Protocol to guide the assessment of mpMRI prostate diagnostic scans for diagnosis of prostate cancer

February 2016

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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 draft decision analytic protocol that will be used to guide the assessment of an intervention for a particular population of patients. The draft protocol will be finalised after inviting relevant stakeholders to provide input to the protocol. The final protocol will provide the basis for the assessment of the intervention.

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

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Purpose of application

A proposal for an application requesting MBS listing of (1) multiparametric MRI (mpMRI) scans of the prostate, and (2) MR-guided prostate biopsy in men with a high or concerning Prostate Specific Antigen and under suspicion of harbouring prostate cancer, was received from the Australian and New Zealand Association of Urological Surgeons and the Australian Diagnostic Imaging Association by the Department of Health in August 2014.

Following the August 2015 meeting, PASC advised that Application 1397 should be spilt into two applications.

1. Intervention for Diagnostic mpMRI; and
2. Intervention for MR-guided biopsy.

This recommendation is intended to assist with the preparation and evaluation of the contracted assessments by the Economic Sub-Committee (ESC) and Medical Services Advisory Committee (MSAC).

Intervention

Description

In cancers, cells replicate in an abnormal, uncontrolled manner, forming a mass of cells called a tumour. Prostate cancer is the result of such abnormal replication in the prostate. While the cause(s) of prostate cancer are not yet completely understood, the following factors are thought to play a role: age, family history, ethnic background, lifestyle, and environmental factors. After heart disease, lung cancer, and cerebrovascular diseases, prostate cancer is the fourth leading cause of death amongst Australian men. In 2011, there were nearly 3300 deaths from prostate cancer, and the age-standardised mortality rate for prostate cancer was 31 per 100,000. It is projected that by 2020, the number of deaths will reach 3900 and the age-standardised mortality rate will decrease to 26 per 100,000 (AIHW 2013).

Currently in Australia, the signs of prostate cancer are detected with a prostate-specific antigen test (PSA test)[1] and/or a digital rectal examination (DRE).

PSA is a protein that is made by the prostate to aid the fertilisation of eggs by spermatozoa. Prostate-specific antigen test is a blood test that quantifies PSA in the blood stream. The PSA may be present in the blood stream for many reasons – including infection or trauma to the prostate, benign prostatic enlargement (BPE), and prostate cancer. The most common reason for elevated PSA levels is BPE, and not all prostate cancers have elevated PSA levels. Consequently, the PSA test has a low

[1] PASC notes that the use of PSA as a screening test for prostate cancer is not currently supported in Australia. However, PASC accepted the pragmatic view that since the high utilisation of the PSA test could already be considered an ad-hoc screening programme, the proposed adjunct (mpMRI) scan did not substantially alter current practice. PASC agreed that the NHMRC guidelines for PSA testing should be considered in context of the present application if and when they are finalised.

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specificity, in the order of 25-30% (Applicant advice). Overall, an elevated level of PSA may be indicative of an elevated risk of prostate cancer, but requires further investigation. (HealthPact 2014; Barentsz et al 2012).

Digital rectal examination (DRE) involves inserting a finger into the rectum to palpate the prostate; swellings, hardenings or lumps may be signs of prostate cancer. The Applicant advises that the DRE has a low sensitivity, although its positive predictive value is high – hard lumps detected by DRE are very likely to be prostate cancer, and while chronic inflammatory conditions can cause hard lumps, this is rare.

However, PSA and DRE tests are not diagnostic; a diagnosis of prostate cancer is made on the basis of biopsy results. During a biopsy, a needle is inserted into the prostate under the guidance of ultrasound, and a set of random samples of tissue (using between 12-32 needles) are taken from the prostate. The samples are then analysed under the microscope, to see if cancer cells are present (Siddiqui et al 2015; AIHW 2013). Prostate cancers are graded using the Gleason system: Gleason score of 6 or less is considered low risk, a Gleason score of 7 is considered intermediate risk, and a score of 8 or above is considered to be high risk (HealthPact 2014). Another risk stratification measure in use is the TNM Classification of Malignant Tumours (TNM), where T describes the size of the tumour, N describes the affected lymph nodes, and M describes the metastases (Cancer Council Australia, 2015).

In magnetic resonance imaging, a magnet together with radio-waves is used to produce images of soft tissues. In multi-parametric MRI, three pulse sequences are used: T2 weighted (T2W), diffusion weighted (DWI) and dynamic-contrast enhanced (DCE). These are combined and analysed together. If the findings are suspicious, a biopsy is conducted to confirm the presence or absence of cancer. Both 1.5 and 3.0 Tesla MRI scanners are available in Australia; either one may be used to carry out multi-parametric scans (HealthPact 2014). However, the Applicant advises that although the new generation 1.5 Tesla MRI scanners may be adequate for mpMRI, the older generation machines are not, as they are unable to acquire the diffusion weighted image (DWI). DWI is a measure of the tissue density of a lesion in the prostate and is a vital tool in diagnosis of cancer within the prostate, as >95% of prostate cancers are more dense than normal prostate tissue.

