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Final Protocol to
guide the assessment
of Breast Magnetic
Resonance Imaging
(MRI)

June 2014

Table of Contents

Table of Contents	2
List of tables	4
MSAC and PASC	5
Purpose of this document.....	5
Purpose of application	6
Intervention	6
Description	6
Administration, dose, frequency of administration, duration of treatment	7
Co-administered interventions	7
Background	8
Current arrangements for public reimbursement	8
Regulatory status	8
Patient population	8
Proposed MBS listing	10
Clinical place for proposed intervention	11
Comparator	13
Mammography	13
Ultrasound	14
Utilisation	14
Clinical management algorithms	15
Clinical claim	20
Outcomes and health care resources affected by introduction of proposed intervention	23
Outcomes	23
Health care resources	24
Proposed structure of economic evaluation (decision-analytic)	24
Appendix A: Existing MBS item descriptors for breast MRI and conventional breast imaging	28

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List of tables

Table 1	Proposed MBS listing for breast MRI	10
Table 2	Proposed MBS listing for breast MRI guided biopsy	11
Table 3:	Classification of an intervention for determination of economic evaluation to be presented	22
Table 4:	List of resources to be considered in the economic analysis	24
Table 5:	Summary of PICO to define research question – population 1a, women undergoing neo-adjuvant chemotherapy	24
Table 6:	Summary of extended PICO to define research question – population 1b, women with lobular breast cancer	25
Table 7:	Summary of extended PICO to define research question- population 2, women with metastatic breast cancer where the source has not been determined.....	26
Table 8:	Summary of extended PICO to define research question – population 5, the use of MRI guided biopsy	27
Table 9	Existing MBS item descriptor for breast MRI	28
Table 10	Mammography MBS items.....	30
Table 11	Breast ultrasound MBS items.....	31

MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Minister for Health (the Minister) to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

Purpose of this document

This document is intended to provide a protocol that will be used to guide the assessment of an intervention for a particular population of patients. Protocols are finalised after inviting relevant stakeholders to provide input.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

- Patients** – specification of the characteristics of the patients in whom the intervention is to be considered for use;
- Intervention** – specification of the proposed intervention
- Comparator** – specification of the therapy most likely to be replaced by the proposed intervention
- Outcomes** – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention

Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing primarily of breast MRI to guide treatment in women newly diagnosed with breast cancer was received from Breast Surgeons of Australia and New Zealand Incorporated (BreastSurgANZ) by the Department of Health and Ageing in September 2012.

The use of breast MRI is proposed to offer improved local staging and/or early treatment monitoring and planning. The proposed indications are:

- 1) women newly diagnosed with breast cancer and undergoing preoperative (neo-adjuvant) chemotherapy
- 2) women newly diagnosed with the lobular subtype of breast cancer
- 3) women newly diagnosed with breast cancer who are
 - a) aged <50 years and/or
 - b) have very dense breasts which preclude mammographic assessment, and/or
 - c) have a significant size discrepancy (≥ 1 cm) between mammogram and ultrasound findings
 - d) have suspicious/malignant calcifications which may underestimate the extent of ductal carcinoma in situ (DCIS) disease
- 4) Women presenting with metastatic breast cancer in the lymph nodes where conventional imaging and examination fails to show the source of the tumour.

The use of breast MRI is also proposed for:

- 5) MRI guided biopsy in patients with suspected breast cancer where the lesion is only identifiable by MRI

Breast MRI is not currently listed on the MBS for these purposes and therefore, this application is for five new MBS items for women of any age who have been diagnosed with breast cancer.

Intervention

Description

Magnetic resonance imaging (MRI) uses a strong external magnetic field to produce images of biological tissues. This magnetic field acts on hydrogen protons (elementary particles) in body tissues and a radiofrequency pulse is used to produce signals that vary according to their local chemical, structural and magnetic environment. MRI is particularly well suited to distinguishing between blood vessels, other fluid filled structures and surrounding soft tissues, and as such is especially useful in imaging the brain, muscles and the heart as well as detecting abnormal tissues such as tumours.

Breast MRI is performed in a dedicated MRI room using an MRI machine with minimum magnet strength of 1.5 Tesla. A dedicated breast coil, comprising of 7 or more channels is also required and intravenous contrast is administered by powered or electronic injector. As breast tissue generally

has similar signal intensity to tumour tissue on routine MRI, the intravenous administration of a contrast agent containing gadolinium chelate is used to enhance breast lesions.

During the examination the patient lies prone on the MRI table with the breast dependant in the dedicated breast coil. A number of imaging sequences are obtained, prior to the administration of the contrast agent gadolinium. Following contrast injection further sequences are obtained including evaluation of the uptake and washout of contrast by breast tissue and any focal lesion over several minutes.

The MRI sequences obtained are interpreted by a radiologist to analyse the findings on the various sequences, including enhancement patterns. The aim is to distinguish between normal, benign and malignant findings. Malignant lesions usually display an enhancement pattern with rapid uptake and washout of contrast. In benign masses the contrast uptake is usually slower and more prolonged. Some lesions have atypical or indeterminate findings.

Administration, dose, frequency of administration, duration of treatment

MRI can be used in both screening and diagnosis of breast cancer. This includes the identification of breast cancer in women with a high risk of breast cancer due to family history or genetic predisposition. Breast MRI is also used in preoperative staging, evaluating response to treatment, screening of women with breast augmentation or reconstruction and identification of occult breast cancer in women with metastatic disease.

Breast MRI generally takes up to 1 hour. Patients undergoing neoadjuvant chemotherapy (population #1) would require initial breast MRI and follow-up 3 months later to assess response to the chemotherapy. Patients with lobular breast cancer (population #2), breast cancer patients who are young and/or have very dense breasts and/or have a discrepancy between conventional imaging (population #3), and patients with metastatic breast cancer of unknown primary site (population #4) would require only one MRI.

Patients requiring MRI guided biopsy because lesions are not visualized on conventional imaging would have had an initial breast MRI and would subsequently require a MRI guided biopsy.

To perform breast MRI, a radiographer is required with specialised training for setup and scanning. The supervising radiologist should have expertise in breast imaging and MRI interpretation. In addition, for an MRI scan to attract a Medicare rebate, the patient must fulfil the proposed eligibility criteria (see Table 1). The scan must be requested by a specialist or consultant physician (not a GP) and be performed on a Medicare-eligible MRI unit by a Medicare-eligible provider, and be an MRI service listed in the MBS.

Co-administered interventions

After identifying a symptom, women would first have a medical consultation including a clinical breast examination (CBE) (MBS items 3, 23, 36 and 44) and then be referred for a mammogram (MBS 59300 and 59301) and/or a specialist appointment (MBS items 104, 105, 110). An ultrasound (MBS

items 59300-59318) may also be requested. To attract a rebate for a breast MRI, women will need to have a referral from a specialist medical practitioner or consultant physician (MBS items 104, 110).

For women in whom MRI is being used to assess response to neo-adjuvant chemotherapy, this will be a co-administered intervention. Neo-adjuvant chemotherapy will vary according to the individual patient but would commonly be Adriamycin and cyclophosphamide (AC), variations include 5-fluorouracil, epirubicin, cyclophosphamide (FEC) and paclitaxel (Taxol), cyclophosphamide (TC). Women with HER2+ breast cancer may also receive trastuzumab.

Background

Current arrangements for public reimbursement

Breast MRI is currently reimbursed for surveillance in asymptomatic high risk women under the age of 50 and for women who have had an abnormality detected through that surveillance (MBS item numbers 63464, 63457, 63458 and 63467. See Appendix A, Table 10). Breast MRI for surveillance was listed as an interim item in February 2009 following advice received from MSAC in 2007 and is currently being reassessed (MSAC Assessment 1098.1). The new assessment proposes expanding the listing to also include women with a prior history of invasive breast cancer, women with a prior history of DCIS and LCIS and women with a previous history of irradiation to the chest from 10 to 35 years of age.

Regulatory status

MRI is currently available in public and private facilities in major centers in each state and territory. Three hundred and thirty seven MRI units have been licensed by the Department of Health to provide services that are eligible for funding under the MBS.

Breast MRI requires both a breast coil and the use of a gadolinium-containing contrast agent. The Australian Register of Therapeutic Goods (ARTG) lists several coils and gadolinium-containing contrast agents that have been approved by the Therapeutic Goods Administration for use in diagnostic imaging procedures.

Patient population

The pre-operative use of breast MRI in newly diagnosed breast cancer is controversial (Houssami & Morrow 2013; McLaughlin et al 2013) and it will therefore be essential to clearly define the patients in whom this imaging is justified. Guidelines from international agencies have made the following recommendations regarding the appropriate use of preoperative breast MRI.

