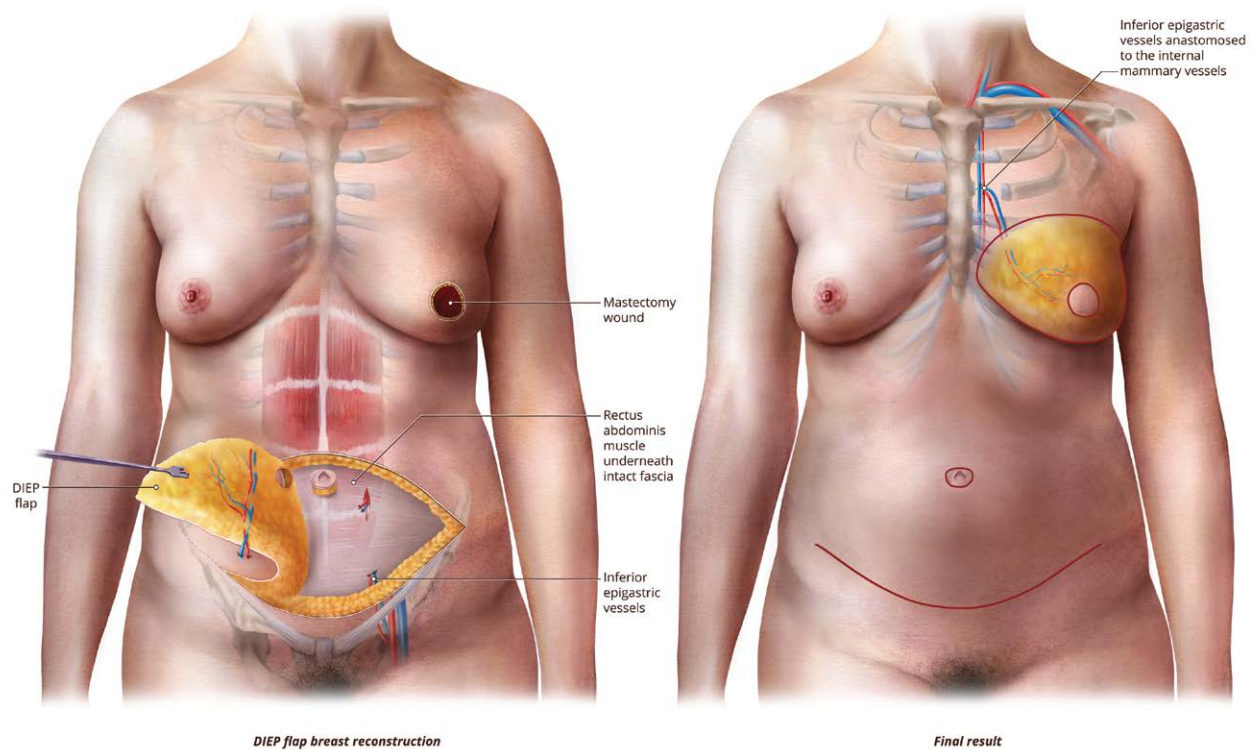


Figure 5. Deep inferior epigastric perforator (DIEP) autologous reconstruction.

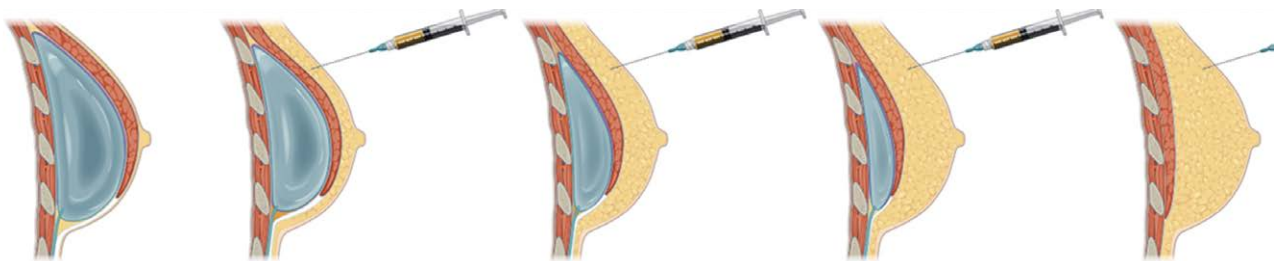


Figure 6: Primary lipofilling reconstruction.