Estimated utilisation

Men with suspected prostate cancer

In 2012, there were nearly 778,500 PSA tests performed in Australia (AIHW 2013). There are no reliable data available that estimate the proportion of these tests that resulted in a high or concerning PSA level. Consequently, it is difficult to accurately estimate the number of men in Australia with suspected prostate cancer who would be eligible for mpMRI of the prostate. PASC noted that the availability of rebates for mpMRI prostate scans may also increase the number of patients choosing to have regular PSA testing, because affordable access to an adjunct confirmation test would enhance the usefulness of the screening PSA test.

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One method for estimating the number of eligible men is to assume that all men who currently receive a prostate biopsy would have an mpMRI scan if the service was listed on the MBS. Between July 2014 and June 2015, there were 20,149 services claimed on the MBS for ultrasound-guided prostate biopsy (MBS item 37219). From this, there would potentially be 20,149 mpMRI services for men with suspected prostate cancer. This is likely an underestimation of utilisation, as men who refused a prostate biopsy may opt to undergo mpMRI scanning.

Men diagnosed with low or intermediate risk prostate cancer undertaking active surveillance

The AIHW reported that at the end of 2009, the 5-year prevalence of prostate cancer was 86,207 men in Australia (AIHW 2014). Data from the Victorian Prostate Cancer Registry indicates that 15.3% of patients newly diagnosed with prostate cancer are opting to have their disease managed with active surveillance (Weerakoon 2015). Applying this to the prevalence data, there may be approximately 13,190 men undergoing active surveillance for prostate cancer. This may be an overestimate of the current use of active surveillance, as it is an emerging management strategy.

Under the proposed protocol for mpMRI in active surveillance (see Figure 4), men would have a scheduled mpMRI scan at 12 months and then every three years thereafter. Men can also have an mpMRI scan at any time if there is concern about clinical or PSA changes. If you assume that, on average, men on active surveillance will have an mpMRI scan once every two years, then this would equate to 6,595 services for mpMRI per year.

Administration, dose, frequency of administration, duration of treatment

An MBS listing is requested for multiparametric MRI (mpMRI) scans of the prostate for two populations:

1. men who are suspected of having prostate cancer on the basis of a high or concerning PSA; and
2. men diagnosed with low or intermediate risk prostate cancer undertaking Active Surveillance (AS).

An mpMRI scan of the prostate, which is an image acquisition protocol, uses T2W, DWI and DCE, as outlined above. The time required to perform the scan will vary, depending on the protocol and machine used. The Applicant advises that the detection protocol using a 3T scanner would take 35 minutes for an mpMRI, and 45 minutes for an mpMRI of the prostate as well as the bones and nodes. The same protocols on a 1.5T machine would take approximately 50% longer.

Applicants advise that consensus on the question of appropriate frequency of mpMRI scanning has not yet been reached. However, for monitoring purposes, the scans can be repeated after 12 months (as prostate cancer grows very slowly). Active surveillance patients may be scanned every 12 months for a period of time, and then may be switched to 3-yearly scans.

All mpMRI scans of the prostate are performed in a radiology department. PASC and the Applicant agreed that the proposed service will require specialist referral from an urologist, radiation oncologist, or medical oncologist. The reporting radiologist must have MRI accreditation with RANZCR.

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Co-administered interventions

Multiparametric MRI (mpMRI) scans of the prostate involve the following co-administered interventions:

- mp-capable MRI machine
- Gadolinium contrast agent (omitted in patients with renal insufficiency)
- Injection of Buscopan (to limit bowel peristalsis)
- Oral medication (for patients with claustrophobia)
- Pulse oximetry equipment (in patients who require sedation)
- Intravenous access disposables

Of note, the 2015 revision of PI-RADS requires T2WI, DWI and DCE unless contrast administration contraindicated.