The UK's NICE guidelines on early and locally advanced breast cancer diagnosis and treatment (National Collaborating Centre for Cancer 2009) state:

- The routine use of MRI of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or DCIS.

- Offer MRI of the breast to patients with invasive breast cancer:
 - if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
 - if breast density precludes accurate mammographic assessment
 - to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer.

The US-based NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for Breast Cancer state the following as clinical indications and applications for breast MRI testing for newly diagnosed patients with breast cancer (National Comprehensive Cancer Network (NCCN) 2014):

- May be used for staging evaluation to define extent of cancer or presence of multifocal or multicentric cancer in the ipsilateral breast, or as a screening of the contralateral breast cancer at the time of initial diagnosis (category 2B¹). There are no high-level data to demonstrate that the use of MRI to facilitate local therapy decision-making improves local recurrence or survival (Houssami et al 2008)
- May be helpful for breast cancer evaluation before and after neo-adjuvant therapy to define extent of disease, response to treatment, and potential for breast-conserving therapy.
- May be useful to detect additional disease in women with mammographically dense breast, but available data do not show differential detection rates by any subset by breast pattern (breast density) or disease type (DCIS, invasive ductal carcinoma, invasive lobular cancer)
- May be useful for identifying primary cancer in women with axillary nodal adenocarcinoma or with Paget's disease of the nipple with breast primary not identified on mammography, ultrasound or physical examination.
- False-positive findings on breast MRI are common. Surgical decisions should not be based solely on the MRI findings. Additional tissue sampling of areas of concern identified by breast MRI is recommended.

¹ All recommendations are category 2A unless otherwise indicated.

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.

Proposed MBS listing

Table 1 Proposed MBS listings for breast MRI

Category 5 – Diagnostic imaging services
<p>[MBS item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the patient has been diagnosed with a breast cancer and is undergoing or about to undergo neo-adjuvant chemotherapy</p> <p>Fee: \$[Proposed fee] As per current fee (\$690) for screening MRI in high risk women [Proposed relevant explanatory notes]</p>
<p>[MBS item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the patient has been diagnosed with a breast cancer of the lobular sub-type, and has not had definitive surgical treatment.</p> <p>Fee: \$[Proposed fee] As per current fee (\$690) for screening MRI in high risk women [Proposed relevant explanatory notes]</p>
<p>[MBS item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the patient has been diagnosed with a breast cancer, and</p> <p style="margin-left: 20px;">i) is aged ≤50 years, and/or</p> <p style="margin-left: 20px;">ii) has very dense breasts, and/or</p> <p style="margin-left: 20px;">iii) has a significant discrepancy (>1 cm) between mammogram and ultrasound findings and has not had definitive surgical treatment</p> <p style="margin-left: 20px;">iv) has suspicious/malignant calcifications which may underestimate the extent of ductal carcinoma in situ (DCIS) disease.</p> <p>Fee: \$[Proposed fee] As per current fee (\$690) for screening MRI in high risk women [Proposed relevant explanatory notes]</p>
<p>[MBS item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the patient has been diagnosed with metastatic breast cancer restricted to the regional lymph nodes and clinical examination and conventional imaging have failed to identify the primary cancer</p> <p>Fee: \$[Proposed fee] As per current fee (\$690) for screening MRI in high risk women [Proposed relevant explanatory notes]</p>

Table 2 Proposed MBS listing for breast MRI guided biopsy

Category 5 – Diagnostic imaging services
<p>[MBS item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>MAGNETIC RESONANCE IMAGING-GUIDED BIOPSY performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the patient has a suspicious lesion seen on MRI but not conventional imaging, and is therefore not amenable to biopsy by conventional imaging</p> <p>Fee: \$[Proposed fee] \$690 as per current MRI plus extra imaging labour costs (\$300) and consumables (\$450) thus a total of \$1440</p> <p>NOTE 1: This item is intended for biopsy of imaging abnormalities diagnosed on MRI scan described by item XXXXX</p>

The proposed fee is the same as the existing fee paid for breast MRI on the MBS, which is \$690. PASC has requested justification of this fee.

The proposed fee for Breast MRI guided biopsy is based on the current fee for breast MRI plus the extra consumables (\$450, including biopsy gun and clip for placement at the lesion site) and labour costs (\$300, one extra hour of radiologist and radiographer time) required to conduct a biopsy for a total of \$1440. This is in-line with the requirements but a more detailed justification of costs may be required.

Clinical place for proposed intervention

In Australia, invasive breast cancer is the most frequently diagnosed cancer in women with 13,688 new cases and an age standardised incidence rate in women of 114 per 100,000 women in 2009. Incidence varies by age: over half of invasive breast cancers diagnosed occurred in women aged 50-69 years and fewer than one in four (24%) in women who are less than 50 years (Australian Institute of Health and Welfare & Cancer Australia 2012).

In 2008, more than three-quarters (78% or 10,527 cases) of breast cancers in females were classified as *invasive ductal carcinoma* (that is, cancers originated in the ducts). Meanwhile, 11% (1,457 cases) of breast cancers were classified as *invasive lobular carcinoma* (that is, cancers originated in the lobules); while a further 5% of breast cancers were classified as unspecified (Australian Institute of Health and Welfare & Cancer Australia 2012).

There are five proposed patient groups defined as follows:

- 1) women newly diagnosed with breast cancer and undergoing preoperative (neo-adjuvant) chemotherapy where breast MRI is proposed to better determine response to therapy;
- 2) women newly diagnosed with the invasive lobular subtype of breast cancer, where conventional imaging frequently underestimates the extent of disease;
- 3) women newly diagnosed with the invasive breast cancer who are
 - a) <50 years of age, and/or

- b) with very dense breasts, and/or
- c) with a significant discrepancy (>1cm) between mammography and ultrasound, where conventional imaging frequently underestimates the extent of the disease
- 4) *have suspicious/malignant calcifications which* may underestimate the extent of ductal carcinoma in situ (DCIS) disease Women presenting with metastatic breast cancer in the lymph nodes, but not elsewhere in the body, where conventional imaging and examination fails to show the source of the tumour. The use of MRI to identify the primary tumour may enable breast conserving surgery to be performed rather than mastectomy.
- 5) The use of MRI guided biopsy in patients with suspected breast cancer where the lesion is only identifiable by MRI.

The applicant states that MRI is primarily proposed for use in incident cases (approximately 14,000 cases per year) rather than prevalent cases and that 'the vast majority of these incident cases are more than adequately worked up with conventional imaging.' The following estimations of utilisation can be made:

- 1) To assess response to neo-adjuvant chemotherapy
 - 2 MRIs required per patient in a year and
 - 6% of patients have neo-adjuvant chemotherapy (from application, no source provided)
 - 840 women per annum each having 2 MRIs
 - Total of 1,680 MRIs per annum
- 2) Women with lobular cancers
 - In 2008, there were 1,457 invasive lobular cancers diagnosed in Australian women (Australian Institute of Health and Welfare & Cancer Australia 2012)
 - Therefore there would be up to 1,500 tests per annum
- 2) Women aged <50 years and/or with very dense breasts and/or with a discrepancy between imaging findings
 - In 2008 there were 3,208 invasive cancers diagnosed in Australian women aged <50 years
 - Breast density declines with age, particularly with menopausal changes, however there will still be some women over 50 years who have dense breasts. The American College of Radiology notes that the reporting of breast density is not reliably reproducible² and therefore the potential size of this patient population is dependent on how women with very dense breasts are defined. One study which reviewed mammographic screens and used the BI-RADS classification of breast density identified that 8% of women aged 50-59 and 4% of women aged 60-79 had extremely dense breasts (Checka et al 2012). If women diagnosed with breast cancer in Australia were assumed to have similar rates of high breast density then, using AHIW data (2012), in 2008, there were 3,471 cases of breast cancer in women aged 50-59 of whom 8% or 278 may have extremely dense breasts and there were 5,427 cases in women aged 60-79 of which 4% or 217 may have extremely dense breasts.

² <http://www.acr.org/About-Us/Media-Center/Position-Statements/Position-Statements-Folder/Statement-on-Reporting-Breast-Density-in-Mammography-Reports-and-Patient-Summaries>

- It is not possible to estimate how many women would have a discrepancy between imaging findings.
 - The total estimate for this population is 3,703 although there is some double counting of women who have the lobular sub-type (10.7% of breast cancers) so there is an estimate of approximately 3,300 tests per annum
- 3) Metastatic breast cancer where the source of the tumour is undefined
- Applicant's estimate is <0.5%
 - no more than 70 cases per annum
- 4) MRI guided biopsy
- Applicants estimate that 10-20% of patients undergoing MRI will require MRI guided biopsy

The Australian Institute of Health and Welfare project that, by 2020, there will be 17,210 new cases of breast cancer diagnosed in women (Australian Institute of Health and Welfare & Cancer Australia 2012). Based on the AIHW estimate, about 500 additional new breast cancers will be diagnosed each year, which is an annual growth rate of about 3%.