Answer 4

Explain to Belle that contralateral prophylactic mastectomy is usually not indicated unless there is a known high-risk genetic variant such as *BRCA1/BRCA2*.

Nonetheless, because autologous reconstructions such as deep inferior epigastric perforator fold can only be done once in a lifetime, some patients may consider contralateral prophylactic mastectomy at the same time. There is, however, no evidence that contralateral prophylactic mastectomy improves survival and having a contralateral operation essentially doubles the risks of the procedure.

Answer 5

Explain to Belle that not all mastectomy patients receive radiotherapy, but that it is a standard treatment in patients who have:

- a tumour size >5 cm with no high-risk features (not a hard indication)
- lymph node disease
- a tumour size ≤5 cm with other risk factors: grade 3, young age (<50 years), lymphovascular invasion, triple-negative cancer.

Explain to Belle that postmastectomy radiotherapy can affect reconstruction in many ways, specifically, in implant and autologous reconstruction.

Table 2. Reconstruction options, advantages and limitations

Reconstruction type	Description	Advantages	Limitations
Implant	<ul style="list-style-type: none"> • Silicone implant with or without mesh 	<ul style="list-style-type: none"> • Shorter recovery period 	<ul style="list-style-type: none"> • Often requires revision every 15–20 years • Breast sites up and does not age like normal breasts; can cause symmetry issues • Can cause ALCL
Autologous	<ul style="list-style-type: none"> • Uses patient's own subcutaneous tissue • Requires microvascular surgery • Can be taken from lower abdomen (DIEP flap), inner thigh (TUG flap), back (LD flap), buttock (SGAP flap) 	<ul style="list-style-type: none"> • Ages like normal breast • Fluctuates with weight 	<ul style="list-style-type: none"> • Each donor site can only be used once in the patient's lifetime • Larger operation • Longer recovery period
Combination	<ul style="list-style-type: none"> • For eg, LD with implant underneath. Often used for patients who do not have a lot of subcutaneous tissue or the required skin coverage 	<ul style="list-style-type: none"> • Ages like normal breast • Fluctuates with weight 	<ul style="list-style-type: none"> • Each donor site can only be used once in the patient's lifetime • Larger operation • Longer recovery period
Primary fat grafting	<ul style="list-style-type: none"> • Building the breast with fat grafting • May need an implant first 	<ul style="list-style-type: none"> • Usually only for patients with small breasts 	<ul style="list-style-type: none"> • Requires around 3–5 operations (depending on size of breasts)

ALCL, anaplastic large cell lymphoma; DIEP, deep inferior epigastric perforator; LD, latissimus dorsi; SGAP, superior gluteal artery perforator; TUG, transverse upper gracilis.

With implant reconstruction it can cause capsular contracture and contraction of the implant pocket over time. This can cause significant pain and discomfort and decrease the cosmetic outcome of the reconstruction. Surgical management of capsule excision with lipofilling has been shown to be effective at alleviating some of the contraction.

With autologous reconstruction postmastectomy, radiotherapy can decrease the size of the reconstruction, creating a smaller breast and asymmetry. It can also cause fat necrosis, resulting in a hardened, lumpy breast.

Due to the negative effects of postmastectomy radiotherapy on reconstruction, and as a way of navigating this, reverse sequencing has now become an option for treatment.³ Reverse sequencing radiotherapy is given prior to surgical management of the breast with autologous reconstruction; radiotherapy is given to the native breasts and not to the reconstructed autologous tissue. Surgery is usually done within six weeks of completion of radiotherapy before fibrosis of the tissues sets in. Reverse sequencing is not usually recommended for patients undergoing implant reconstruction due to the higher risk of wound complications.