Background

Current arrangements for public reimbursement

Current MBS item for ultrasound scans of the prostate, include:

Table 1: Current MBS item descriptors for scans of the prostate

Subgroup 4 - Urological
MBS item 55600 Prostate, bladder base and urethra, ultrasound scan of, if performed: (a) personally by a medical practitioner (not being the medical practitioner who assessed the patient as specified in paragraph (c)) using one or more transducer probes that: (i) have a nominal frequency of 7 to 7.5 MHz or a nominal frequency range that includes frequencies of 7 to 7.5 MHz; and (ii) can obtain both axial and sagittal scans in 2 planes at right angles; and (b) after a digital rectal examination of the prostate by that medical practitioner; and (c) on a patient who has been assessed by a specialist in urology, radiation oncology or medical oncology, a consultant physician in medical oncology, who has: (i) examined the patient in the 60 days before the scan; and (ii) recommended the scan for the management of the patient's current prostatic disease (R) (K) *(See para DIQ of explanatory notes to this Category)* **Fee:** $109.10 **Benefit:** 75% = $81.85 85% = $92.75
MBS item 55601 PROSTATE, bladder base and urethra, ultrasound scan of, where performed: (a) personally by a medical practitioner (not being the medical practitioner who assessed the patient as specified in (c)) using a transducer probe or probes that: (i) have a nominal frequency of 7 to 7.5 megahertz or a nominal frequency range which includes frequencies of 7 to 7.5 megahertz; and (ii) can obtain both axial and sagittal scans in 2 planes at right angles; and (b) following a digital rectal examination of the prostate by that medical practitioner; and (c) on a patient who has been assessed by a specialist in urology, radiation oncology or medical oncology or a consultant physician in medical oncology who has: (i) examined the patient in the 60 days prior to the scan; and (ii) recommended the scan for the management of the patient's current prostatic disease (R) (NK) *(See para DIQ of explanatory notes to this Category)* **Fee:** $54.55 **Benefit:** 75% = $40.95 85% = $46.40
MBS item 55603 PROSTATE, bladder base and urethra, ultrasound scan of, where performed: (a) personally by a medical practitioner who undertook the assessment referred to in (c) using a transducer probe or probes that:

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(i) have a nominal frequency of 7 to 7.5 megahertz or a nominal frequency range which includes frequencies of 7 to 7.5 megahertz; and (ii) can obtain both axial and sagittal scans in 2 planes at right angles; and (b) following a digital rectal examination of the prostate by that medical practitioner; and (c) on a patient who has been assessed by a specialist in urology, radiation oncology or medical oncology or a consultant physician in medical oncology who has: (i)examined the patient in the 60 days prior to the scan; and (ii)recommended the scan for the management of the patient's current prostatic disease (R) (K) *(See para DIQ of explanatory notes to this Category)* **Fee:** $109.10 **Benefit:** 75% = $81.85 85% = $92.75
MBS item 55604 PROSTATE, bladder base and urethra, ultrasound scan of, where performed: (a) personally by a medical practitioner who undertook the assessment referred to in (c) using a transducer probe or probes that: (i) have a nominal frequency of 7 to 7.5 megahertz or a nominal frequency range which includes frequencies of 7 to 7.5 megahertz; and (ii) can obtain both axial and sagittal scans in 2 planes at right angles; and (b) following a digital rectal examination of the prostate by that medical practitioner; and (c) on a patient who has been assessed by a specialist in urology, radiation oncology or medical oncology or a consultant physician in medical oncology who has: (i) examined the patient in the 60 days prior to the scan; and (ii) recommended the scan for the management of the patient's current prostatic disease (R) (NK) *(See para DIQ of explanatory notes to this Category)* **Fee:** $54.55 **Benefit:** 75% = $40.95 85% = $46.40

The current MBS item for the biopsy portion of ultrasound-guided biopsy of the prostate is as follows:

Table 2: Current MBS item descriptor for item 37219

Group T8 – Surgical Operations
MBS item 37219 PROSTATE, needle biopsy of, using prostatic ultrasound techniques and obtaining 1 or more prostatic specimens, being a service associated with a service to which item 55600 or 55603 applies Multiple services rule. (Anaes.) (Assist.) **Fee:** $280.85 **Benefit:** 75% = $210.65 85% = $238.75

Regulatory status

A number of MRI systems are TGA-approved for use in Australia. A recent horizon scan of MRI screening for prostate cancer in Australia has identified the following TGA-listed manufacturers of MRI full-body scanners: Emergo Asia Pacific Pty Ltd (ARTG # 136622); GE Healthcare Australia Pty Ltd (ARTG # 135096; 169744; 169036; 223115); Philips Electronics Australia Ltd (ARTG # 98887, 212690); Siemens Ltd (ARTG # 98319, 98485, 144221, 154128) and Toshiba Australia Pty Ltd (ARTG # 126911). (AIHW 2013)

Patient population

The patient population for mpMRI scans of the prostate are:

1. men who are suspected of having prostate cancer on the basis of a high or concerning PSA; and
2. men diagnosed with low or intermediate risk prostate cancer undertaking active surveillance.

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PASC agreed that whether the PSA result is "high or concerning" is a matter of clinical judgement, which involves interpreting the PSA result in relation to the patient's age, family history, the prostate volume, increase in PSA score over a 12 month period and the results of DRE examinations.