Comparator

Mammography

Mammography is the most common form of breast imaging for asymptomatic and symptomatic women and may be used for screening or diagnosis.

Mammography is the primary breast imaging modality for the investigation of symptomatic women 35 years and over, for the follow-up of women with a previous diagnosis of breast cancer and for the screening of asymptomatic women (National Breast Cancer Centre 2002). A mammogram gives a two-dimensional radiographic image of most (and sometimes all) of the breast tissue. The MBS provides a rebate for diagnostic mammography where there is a reason to suspect the presence of a malignancy, for example in women with breast symptoms and women with a personal or family history of breast cancer (MBS 59300, 59301, 59303 and 59304, see Appendix A, Table 11).

The MBS specifically excludes rebates for mammography for screening purposes except for personal or family history. However, it is apparent that some mammography services accessed through the MBS are for non-diagnostic purposes (IMS Health 2009).

The standard mammographic examination includes two views, medio-lateral oblique (side) and cranio-caudal (top). Correct positioning and compression of the breast is required for optimal quality.

Digital mammography is replacing film mammography in Australia. Digital mammography uses a digital detector rather than the traditional film x-ray and was assessed by MSAC in 2007 (Reference 37) and found to be as safe and effective as film mammography.

The sensitivity of mammography for detecting any abnormality will depend upon:

- The nature of the breast lesion
- The radiographic density and overall nodularity of the breast tissue
- The location of the abnormality within the breast
- The technical quality of the mammograms
- The radiologist's expertise in interpreting the imaging appearances (National Breast Cancer Centre 2002).

Ultrasound

Breast ultrasound may be used to complement mammography (MBS 55059, 55060, 55061, 55062, 55070, 55073 and 55076, see Appendix A, Table 12). Even with excellent quality mammography technique and interpretation, a lesion may not be visible on the mammogram or the mammographic findings may be indeterminate. Ultrasound is the most common complement to mammography and may be the primary and only imaging modality used for the investigation of breast symptoms in women less than 35 years. Ultrasound is the preferred initial imaging technique in women who are pregnant or lactating.

Utilisation

In the 2012 calendar year there were 374,310 claims processed for mammography and 533,653 for breast ultrasound on the MBS. Both imaging modalities have increased utilisation over the past ten years however, the increase has been more rapid for ultrasound than mammography (Australian Government Department of Human Services 2013) such that the age standardised incidence rate of MBS funded mammography services has declined from 33.6 per 100,000 women in 2002 to 29.5 per 100,000 women in 2011 (Australian Institute of Health and Welfare & Cancer Australia 2012).

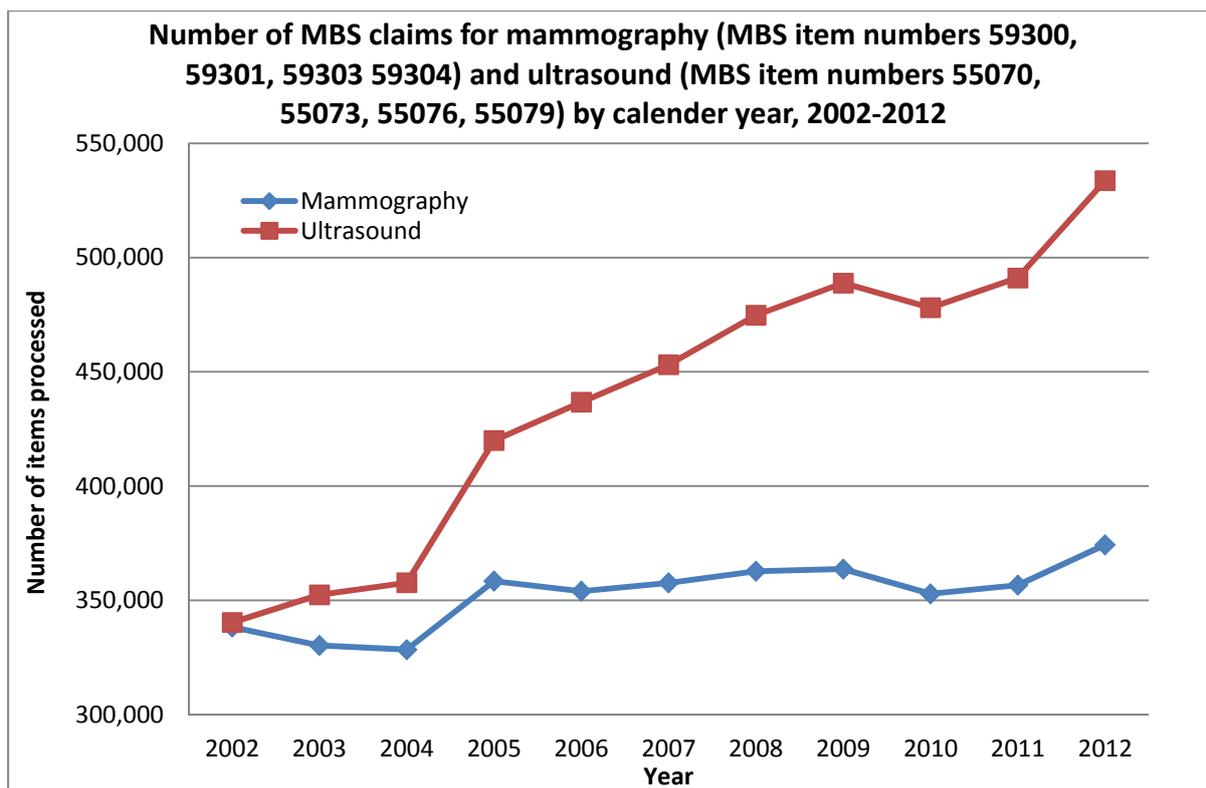
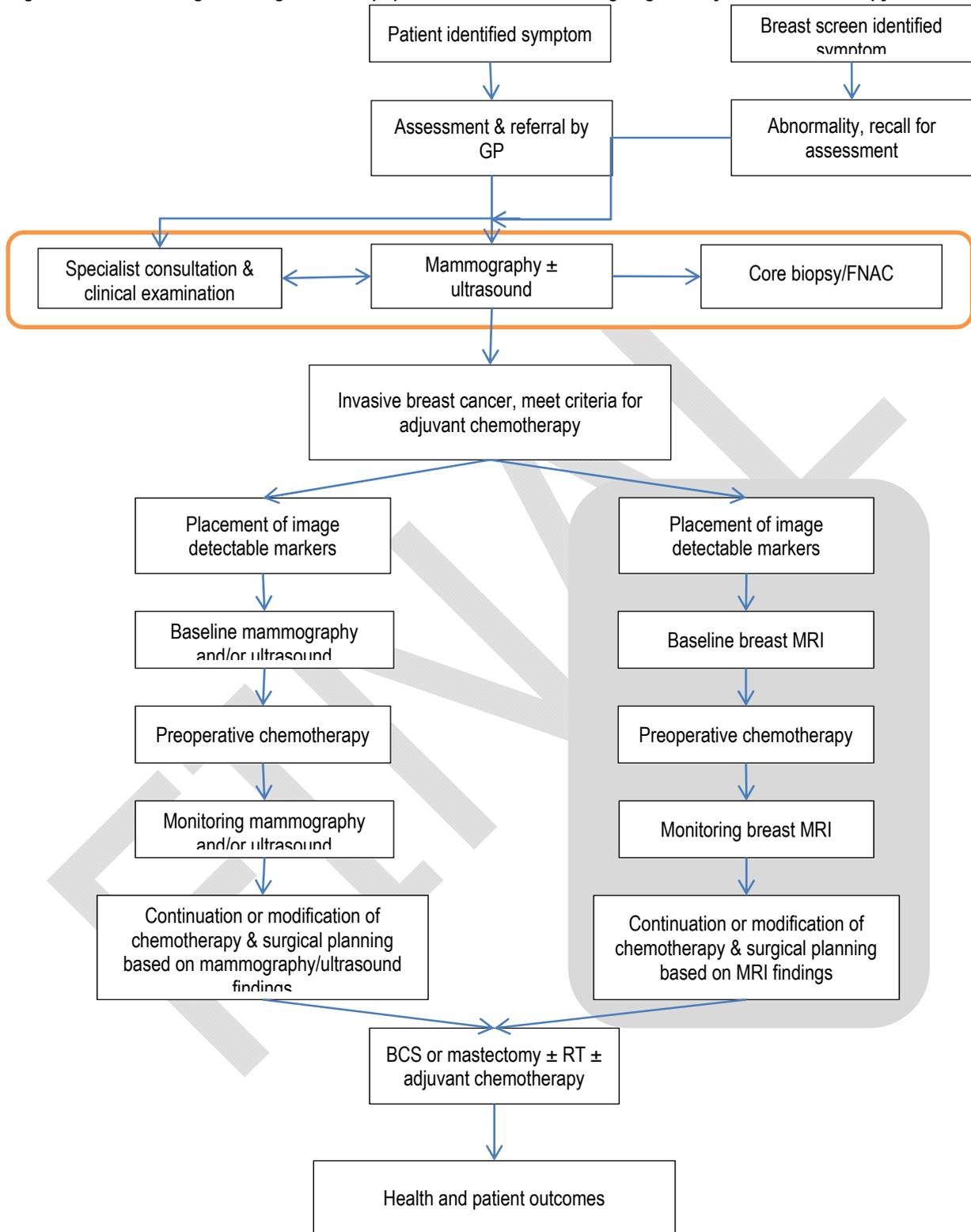