Answer 6

Belle now requires adjuvant endocrine therapy. This may be in the form of aromatase inhibitors or a selective oestrogen receptor modulator such as tamoxifen. Most women tolerate these better postmenopause than premenopause. Side effects, if they occur, often settle within 6–8 weeks. If the side effects are overwhelming, rather than ceasing medication, dose reduction, switching the class of aromatase inhibitor or switching from an aromatase inhibitor to a selective oestrogen receptor modulator is encouraged, in consultation with the medical oncologist.

A summary of the possible side effects of endocrine therapies and how to manage them is given in Table 3.

Table 3. Side effects of endocrine therapies and options for management

Side effect	Management options
Hot flushes, mental fog, labile moods	<ul style="list-style-type: none"> • Oxybutynin • Cognitive behavioural therapy • Acupuncture • Selective serotonin reuptake inhibitors: Venlafaxine (may interact with tamoxifen) • Antidepressants: Escitalopram
Vaginal dryness	<ul style="list-style-type: none"> • Vaginal moisturisers • Simple lubrication • Ovestin cream
Osteoporosis	<ul style="list-style-type: none"> • Weight-bearing exercises • Vitamin D and calcium • Bisphosphonates

Resources for patients

- Breast Cancer Trials – Information on invasive lobular carcinoma, www.breastcancertrials.org.au/what-is-invasive-lobular-carcinoma
- BRECONDA – Breast reconstruction decision aid, <https://breconda.bcna.org.au>
- Cancer Council – Advice on cancer prevention, www.cancer.org.au/cancer-information/causes-and-prevention/early-detection-and-screening/get-checked-women

Resources for doctors

- Cancer Australia and Cancer Council – Quick guide to optimal care, www.cancer.org.au/assets/pdf/breast-cancer-quick-reference-guide
- Cancer Council – Optimal care pathways, www.cancer.org.au/health-professionals/optimal-cancer-care-pathways
- ESMO – Clinical practice guideline for early breast cancer, www.esmo.org/guidelines/guidelines-by-topic/esmo-clinical-practice-guidelines-breast-cancer/early-breast-cancer

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CASE

5 | Lucy needs a follow-up plan

Lucy, a schoolteacher aged 49 years, felt a lump in her breast while in the shower and promptly visited you to have it checked. You organised a diagnostic mammogram with tomosynthesis and bilateral breast ultrasound. Her mammogram shows dense breast tissue (BI-RADS category C) with an area of microcalcification in the medial aspect of her left breast and a 2-cm hypochoic, irregular mass at 8 o'clock in her left breast on ultrasound. Core biopsy of this lesion shows a moderately differentiated, ER-positive, PR-positive, HER2-negative invasive carcinoma (no special type) with associated ductal carcinoma in situ.

You refer Lucy for a surgical opinion.

Question 1 (D2)

What are the important issues to elicit when taking a history from Lucy?

Further information

Lucy is otherwise well and has never had any concerns about her breasts in the past. Her maternal grandmother developed breast cancer in her seventies and her mother passed away with ovarian cancer aged 64. Lucy continues to have a regular menstrual cycle and has been using a NuvaRing for contraception since her last child was born. Her daughters are aged 16, 14 and nine years, and she breastfed all three for 12 months each. Lucy was prescribed a selective serotonin reuptake inhibitor two years ago, after her mother passed away, to help with mild depressive symptoms. Her mental health is currently stable. She drinks two standard glasses of wine a night with two alcohol-free days a week and is a non-smoker. She walks the dog most mornings. She enjoys cooking with her family, takes her lunch to work and eats most meals at home.

Question 2 (D2)

What other issues now need to be addressed as Lucy embarks on her breast cancer treatment?

Question 3 (D2)

What contraception is safe for Lucy now she has been diagnosed with breast cancer?