Proposed MBS listing

The proposed MBS listing for mpMRI scans of the prostate is presented in Table 3 below.

Table 3: Proposed MBS item descriptors for mpMRI scans of the prostate

Category 5 – Diagnostic Imaging Services
MBS [item number] Multiparametric Magnetic Resonance Imaging (mpMRI) performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by an urologist, radiation oncologist, or medical oncologist and where: a) a standardised image acquisition protocol involving T2 weighted imaging, Diffusion Weighted Imaging, and Dynamic Contrast Enhancement (unless contraindicated)is used; and b) the man is suspected of having prostate cancer on the basis of a high or concerning PSA. Scan of the prostate for: – detection of cancer (R)(Contrast) Fee: [Applicant advises that current fee charged is $600] [Relevant explanatory notes]
MBS [item number] Multiparametric Magnetic Resonance Imaging (mpMRI) performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by an urologist, radiation oncologist, or medical oncologist and where: a) a standardised image acquisition protocol involving T2 weighted imaging, Diffusion Weighted Imaging, and Dynamic Contrast Enhancement (unless contraindicated) is used; and b) the man has an existing diagnosis of low or intermediate risk prostate cancer and is undertaking Active Surveillance. Scan of the prostate for: – assessment of cancer (R)(Contrast) Fee: [Applicant advises that current fee charged is $600] [Relevant explanatory notes]

Contrast application – MBS item 63491

PASC noted that the cost for the contrast agent is included in the proposed fees. PASC suggested that the cost of the contrast agent should be listed separately, as for other MRI items.

Clinical place for proposed intervention

Clinical scenario 1: men who are suspected of having prostate cancer

Currently, the signs of prostate cancer are detected with a prostate-specific antigen test (PSA) and/or a digital rectal examination (DRE). PSA and DRE are not diagnostic; diagnosis is obtained via ultrasound-guided biopsy (either TRUSGB or TPUSGB). Patients who receive a negative biopsy result will remain under observation and have a follow-up PSA test after twelve months. Patients with a biopsy result indicating intermediate or low risk cancer will be offered active surveillance, which is

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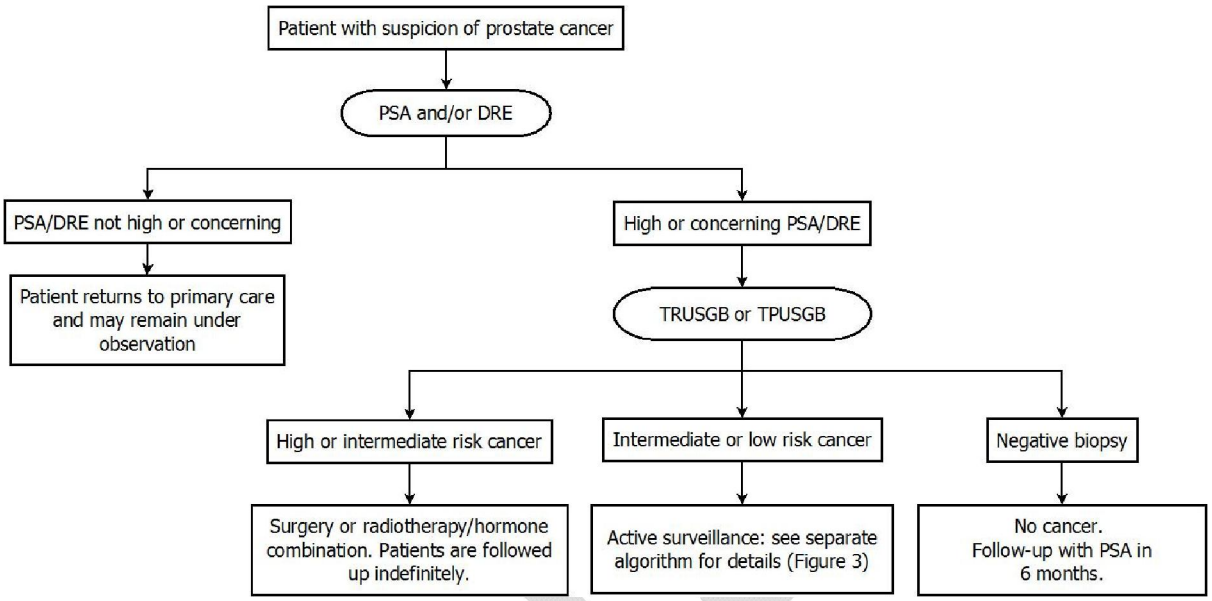
detailed in Figure 3. Patients with a biopsy result indicating high risk or intermediate risk cancer will be offered surgery or a radiotherapy/hormone therapy combination.