Figure 1 Utilisation of mammography and ultrasound on the MBS, 2002-2012.
Source: (Australian Government Department of Human Services 2013)

Clinical management algorithms

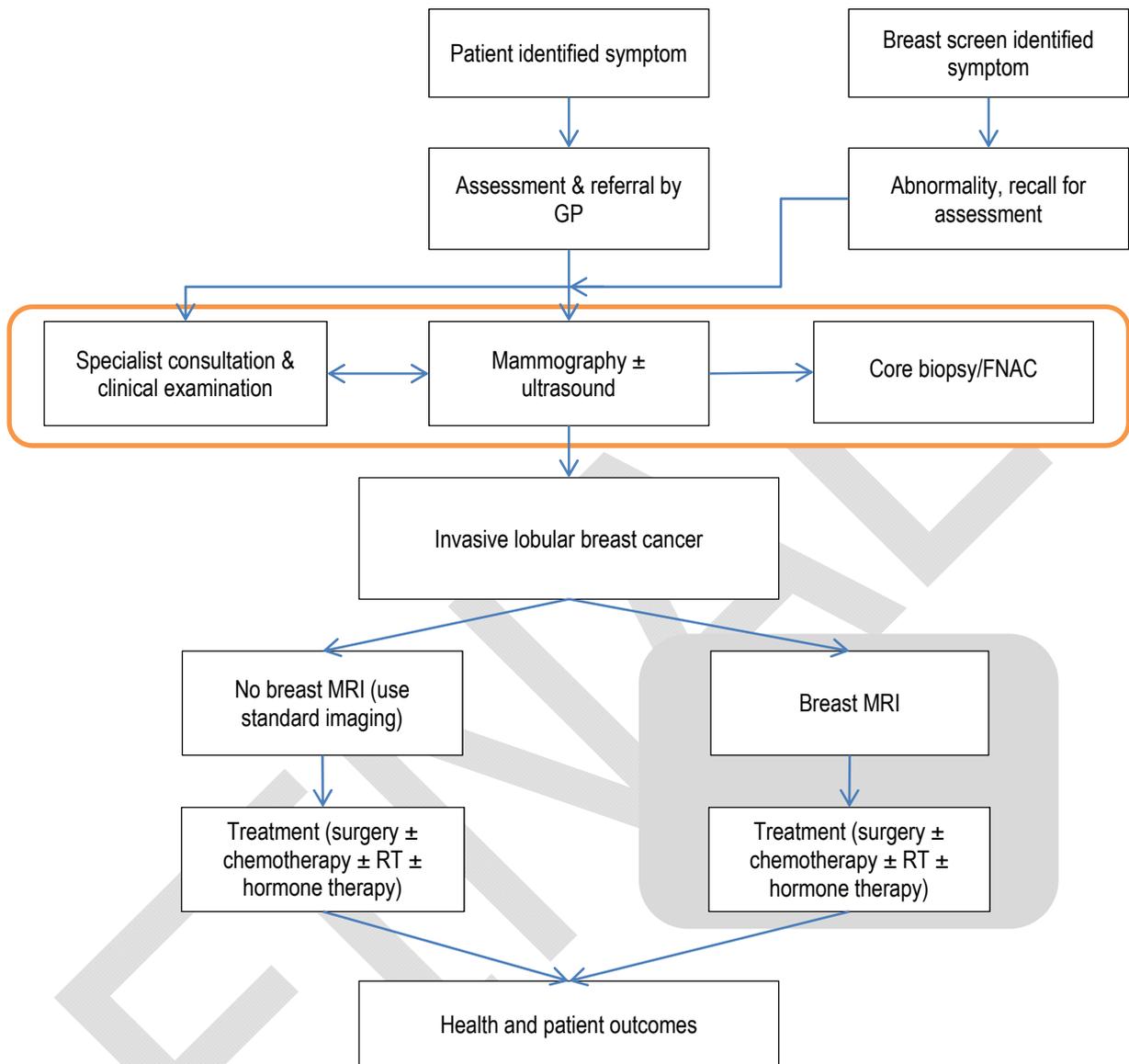
For population 1, breast MRI is proposed *to replace* mammography and/or ultrasound for the monitoring of response to neo-adjuvant chemotherapy.

Figure 2 Clinical management algorithm for population 1 – women undergoing neo adjuvant chemotherapy



For population 2, women diagnosed with invasive lobular breast cancer, breast MRI is proposed to be used *in addition* to mammography and ultrasound in the initial staging of the breast cancer.

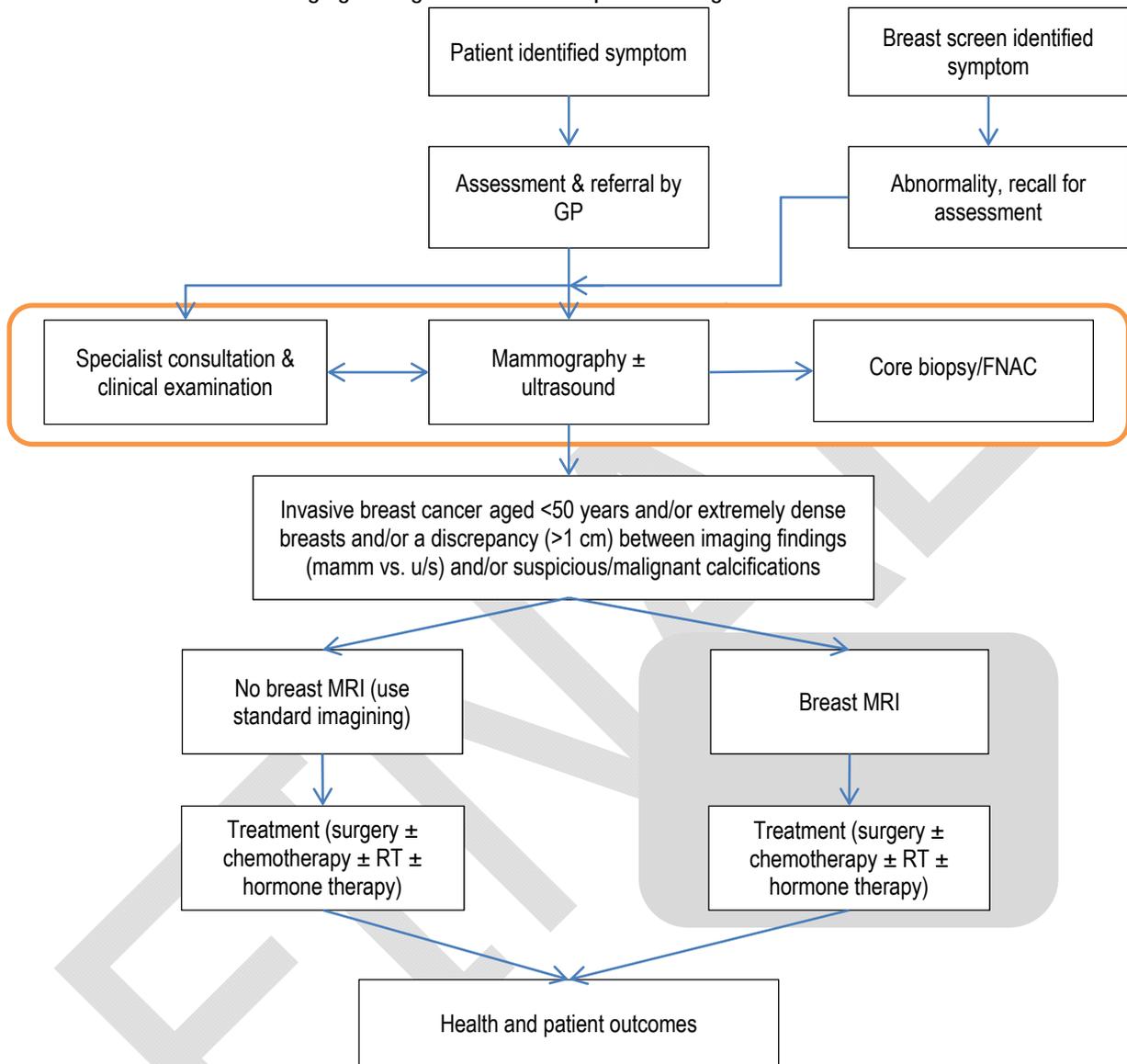
Figure 3 Clinical management algorithm for population 2 – women diagnosed with invasive lobular breast cancer



For population 3, women diagnosed with invasive breast cancer who are either aged <50 years and/or have extremely dense breasts and/or have a discrepancy between imaging findings, breast MRI is proposed to be used *in addition* to mammography and ultrasound in the initial staging of the breast cancer.