Further information

Following a breast MRI and positron emission tomography scan, which show no further breast lesions or evidence of distant metastases, Lucy has an ultrasound-guided, hook-wire guided wide local excision and sentinel lymph node biopsy. This shows a 22-mm, grade 2 invasive ductal carcinoma (no special type), with 15 mm of surrounding high-grade ductal carcinoma in situ. The surgical margins are clear of tumour. One of three sentinel lymph nodes shows a 2-mm metastasis.

Question 8 (D2)

If Lucy has any vaginal bleeding while on tamoxifen, what needs to be considered and what are the appropriate investigations?

Question 9 (D2)

Lucy is back working full time and is keen to know what ongoing treatment and surveillance she requires. What ongoing follow-up will Lucy require in the years to come?

CASE 5 **Answers**

Answer 1

Important details to get from your history-taking include Lucy's:

- past medical and surgical history including breast surgery
- family history of malignancy, especially breast, ovarian, prostate and pancreatic cancers
- menstrual history
- contraceptive history
- obstetric history including use of in-vitro fertilisation treatments

- current medications
- social situation
- smoking habits
- alcohol use
- exercise and dietary habits.

Answer 2

As Lucy is currently using a NuvaRing, you are not able to determine whether she is menopausal or not. The NuvaRing provides exogenous oestrogen and progesterone via the transvaginal delivery method. Its use is therefore contraindicated in women diagnosed with breast cancer.²

Lucy is theoretically still fertile and requires a non-hormonal form of contraception until her menopausal status can be determined.

Answer 3

There are a number of non-hormonal forms of contraception that are safe for Lucy to use:

- copper intrauterine contraceptive device
- condoms
- diaphragm
- vasectomy
- tubal ligation
- abstinence.

Answer 4

Following wide local excision and sentinel lymph node biopsy, Lucy requires radiotherapy to the breast to treat any microscopic residual disease, along with chemotherapy and hormone therapy. For women with early-stage ER-positive breast cancer, adjuvant tamoxifen reduces 15-year breast cancer mortality by one-third.¹

Management options for the micrometastasis in the sentinel lymph node, which should be discussed at the multidisciplinary meeting, include axillary clearance and adjuvant radiotherapy to the axilla.

Answer 5

As Lucy's breast cancer is ER-positive, endocrine therapy will play an important role in her ongoing treatment to decrease her risk of disease recurrence.³ The initial choice of endocrine therapy will depend on her menopausal status; 76% of premenopausal women experience chemotherapy-related amenorrhoea and 40% resume menstruating after their treatment is completed.⁴ As Lucy has had a period within the last two years, she is considered premenopausal and her periods may return after chemotherapy.

Lucy is also on a selective serotonin reuptake inhibitor, which may reduce the efficacy of her tamoxifen, if this is the chosen

endocrine agent. Antidepressants such as paroxetine, fluoxetine, bupropion and duloxetine may reduce the effectiveness of tamoxifen as they inhibit cytochrome P450, which is involved in the conversion of tamoxifen to more active metabolites. Antidepressants that are weaker inhibitors of cytochrome P450 2D6 include citalopram, escitalopram, desvenlafaxine and sertraline. Venlafaxine seems to have little or no effect on cytochrome P450 2D6.^{5,6} (See Table 2 in Kim et al, Use of antidepressants in patients with breast cancer taking tamoxifen.⁶)

Tamoxifen increases the risk of thromboembolic disease,⁷ so any history of this needs to be considered, and Lucy's bone density should be measured as a baseline prior to commencing endocrine therapy. Aromatase inhibitors can reduce bone density, so if Lucy is osteopenic or osteoporotic before starting treatment, non-pharmacological and pharmacological strategies to mitigate further bone loss, or even to build bone, should be considered. These include improving dietary calcium, ensuring vitamin D levels are adequate and undertaking weightbearing and resistance exercise. Limiting alcohol consumption and avoiding smoking are also important for maintaining bone density. Bisphosphonates have the additional benefit of decreasing breast cancer recurrence.⁸

Answer 6

Aromatase inhibitors are medications that block the activity of the enzyme aromatase, which is responsible for converting androgens (male hormones) produced in the fat, liver and muscle into oestrogens (female hormones). This is the main source of oestrogen in postmenopausal women. Tamoxifen is useful in postmenopausal women who do not tolerate aromatase inhibitors.