Figure 1: Current clinical management algorithm without the proposed intervention



Abbreviations: PSA=prostate-specific antigen test; DRE=digital rectal examination; TRUSGB=trans-rectal ultrasound-guided biopsy; TPUSGB=trans-perineal ultrasound-guided biopsy.

Under the proposed clinical management algorithm for patients with suspected prostate cancer, patients would be imaged using multi-parametric MRI (mpMRI). Criteria for suspected prostate cancer, for the purposes of this protocol is defined as:

- PSA > 3μg/L (or lower level if < 50 years of age – see guidelines) or
- Positive Family History (includes BRCA gene mutation) or
- Free/Total PSA ratio < 25%)

Patients with PI-RADS scores 1, 2, or 3 with low clinical concern, will return to primary care and may remain under observation. Patients with PI-RADS score of 1, 2 or 3 with very high or intermediate clinical concern may have a template biopsy and patients with PI-RADS scores 4 and 5 will have a targeted biopsy of the lesion (either magnetic resonance guided biopsy; MRGB, Fusion, or cognitive). High or intermediate concern is defined as:

- Positive family history/ BRCA gene mutation or
- Free/Total PSA Ratio < 12% or
- PSA density > 0.15.

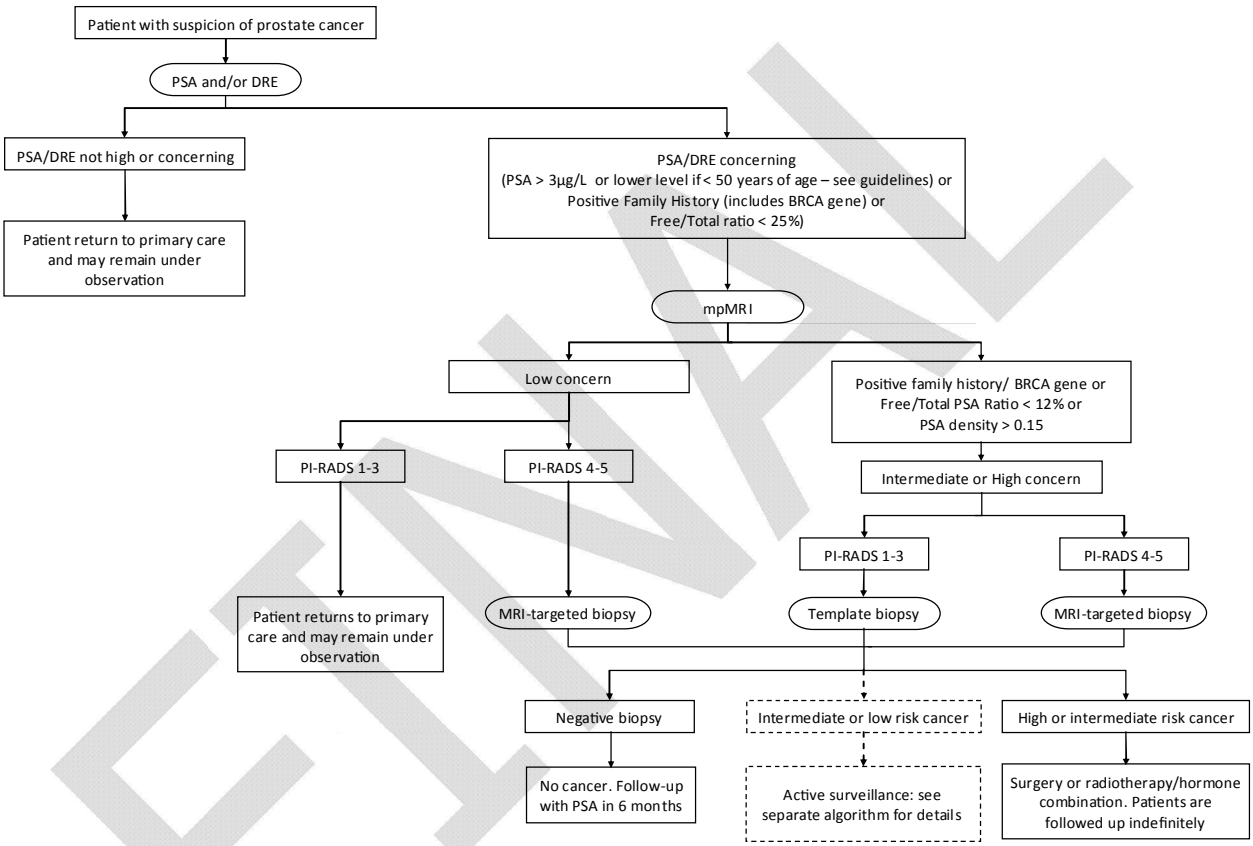
Low concern is defined as patients who have suspected prostate cancer but do not meet the criteria for high or intermediate concern.