Figure 4

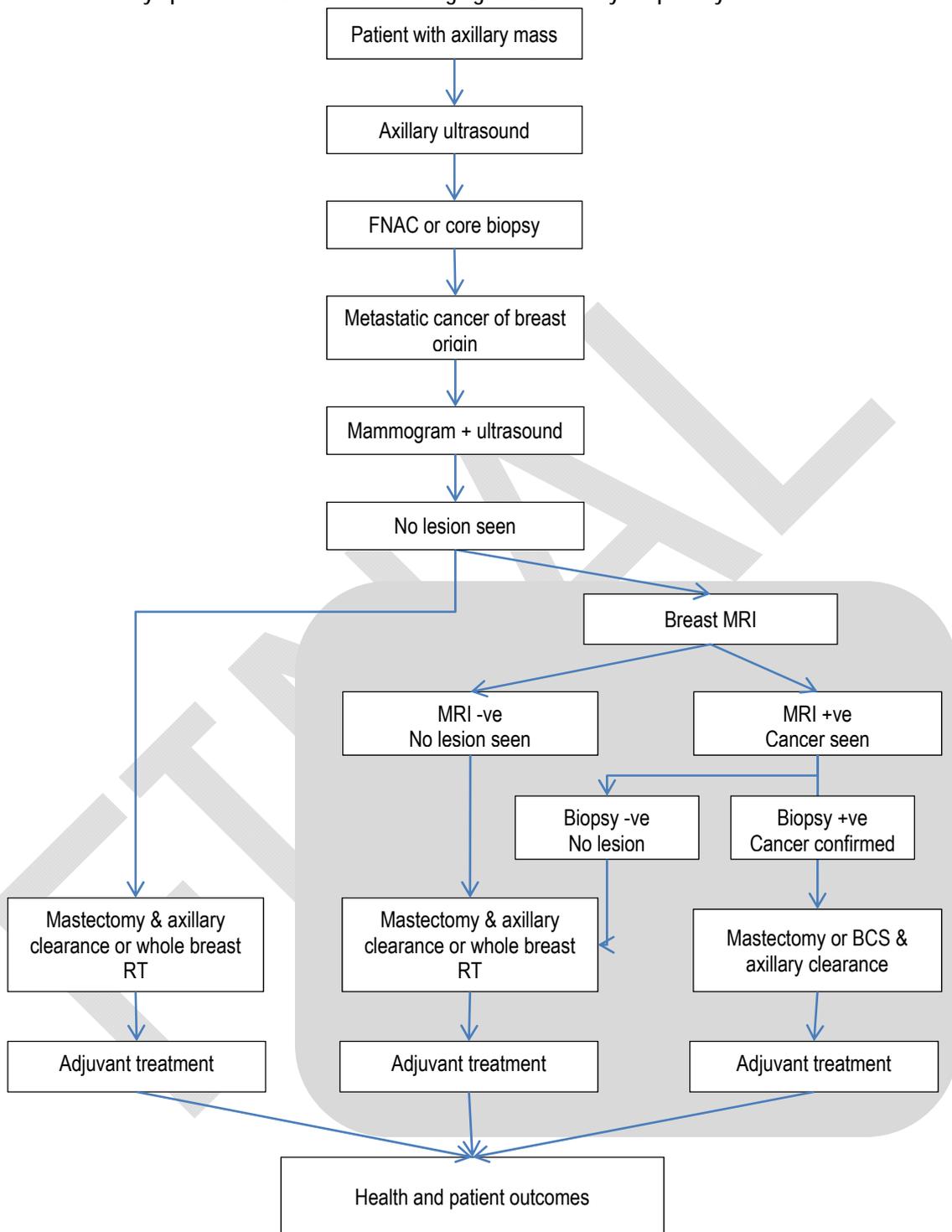
Clinical management algorithm for population 3 – women diagnosed with invasive breast cancer who are either aged <50 years and/or have extremely dense breasts and/or have a discrepancy between imaging findings and/or have suspicious/malignant calcifications



For population 4, women presenting with metastatic cancer in the lymph nodes where conventional imaging fails to identify the primary tumour, breast MRI is proposed to be used *in addition* to mammography and ultrasound.

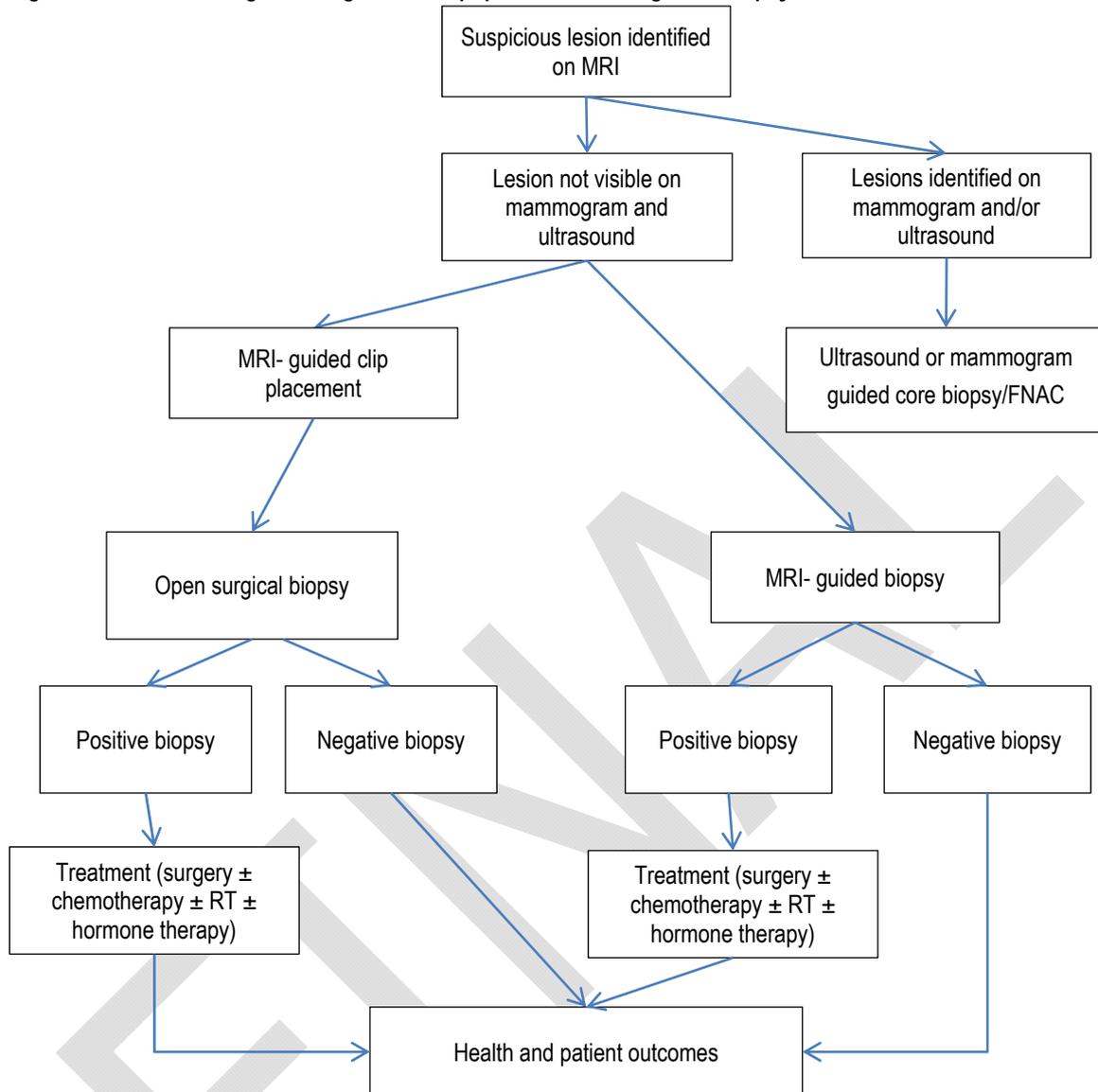
Figure 5

Clinical management algorithm for population 4 – women presenting with metastatic cancer in the lymph nodes and conventional imaging fails to identify the primary tumour



For population 5, MRI guided biopsy there is no true comparator, an MRI would be required to either to perform an MRI guided biopsy or to place a clip in order to undertake an open surgical biopsy.