In premenopausal women, most oestrogen is produced by the ovaries, not by enzyme conversion.

Therefore, in premenopausal women, ovarian suppression is required to decrease circulating oestrogen, combined with blocking the effect of oestrogen at its target cell by blocking the oestrogen receptor, which is how tamoxifen and other selective oestrogen receptor modulators work. Aromatase inhibitors can be used in premenopausal women in conjunction with ovarian suppression with a gonadotropin-releasing hormone agonist, or following oophorectomy.

Answer 7

Breast cancer is a complex disease involving both genetic and environmental factors. The main lifestyle-related risk factors include alcohol use, smoking habits, obesity, diabetes and physical inactivity. Research has shown that even minimal amounts of daily exercise and a healthy diet mitigate the side effects of cancer treatment and reduce the recurrence of cancer in survivors.⁹⁻¹¹ Aim for a healthy body mass index and inform Lucy of the linear trend with alcohol use and breast cancer risk.

As Lucy's general practitioner you are in a position to employ motivational interviewing techniques, to engage allied health

practitioners such as a physiotherapist, exercise physiologist, dietitian and psychologist, and to suggest community programs to assist with her physical and mental wellbeing.

Exercise independently reduces the risk of a range of cancers, including breast. Exercise is good for management of the side effects of treatment including tiredness and musculoskeletal pain. Recommend 30 minutes of walking a day, yoga, Pilates and swimming. Exercise is also a well-recognised tool to assist with the improvement of mental health, especially symptoms of depression and anxiety.

Answer 8

Tamoxifen acts in a pro-oestrogenic manner at the endometrium, increasing the risk of endometrial hyperplasia and endometrial cancer. Therefore, any new bleeding after amenorrhoea needs to be investigated in women using tamoxifen. This should consist of a physical examination, a cervical screening test and swabs as indicated, transvaginal pelvic ultrasound and sampling of the endometrium with pipelle or hysteroscopy and curettage.

Answer 9

Lucy needs to be seen by one or more of her treating team (surgeon, medical oncologist, radiation oncologist, breast physician) for at least the first five years after diagnosis. Her visits should be every 3-6 months for the first 2-3 years and then annually. Each visit should consist of history related to current symptomology and potential distant disease, as well as side effects from treatment. Her general health, social and mental well-being should also be discussed.

She will need to be examined regularly to assist in the detection of recurrent disease as well as in the assessment of surgical outcomes and long-term complications related to radiation treatment. Ongoing imaging should consist of a mammogram (two- or three-dimensional) with or without an ultrasound every 12 months. An MRI may also be indicated depending on her breast density and complexity and her personal preference. As of November 2022, women who were diagnosed with breast cancer before the age of 50 are eligible for an annual Medicare-rebatable breast MRI (Medicare Benefits Schedule item 63464), on request from a specialist, until the age of 60.

Resources for patients

- Breast Cancer Network Australia – Information and support, www.bcna.org.au
- Cancer Australia – Information and support, www.canceraustralia.gov.au/cancer-types/breast-cancer/overview

Resources for doctors

- National Institute for Health and Care Excellence – Guidance on diagnosis and management of early and locally advanced breast cancer, www.nice.org.uk/guidance/ng101/chapter/Recommendations-for-research

- Heery M, Corbett P, Zelkowitz R – Precautions for patients taking tamoxifen, www.ncbi.nlm.nih.gov/pmc/articles/PMC6296418
- Sella T, Ruddy KJ, Carey LA, Partridge AH – Optimal endocrine therapy in premenopausal women, <https://ascopubs.org/doi/full/10.1200/OP.21.00482>
- CanRisk – Online tool for calculating patient’s risk of developing breast and ovarian cancer, www.canrisk.org
- Cancer Australia – Follow-up care for early breast cancer, www.cancer australia.gov.au/sites/default/files/publications/shared-follow-and-survivorship-care-information-health-professionals/pdf/scbch_information_for_health_professionals.pdf

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Multiple-choice questions

Case 1 – Louise

Louise, aged 37 years, is attending for breast cancer risk assessment. There are a number of different risk assessment models available.