Based on the results of the biopsy, patients will either:

- return to primary care under observation, with a follow-up PSA test after six months; or
- undergo active surveillance; or
- have surgery or a radiotherapy/hormone therapy combination for their cancer.

The details of the active surveillance protocol are set out in Figures 3 and 4 have been based on the Applicant's advice and the recent NICE guidelines (2014).

Figure 2: Proposed clinical management algorithm for diagnostic mpMRI



Abbreviations: PSA=prostate specific antigen test; DRE=digital rectal examination; PI-RADS=Prostate Imaging-Reporting and Data System; MR=magnetic resonance; mpMRI=multi-parametric magnetic resonance imaging; MRGB=magnetic resonance guided biopsy; US=ultrasound.
*Indications of increased cancer risk may include patient's age, positive family history, abnormal DRE, PSA doubling time < 2 years, PSA density > 0.15, free/total PSA ratio < 25%, Prostate Health Index > 25, known BRCA1 or BRCA2 gene mutation.

Clinical scenario 2: men diagnosed with prostate cancer undertaking active surveillance

Men who have a diagnosis of intermediate or low risk cancer may choose to participate in Active Surveillance. During active surveillance men will undergo scheduled testing (PSA, PSA kinetics and DRE) over a period of five years or more. Men also have scheduled prostate biopsies at 12 months and then every three years thereafter. At any point in time, if there is concern about clinical or PSA/DRE changes, men can opt to have an additional prostate biopsy. Based on the results of these biopsies, men will either continue on active surveillance or be offered surgery or a radiotherapy/hormone therapy combination for their cancer. The full details of the current active

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surveillance protocol are set out in Figure 3 have been based on the Applicant's advice and the recent NICE guidelines (2014).

If the proposed mpMRI service is added to the active surveillance protocol it will be used as an additional test prior to prostate biopsy. Men who are due for their scheduled biopsy and men who have concern about clinical or PSA/DRE changes would first have an mpMRI scan. The criteria for concern are the same as for clinical scenario 1 (PSA > 3μg/L or lower level if < 50 years of age, positive family history or free/total PSA ratio < 25%). Men with PI-RADS scores 1, 2, and 3 with low clinical suspicion will return to active surveillance. Men with intermediate/high risk (defined the same as in clinical scenario 1: positive family history, free/total PSA ratio < 12% or PSA density > 0.15, regardless of PI-RADS score), and men with low risk and a PI-RADS score of 4-5 will continue with a re-biopsy. Patients with a PI-RADS score of 4-5 would have an in-gantry MRGB or an US-MR (Ultrasound-Magnetic resonance) fusion-guided biopsy (both are MRI-targeted biopsy techniques), while patients with a PI-RADS score of 1-3 (intermediate/high risk) would have a template biopsy. Based on the results of these biopsies, men will either continue on active surveillance or be offered surgery or a radiotherapy/hormone therapy combination for their cancer. The details of the proposed protocol for active surveillance are presented in Figure 4. The clinical claim for either in-gantry MRGB or US-MR fusion-guided biopsy can be assessed after the completion of Application 1424.