Figure 6 Clinical management algorithm for population 5 – MRI guided biopsy



Clinical claim

For women undergoing neo-adjuvant chemotherapy, the role of breast MRI is to more accurately assess response to treatment in order to assist with surgical treatment planning. The potential advantages of using MRI in this indication are:

- Breast MRI is a more sensitive test (correct identification of responders)
- May lead to improved health outcomes by
 - Improving the selection of patients for breast conserving surgery rather than mastectomy
 - Determining earlier those patients who are responders and altering treatment to achieve complete response

The potential disadvantages of using breast MRI in this indication are:

- Lower test specificity (correct identification of non-responders)
- May lead to potential harms such as
 - *Possibility that more women may have mastectomy due to MRI detected foci which could have been adequately managed by breast conserving therapy. In other words foci detected by MRI could potentially be misclassified as requiring aggressive treatment (false positive) where in fact less aggressive treatment is only needed.*
 - *Possibility of ceasing or altering of treatment due to MRI detected foci which could have benefited for continued treatment. In other words foci detected by MRI could potentially be misclassified as requiring no further treatment (false negative) where in fact ongoing treatment is more appropriate.*
- The exclusion of women with contraindications (eg. MRI-incompatible implantable devices)
- The higher cost of the test

With reference to Table 3, it is expected that in this indication breast MRI has non-inferior safety and the claim is that it has superior effectiveness; that is it is more accurate which leads to a change in surgical management which then translates into improved health outcomes. Therefore, the approach to the economic evaluation is expected to be a cost-effectiveness analysis or a cost utility analysis.

For women diagnosed with invasive lobular carcinoma and those diagnosed with other breast cancers who are under 50 years of age and/or have very dense breasts and/or have a discrepancy in imaging findings and/or have suspicious/malignant calcifications, the role of breast MRI is to more accurately stage the disease and it is expected that this will alter treatment for some women, usually from breast conserving surgery to mastectomy, which then translates into improved health outcomes. The advantages of using MRI in these indications are:

- Breast MRI is a more sensitive test
- May lead to improved health outcomes by better selecting patients for breast conserving surgery thus,
 - Increasing rates of negative margins
 - Reducing rates of reintervention
 - Decreasing conversion from breast conservation to mastectomy
 - Reducing breast cancer recurrence.

The potential disadvantages of using breast MRI in this indication are:

- Lower test specificity
- May lead to reduced health outcomes by
 - Increasing rates of unnecessary mastectomies
 - Increasing time between diagnosis and treatment
- The additional cost of the test

With reference to Table 3, in these indications breast MRI is proposed to have non-inferior safety and superior effectiveness and therefore, the approach to the economic evaluation is expected to be a cost-effectiveness analysis or a cost utility analysis.

For women with metastatic breast cancer in the lymph nodes where conventional imaging has failed to identify the source of the tumour, the role of MRI is to have increased incremental sensitivity over conventional imaging, thus enabling the primary tumour to be identified allowing treatment to be altered such that it is less extensive (i.e. from whole breast radiotherapy or mastectomy to breast conserving therapy).

The advantages of using MRI in these indications are:

- Breast MRI is a more sensitive test
- May lead to improved health outcomes by enabling less extensive surgery/treatment

The potential disadvantages in this indication are:

- May increase the time from diagnosis to treatment
- Low specificity may lead to additional biopsies for no clinical gain
- Increased costs

The use of MRI guided biopsy is proposed to allow women with a suspected breast cancer identified by MRI but not by other imaging modalities to have an image-guided biopsy.

The potential advantages of MRI guided biopsy are:

- MRI guided biopsy is a less invasive procedure than a surgical biopsy:
 - Better healing
 - Fewer days of leave
 - Less scarring

The potential disadvantages of MRI guided biopsy are:

- Complex and costly procedure.

Table 3: Classification of an intervention for determination of economic evaluation to be presented

		Comparative effectiveness versus comparator				
		Superior	Non-inferior	Inferior		
Comparative safety versus comparator	Superior	CEA/CUA	CEA/CUA	Net clinical benefit	CEA/CUA	
				Neutral benefit	CEA/CUA*	
				Net harms	None [^]	
	Non-inferior	CEA/CUA	CEA/CUA*	None [^]		
	Inferior	Net clinical benefit	CEA/CUA	None [^]	None [^]	
		Neutral benefit	CEA/CUA*			
Net harms		None [^]				

Abbreviations: CEA = cost-effectiveness analysis; CUA = cost-utility analysis

* May be reduced to cost-minimisation analysis. Cost-minimisation analysis should only be presented when the proposed service has been indisputably demonstrated to be no worse than its main comparator(s) in terms of both effectiveness and safety, so the difference between the service and the appropriate comparator can be reduced to a comparison of costs. In most cases, there will be some uncertainty around such a conclusion (i.e., the conclusion is often not indisputable). Therefore, when an assessment concludes that an intervention was no worse than a comparator, an

assessment of the uncertainty around this conclusion should be provided by presentation of cost-effectiveness and/or cost-utility analyses.

[^] No economic evaluation needs to be presented; MSAC is unlikely to recommend government subsidy of this intervention

Outcomes and health care resources affected by introduction of proposed intervention

Outcomes

The health outcomes, upon which the comparative clinical performance of breast MRI in addition to mammography and ultrasound will be measured, are:

Effectiveness

Health outcomes:

- Overall survival
- Breast cancer specific mortality
- Breast cancer recurrence
- Rates of negative surgical margins
- Rates of reintervention
- Time from diagnosis to treatment
- Rates of mastectomy vs. BCS
- Quality of life
- Patient preference
- Satisfaction, anxiety
- Patient compliance
- Overtreatment

Diagnostic accuracy:

- negative & positive predictive value,
- sensitivity & specificity,
- additional true/false positives
- Intra and inter individual variability/reproducibility

Change in management:

- Definitive treatment instigated/avoided
- Biopsy rate
- Change of stage

Safety

Any adverse events arising from the addition of breast MRI

- gadolinium reaction
- claustrophobia
- other

Health care resources

Table 4: List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
<u>Resources provided to identify eligible population</u>										
- Weighted average costs of a medical consultation	GP/other	outpatient	100							
- Specialist consultation	Specialist	Outpatient	100							
- Mammogram	Radiologist	Outpatient	100							
- Ultrasound		Outpatient								
<u>Resources associated with the addition of MRI to conventional imaging</u>										
- MRI	Radiologist	Outpatient	100							
- Specialist consultation	Specialist	Outpatient	100							
<u>Resources associated with use of MRI when used to monitor neo-adjuvant chemotherapy</u>										
- Resource 1	TBC									
- Resource 2, etc										
<u>Resources associated with follow-up from imaging</u>										
- Surgical biopsy	Specialist	Outpatient			31506					
- Anaesthetic costs	Specialist	Outpatient								
- Fine needle aspiration biopsy	Specialist	Outpatient			31533					
- Ultrasound guidance	Specialist	Outpatient			55070					
- Core needle biopsy	Specialist	Outpatient			31528					
- Stereotactic biopsy	Specialist	Outpatient			31545					
- Specialist appointment	Specialist	Outpatient								
<u>Resources associated with treatment</u>										
- Breast conserving surgery	Specialist	Inpatient								
- Mastectomy	Specialist	Inpatient								
- Radiotherapy	Specialist	Inpatient/Outpatient								
- Chemotherapy	Specialist	Inpatient/Outpatient								
- Hormone therapy	Specialist	Outpatient								
<u>Resources associated with breast MRI guided biopsy</u>										
- TBC										

Proposed structure of economic evaluation (decision-analytic)

Table 5: Summary of PICO to define research question – population 1, women undergoing neo-adjuvant chemotherapy