Question 1

All of the following risk assessment models are available and appropriate for use with a patient who does not have cancer except:

- A. CanRisk
- B. Tyrer-Cuzick (IBIS tool)
- C. Manchester Scoring System
- D. iPrevent

Question 2

Women with a *PALB2* gene variant:

- A. Have a 55% lifetime risk of breast cancer
- B. Have a 10% lifetime risk of ovarian cancer
- C. Have a 10% lifetime risk of pancreatic cancer
- D. Can have a funded breast MRI from the age of 40 years

Case 2 – Marie

Marie, aged 53 years, has a new lump in her left breast. She has had breast screen mammograms in the past with no suspicious findings.

Question 3

Which of the following would *not* contribute to her risk for breast cancer?

- A. A previous diagnosis of breast cancer, including ductal carcinoma in situ
- B. Being aged >50 years
- C. A previous breast cyst
- D. A significant family history of breast or ovarian cancer

Question 4

Which of the following imaging modality referrals is inappropriate for diagnostic work-up of a breast symptom?

- A. Contrast-enhanced mammography
- B. Breast screen referral
- C. Breast MRI
- D. Breast ultrasound

Case 3 – Fiona

Fiona, aged 31 years, has just been diagnosed with a 48-mm, triple-positive breast cancer. She has no family history of breast cancer.

Question 5

Neoadjuvant chemotherapy is now the standard of care for:

- A. ER/PR/HER2-positive breast cancer, particularly if >15 mm
- B. ER/PR/HER2-positive breast cancer, particularly if >10 mm
- C. All women aged <40 years with breast cancer
- D. ER/PR-positive, HER2-negative with axillary node involvement

Question 6

What criteria does Fiona meet to access Medicare-funded genetic testing?

- A. Diagnosed at age <40 years
- B. Diagnosed with a breast cancer between 2 and 5 cm
- C. Diagnosed with a triple-positive breast cancer
- D. Diagnosed having had three children and having breastfed

Case 4 – Belle

Belle, aged 55 years and postmenopausal, has been having regular breast screening as she has a significant family history of breast cancer. She is asymptomatic. Previous imaging has shown dense breasts, with asymmetrical density, and biopsy has proven a lobular carcinoma.

Question 7

Lobular breast carcinomas:

- A. Account for 30% of breast carcinomas
- B. Are often less extensive than seen on conventional imaging
- C. Are rarely multifocal
- D. Are more likely to be bilateral

Question 8

Post-mastectomy radiotherapy is indicated in patients who have:

- A. Tumour size >4 cm with no high-risk features
- B. No lymph node disease
- C. Tumour ≤5 cm with other risk factors: grade 3, young age, lymphatic invasion, triple negative
- D. Silicone implants

Case 5 - Lucy

Lucy, aged 49 years, has recently completed surgery, chemotherapy and radiotherapy for a 22-mm invasive ER/PR-positive, HER2-negative breast cancer. She had a wide local excision and sentinel node biopsy. One of the three sentinel nodes was involved. Lucy is about to start adjuvant hormone therapy.

Question 9

Tamoxifen is not suitable for women who:

- A. Are premenopausal
- B. Are postmenopausal
- C. Have chemotherapy-induced amenorrhoea
- D. Have a history of thromboembolic disease

Question 10

Use of adjuvant hormone therapy reduces the risk of breast cancer-related death by:

- A. 25%
- B. 33%
- C. 40%
- D. 50%

Question 11

There is good evidence to counsel Lucy in risk-reducing measures that include:

- A. Reducing alcohol intake
- B. Maintaining a healthy body mass index
- C. Exercising for 30 minutes daily
- D. Eating plenty of unprocessed fresh fruit and vegetables
- E. All of the above



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