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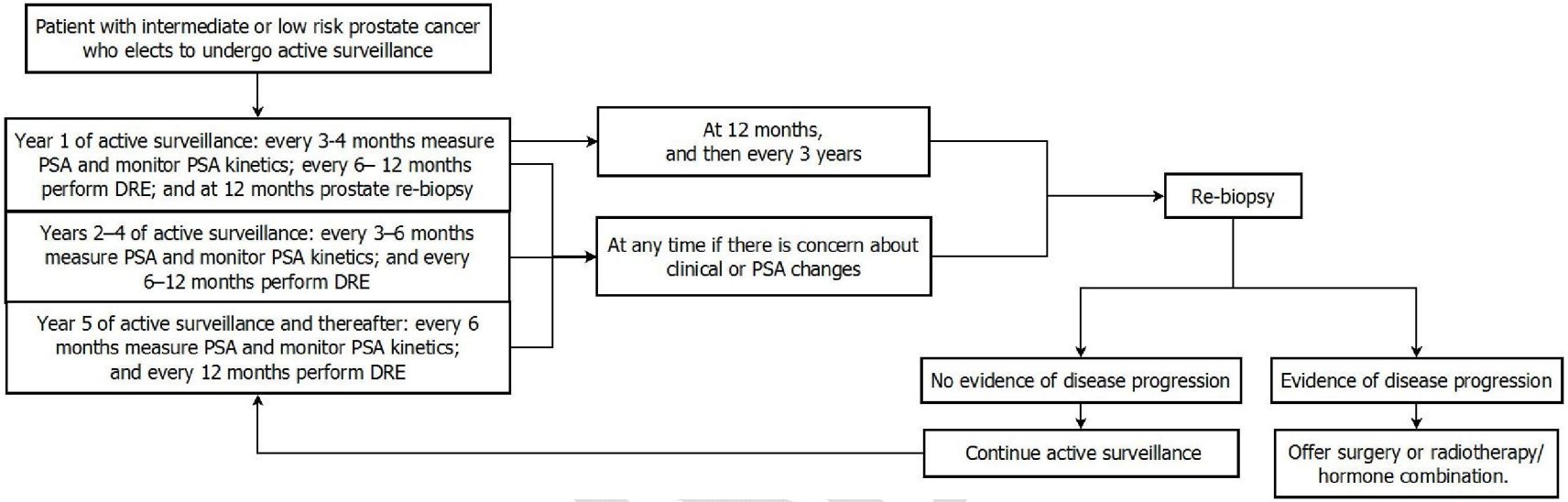
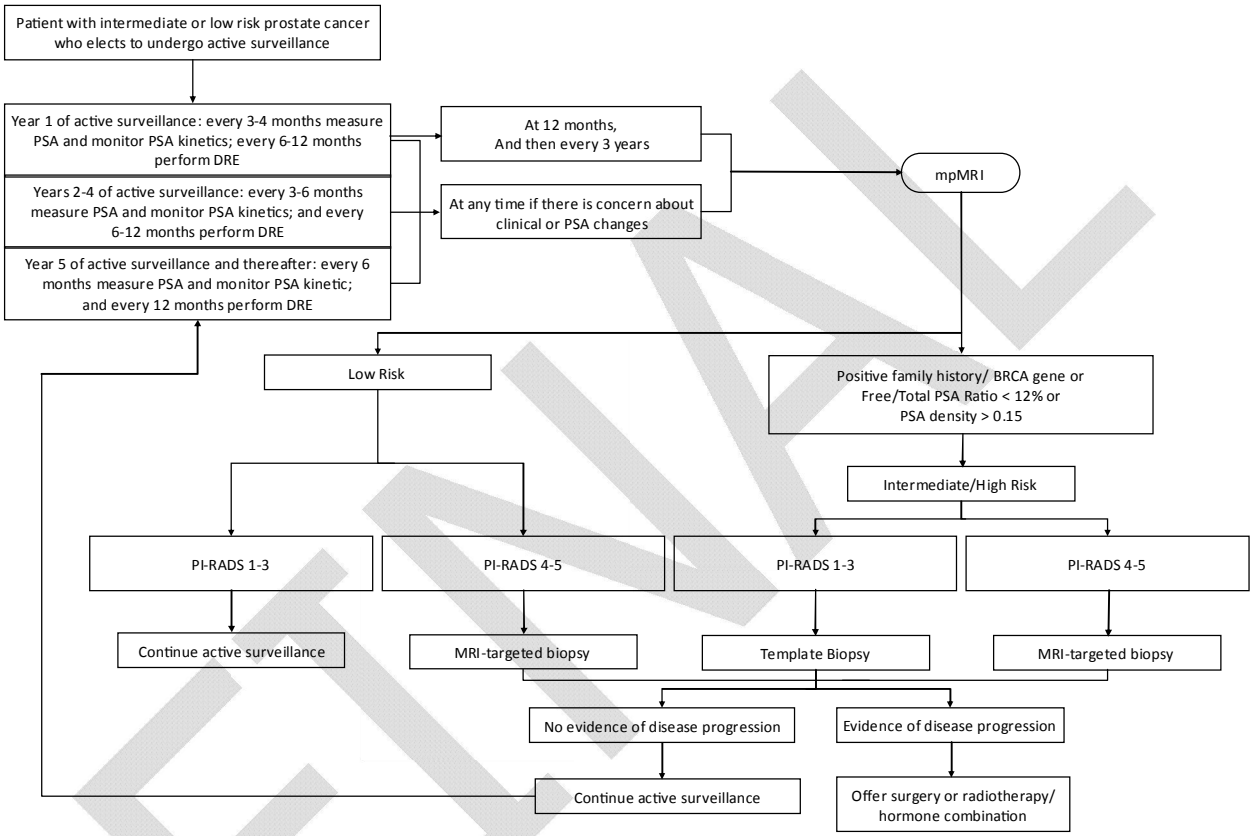
Figure 3 Current protocol for Active Surveillance without the proposed intervention



Abbreviations: PSA=prostate-specific antigen test; DRE=digital rectal examination.

Figure 4 Proposed protocol for Active Surveillance with mpMRI



Abbreviations: PSA=prostate specific antigen test; DRE=digital rectal examination; PI-RADS=Prostate Imaging-Reporting and Data System; MR=magnetic resonance; mpMRI=multi-parametric magnetic resonance imaging; US=ultrasound.