Patients	Intervention	Comparator	Outcomes to be assessed
Women newly diagnosed with breast cancer who are undergoing preoperative (neo-adjuvant) chemotherapy	Breast MRI for monitoring neo-adjuvant chemotherapy	Conventional imaging (mammography ± ultrasound)	<p>Effectiveness</p> <p>Health outcomes:</p> <ul style="list-style-type: none"> • Overall survival • Breast cancer specific mortality • Breast cancer recurrence • Rates of negative surgical margins • Rates of reintervention • Time from diagnosis to treatment • Rates of mastectomy vs. BCS • Quality of life • Patient preference • Satisfaction, anxiety • Patient compliance • Overtreatment <p>Diagnostic accuracy:</p> <ul style="list-style-type: none"> • negative & positive predictive value, • sensitivity & specificity, additional true/false positives • Intra and inter individual variability/reproducibility <p>Change in management:</p> <ul style="list-style-type: none"> • Definitive treatment instigated/avoided • Biopsy rate • Change of stage <p>Safety</p> <p>Any adverse events arising from the addition of breast MRI</p> <ul style="list-style-type: none"> • gadolinium reaction • claustrophobia • other

Table 6: Summary of extended PICO to define research question – population 2, women with lobular breast cancer

Patients	Intervention	Comparator	Outcomes to be assessed
Women newly diagnosed with invasive lobular breast cancer where MRI imaging may alter treatment planning	Conventional imaging (mammography ± ultrasound) PLUS Breast MRI	Conventional imaging (mammography ± ultrasound)	<p>Effectiveness</p> <p>Health outcomes:</p> <ul style="list-style-type: none"> • Overall survival • Breast cancer specific mortality • Breast cancer recurrence • Rates of negative surgical margins • Rates of reintervention • Time from diagnosis to treatment • Rates of mastectomy vs. BCS • Quality of life • Patient preference • Satisfaction, anxiety

			<ul style="list-style-type: none"> • Patient compliance • Overtreatment Diagnostic accuracy: <ul style="list-style-type: none"> • negative & positive predictive value, • sensitivity & specificity, additional true/false positives • Intra and inter individual variability/reproducibility Change in management: <ul style="list-style-type: none"> • Definitive treatment instigated/avoided • Biopsy rate • Change of stage Safety Any adverse events arising from the addition of breast MRI <ul style="list-style-type: none"> • gadolinium reaction • claustrophobia • other
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Table 7: Summary of extended PICO to define research question – population 3, women with lobular breast cancer

Patients	Intervention	Comparator	Outcomes to be assessed
Women newly diagnosed with invasive breast cancer where MRI imaging may alter treatment planning <ul style="list-style-type: none"> • aged ≤50 years old, or • with very/extremely dense breasts, or • with a discrepancy between mammogram and ultrasound findings of ≥1cm 	Conventional imaging (mammography ± ultrasound) PLUS Breast MRI	Conventional imaging (mammography ± ultrasound)	Effectiveness Health outcomes: <ul style="list-style-type: none"> • Overall survival • Breast cancer specific mortality • Breast cancer recurrence • Rates of negative surgical margins • Rates of reintervention • Time from diagnosis to treatment • Rates of mastectomy vs. BCS • Quality of life • Patient preference • Satisfaction, anxiety • Patient compliance • Overtreatment Diagnostic accuracy: <ul style="list-style-type: none"> • negative & positive predictive value, • sensitivity & specificity, additional true/false positives • Intra and inter individual variability/reproducibility Change in management: <ul style="list-style-type: none"> • Definitive treatment instigated/avoided • Biopsy rate • Change of stage Safety Any adverse events arising from the addition of breast MRI

			<ul style="list-style-type: none"> • gadolinium reaction • claustrophobia • other
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Table 8: Summary of extended PICO to define research question- population 4, women with metastatic breast cancer where the source has not been determined

Patients	Intervention	Comparator	Outcomes to be assessed
Women presenting with metastatic breast cancer in the lymph nodes (but not elsewhere) where conventional imaging and examination fails to show the source of the tumour.	Conventional imaging (mammography ± ultrasound) PLUS Breast MRI	Conventional imaging (mammography ± ultrasound)	<p>Effectiveness</p> <p>Health outcomes:</p> <ul style="list-style-type: none"> • Overall survival • Breast cancer specific mortality • Breast cancer recurrence • Rates of negative surgical margins • Rates of reintervention • Time from diagnosis to treatment • Rates of mastectomy vs. BCS • Quality of life • Patient preference • Satisfaction, anxiety • Patient compliance • Overtreatment <p>Diagnostic accuracy:</p> <ul style="list-style-type: none"> • negative & positive predictive value, • sensitivity & specificity, additional true/false positives • Intra and inter individual variability/reproducibility <p>Change in management:</p> <ul style="list-style-type: none"> • Definitive treatment instigated/avoided • Biopsy rate • Change of stage <p>Safety</p> <p>Any adverse events arising from the addition of breast MRI</p> <ul style="list-style-type: none"> • gadolinium reaction • claustrophobia • other

Table 9: Summary of extended PICO to define research question – population 4, the use of MRI guided biopsy

Patients	Intervention	Comparator	Outcomes to be assessed
Patients with suspected breast cancer where the lesion is only identifiable by MRI	MRI guided biopsy	All comparators would require MRI-guidance	<p>Effectiveness</p> <p>Health outcomes:</p> <ul style="list-style-type: none"> • Overall survival • Breast cancer specific mortality • Breast cancer recurrence • Rates of negative surgical margins • Rates of reintervention • Time from diagnosis to treatment • Rates of mastectomy vs. BCS

			<ul style="list-style-type: none"> • Quality of life • Patient preference • Satisfaction, anxiety • Patient compliance • Overtreatment <p>Diagnostic accuracy:</p> <ul style="list-style-type: none"> • negative & positive predictive value, • sensitivity & specificity, additional true/false positives • Intra and inter individual variability/reproducibility <p>Change in management:</p> <ul style="list-style-type: none"> • Definitive treatment instigated/avoided • Biopsy rate • Change of stage <p>Safety</p> <p>Any adverse events arising from the addition of breast MRI</p> <ul style="list-style-type: none"> • gadolinium reaction • claustrophobia • other
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Appendix A: Existing MBS item descriptors for breast MRI and conventional breast imaging

Table 10 Existing MBS item descriptor for breast MRI

	Category 5 – Diagnostic imaging services
<p>MBS 63464</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the woman is asymptomatic and is less than 50 years of age; and</p> <p>(c) the request for scan identifies either:</p> <p style="padding-left: 20px;">(i) that the patient is at high risk of developing breast cancer, due to 1 of the following:</p> <p style="padding-left: 40px;">(A) 3 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer;</p> <p style="padding-left: 40px;">(B) 2 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer, if any of the following applies to at least 1 of the relatives:</p> <ul style="list-style-type: none"> - has been diagnosed with bilateral breast cancer; - had onset of breast cancer before the age of 40 years; - had onset of ovarian cancer before the age of 50 years; - has been diagnosed with breast and ovarian cancer, at the same time or at different times; - has Ashkenazi Jewish ancestry; - is a male relative who has been diagnosed with breast cancer; <p style="padding-left: 40px;">(C) 1 first or second degree relative diagnosed with breast cancer at age 45 years or younger, plus another first or second degree relative on the same side of the family with bone or soft tissue sarcoma at age 45 years or younger; or</p> <p style="padding-left: 20px;">(ii) that genetic testing has identified the presence of a high risk breast cancer gene mutation.</p> <p>Scan of both breasts for:</p> <ul style="list-style-type: none"> - detection of cancer (R) <p>NOTE: Benefits are payable on one occasion only in any 12 month period</p> <p>Bulk bill incentive</p> <p>(Anaes.)</p> <p>Fee: \$690.00 Benefit: 75% = \$517.50 85% = \$613.80</p>	
<p>MBS 63457</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:</p> <p>(a) a dedicated breast coil is used; and</p> <p>(b) the request for scan identifies that the woman is asymptomatic and is less than 50 years of age; and</p> <p>(c) the request for scan identifies either:</p> <p style="padding-left: 20px;">(i) that the patient is at high risk of developing breast cancer, due to 1 of the following:</p> <p style="padding-left: 40px;">(A) 3 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer;</p> <p style="padding-left: 40px;">(B) 2 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer, if any of the following applies to at least 1 of the relatives:</p> <ul style="list-style-type: none"> - has been diagnosed with bilateral breast cancer; - had onset of breast cancer before the age of 40 years; 	

- had onset of ovarian cancer before the age of 50 years;
- has been diagnosed with breast and ovarian cancer, at the same time or at different times;
- has Ashkenazi Jewish ancestry;
- is a male relative who has been diagnosed with breast cancer;

(C) 1 first or second degree relative diagnosed with breast cancer at age 45 years or younger, plus another first or second degree relative on the same side of the family with bone or soft tissue sarcoma at age 45 years or younger; or

(ii) that genetic testing has identified the presence of a high risk breast cancer gene mutation.

Scan of both breasts for:

- detection of cancer (R)

NOTE: Benefits are payable on one occasion only in any 12 month period

(NK)

Bulk bill incentive

(Anaes.)

Fee: \$345.00 Benefit: 75% = \$258.75 85% = \$293.25

MBS 63467

MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:

- (a) a dedicated breast coil is used; and
- (b) the woman has had an abnormality detected as a result of a service described in item 63464 performed in the previous 12 months

Scan of both breasts for:

- detection of cancer (R)

NOTE 1: Benefits are payable on one occasion only in any 12 month period

NOTE 2: This item is intended for follow-up imaging of abnormalities diagnosed on a scan described by item 63464

Bulk bill incentive

(Anaes.)

Fee: \$690.00 Benefit: 75% = \$517.50 85% = \$613.80

MBS 63458

MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:

- (a) a dedicated breast coil is used; and
- (b) the woman has had an abnormality detected as a result of a service described in item 63464 performed in the previous 12 months

Scan of both breasts for:

- detection of cancer (R)

NOTE 1: Benefits are payable on one occasion only in any 12 month period

NOTE 2: This item is intended for follow-up imaging of abnormalities diagnosed on a scan described by item

63464 or 63457

(NK)

Bulk bill incentive

(Anaes.)

Fee: \$690.00 Benefit: 75% = \$517.50 85% = \$613.80

Table 11 Mammography MBS items

Mammography Category 5 – Diagnostic Imaging Services	
MBS 59300	
MAMMOGRAPHY OF BOTH BREASTS, if there is a reason to suspect the presence of malignancy because of: (i) the past occurrence of breast malignancy in the patient or members of the patient's family; or (ii) symptoms or indications of malignancy found on an examination of the patient by a medical practitioner. Unless otherwise indicated, mammography includes both breasts (R)	
Bulk bill incentive	
Fee: \$89.50 Benefit: 75% = \$67.15 85% = \$76.10	
MBS 59301*	
MAMMOGRAPHY OF BOTH BREASTS, if there is a reason to suspect the presence of malignancy because of: (i) the past occurrence of breast malignancy in the patient or members of the patient's family; or (ii) symptoms or indications of malignancy found on an examination of the patient by a medical practitioner. Unless otherwise indicated, mammography includes both breasts (R) (NK)	
Bulk bill incentive	
Fee: \$44.75 Benefit: 75% = \$33.60 85% = \$38.05	
MBS 59303	
MAMMOGRAPHY OF ONE BREAST, if: (a) the patient is referred with a specific request for a unilateral mammogram; and (b) there is reason to suspect the presence of malignancy because of: (i) the past occurrence of breast malignancy in the patient or members of the patient's family; or (ii) symptoms or indications of malignancy found on an examination of the patient by a medical practitioner (R)	
Bulk bill incentive	
Fee: \$53.95 Benefit: 75% = \$40.50 85% = \$45.90	
MBS 59304*	
MAMMOGRAPHY OF ONE BREAST, if: (a) the patient is referred with a specific request for a unilateral mammogram; and (b) there is reason to suspect the presence of malignancy because of: (i) the past occurrence of breast malignancy in the patient or members of the patient's family; or (ii) symptoms or indications of malignancy found on an examination of the patient by a medical practitioner (R) (NK)	
Bulk bill incentive	
Fee: \$27.00 Benefit: 75% = \$20.25 85% = \$22.95	

Table 12 Breast ultrasound MBS items

Ultrasound Category 5 – Diagnostic Imaging Services
<p>MBS 55059</p> <p>BREAST, one, ultrasound scan of, where:</p> <p>(a) the patient is referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies; and</p> <p>(c) the referring medical practitioner is not a member of a group of practitioners of which the providing practitioner is a member (R) (NK)</p> <p>Bulk bill incentive</p> <p>Fee: \$49.15 Benefit: 75% = \$36.90 85% = \$41.80</p>
<p>MBS 55060</p> <p>BREAST, one, ultrasound scan of, where:</p> <p>(a) the patient is not referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies (NR) (NK)</p> <p>Bulk bill incentive</p> <p>Fee: \$17.05 Benefit: 75% = \$12.80 85% = \$14.50</p>
<p>MBS 55070</p> <p>BREAST, one, ultrasound scan of, where:</p> <p>(a) the patient is referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies; and</p> <p>(c) the referring medical practitioner is not a member of a group of practitioners of which the providing practitioner is a member (R)</p> <p>Bulk bill incentive</p> <p>Fee: \$98.25 Benefit: 75% = \$73.70 85% = \$83.55</p>
<p>MBS 55073</p> <p>BREAST, one, ultrasound scan of, where:</p> <p>(a) the patient is not referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies (NR) Bulk bill incentive</p> <p>Fee: \$34.05 Benefit: 75% = \$25.55 85% = \$28.95</p>
<p>MBS 55061</p> <p>BREASTS, both, ultrasound scan of, where:</p> <p>(a) the patient is referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies; and</p> <p>(c) the referring medical practitioner is not a member of a group of practitioners of which the providing practitioner is a member (R) (NK)</p> <p>Bulk bill incentive</p> <p>Fee: \$54.55 Benefit: 75% = \$40.95 85% = \$46.40</p>

<p>MBS 55062</p> <p>BREASTS, both, ultrasound scan of, where:</p> <p>(a) the patient is not referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies (NR) (NK)</p> <p>Bulk bill incentive</p> <p>Fee: \$18.95 Benefit: 75% = \$14.25 85% = \$16.15</p>
<p>MBS 55076</p> <p>BREASTS, both, ultrasound scan of, where:</p> <p>(a) the patient is referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies; and</p> <p>(c) the referring medical practitioner is not a member of a group of practitioners of which the providing practitioner is a member (R)</p> <p>Bulk bill incentive</p> <p>Fee: \$109.10 Benefit: 75% = \$81.85 85% = \$92.75</p>
<p>MBS 55079</p> <p>BREASTS, both, ultrasound scan of, where:</p> <p>(a) the patient is not referred by a medical practitioner; and</p> <p>(b) the service is not associated with a service to which an item in Subgroup 2 or 3 of this group applies (NR) Bulk bill incentive</p> <p>Fee: \$37.85 Benefit: 75% = \$28.40 85% = \$32.20</p>

Capital sensitivity rule for all diagnostic imaging equipment: Most diagnostic imaging services have two different schedule items: schedule K items and schedule NK items. Schedule NK items have a fee approximately half the corresponding K item. Whether a service is a schedule K or a schedule NK service depends on the age of the equipment, whether the equipment has been upgraded or whether a location based exemption of the age requirements has been granted (see <http://www.health.gov.au/capitalsensitivity>). The symbol (R) designates that the services is a requested services subject to the written request requirement.

References

1. Australian Government Department of Human Services 2013, *Medicare Australia Statistics* [Internet]. Available from: https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml [Accessed 25 October 2013].
2. Australian Institute of Health and Welfare & Cancer Australia 2012, *Breast cancer in Australia: an overview*. Cancer series no. 71 Cat. no. CAN 67. Canberra: AIHW.
3. Checka, CM, Chun, JE et al 2012. The Relationship of Mammographic Density and Age: Implications for Breast Cancer Screening, *American Journal of Roentgenology*, 198 (3), W292-W295.
4. Houssami, N, Ciatto, S et al 2008. Accuracy and Surgical Impact of Magnetic Resonance Imaging in Breast Cancer Staging: Systematic Review and Meta-Analysis in Detection of Multifocal and Multicentric Cancer, *Journal of Clinical Oncology*, 26 (19), 3248-3258.
5. Houssami, N and Morrow, M 2013. Does preoperative MRI improve clinical outcomes in breast cancer?, *Breast Cancer Management*, 2 (2), 115-122.
6. IMS Health 2009, *BreastScreen Australia: MBS Mammography Analysis Project*. 11/2009.ACT: Department of Health and Ageing.
7. McLaughlin, S, Mittendorf, E et al 2013. The 2013 Society of Surgical Oncology Susan G. Komen for the Cure Symposium: MRI in Breast Cancer: Where Are We Now?, *Ann Surg Oncol* 1-9.
8. National Breast Cancer Centre 2002, *Breast imaging: a guide for practice*. Camperdown, NSW.
9. National Collaborating Centre for Cancer 2009, *Early and locally advanced breast cancer: diagnosis and treatment*. NICE Clinical Guidelines No.80. Cardiff.
10. National Comprehensive Cancer Network (NCCN) 2014, *Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.1.2014 ®* [Internet]. To view the most recent and complete version of the guideline, go online to www.nccn.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc. [Accessed 16 January 2014].