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Comparator

For men who are suspected of having prostate cancer on the basis of a high or concerning PSA, the comparators are:

1. DRE/PSA + clinical judgement and US-guided trans-rectal or trans-perineal biopsy (TRUSGB or TPUSGB)
2. DRE/PSA + clinical judgement alone, for patients who elect not to undergo TRUSGB or TPUSGB

For men diagnosed with low or intermediate risk prostate cancer undertaking active surveillance, the comparator is the current active surveillance protocol with routine re-biopsy.

Reference standard test

The reference standard is subsequent pathology (testing of the acquired samples).

Clinical claim

Use of mpMRI will result in more accurate selection of patients for biopsy, with approximately half of all men presenting to urologists for suspected prostate cancer avoiding biopsy altogether, if they have a PIRADS 1-2 scan (Pokorny 2014). The higher diagnostic accuracy of mpMRI would result in a reduction of diagnoses of low risk cancer and therefore a reduction in overtreatment in this patient population (Rosenkrantz 2015; Ghai 2015).

The clinical claim is that multiparametric MRI (mpMRI) scans of the prostate are more accurate (hence, more effective) and safer than the current approach. In the event that claims of superior efficacy and safety are supported by the literature, either a cost-utility or a cost-effectiveness analysis would be appropriate.

Table 4: Classification of an intervention for determination of economic evaluation to be presented

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="4">Comparative effectiveness versus comparator</td></tr>
<tr><td colspan="2">Superior</td><td>Non-inferior</td><td colspan="2">Inferior</td></tr>
<tr><td rowspan="5">Comparative safety versus comparator</td><td rowspan="3">Superior</td><td colspan="2" rowspan="3">CEA/CUA</td><td rowspan="3">CEA/CUA</td><td>Net clinical benefit</td><td>CEA/CUA</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
<tr><td>Non-inferior</td><td colspan="2">CEA/CUA</td><td>CEA/CUA*</td><td colspan="2">None^</td></tr>
<tr><td rowspan="3">Inferior</td><td>Net clinical benefit</td><td>CEA/CUA</td><td rowspan="3">None^</td><td colspan="2" rowspan="3">None^</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
</table>

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

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Outcomes and health care resources affected by the proposed intervention

Outcomes

For the multiparametric MRI (mpMRI) scans of the prostate, this assessment will consider:

- Effectiveness
    - Health outcomes: change in overall survival, change in prostate cancer specific mortality, change in incontinence, change in impotence
    - Diagnostic accuracy: sensitivity, specificity, PPV, NPV
    - Change in management: changes in the biopsy rate, changes in the rate of men diagnosed with low risk cancer, change in the rates of surgery
    - Patient outcomes: quality of life, satisfaction, time from diagnosis to treatment
- Safety
    - Adverse events: change in biopsy-induced trauma, change in biopsy-induced haemorrhage
- Cost-effectiveness or cost-utility

PASC noted feedback received from the Royal College of Pathologists of Australasia that is may not be feasible to measure change in overall survival and change in prostate cancer specific mortality due to the long natural history of prostate cancer (typically >10 years from diagnosis to death). The RCPA also advised that the savings in pathology costs are likely to be insignificant compared to the additional cost of mpMRI.

PASC noted feedback from the Urological Society of Australia and New Zealand (USANZ) and the Applicant that the adverse outcomes of biopsy were overstated in the initial application, as there is a growing trend to trans-perineal biopsies in Australia that have a close to 0% risk of sepsis. Adverse outcomes can include admission to an Intensive Care Unit (ICU) or hospital.

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Proposed structure of economic evaluation (decision-analytic)

Table 6: Summary of extended PICO to define research question that assessment will investigate

Patients	Prior test	Intervention	Comparator	Outcomes to be assessed
1. Men who are suspected of having prostate cancer on the basis of a high or concerning PSA level. 2. Men diagnosed with low or intermediate risk prostate cancer undertaking active surveillance.	DRE/PSA	Multiparametric MRI (mpMRI) scans of the prostate	In suspected prostate cancer: • DRE/PSA + clinical judgement + TRUSGB/TPUSGB • DRE/PSA + clinical judgement alone In active surveillance population: • Active surveillance including routine biopsy.	*Effectiveness* ○ Health outcomes: change in overall survival, change in prostate cancer specific mortality, change in incontinence, change in impotence ○ Diagnostic accuracy: sensitivity, specificity, PPV, NPV ○ Change in management: changes in the biopsy rate, changes in the rate of men diagnosed with low risk cancer, change in the rates of surgery ○ Patient outcomes: quality of life, satisfaction, time from diagnosis to treatment *Safety* ○ Adverse events: change in biopsy-induced trauma, change in biopsy-induced haemorrhage *Economic:* ○ Cost-effectiveness or cost-utility

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