1237

Final protocol to guide the assessment of cardiac magnetic resonance imaging of patients with known or suspected coronary artery disease

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MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Australian Government Minister for Health 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 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

Purpose of application

An application requesting MBS listing of magnetic resonance imaging (MRI) for myocardial stress perfusion and myocardial viability imaging in patients with known or suspected coronary artery disease (CAD) was received from The Cardiac Society of Australia and New Zealand by the Department of Health and Ageing in September 2011.

The use of MRI for the investigation of suspected CAD is thought to offer superior safety and diagnostic accuracy compared to existing diagnostic modalities. MRI is through to offer non-inferior diagnostic accuracy and superior safety compared to existing imaging modalities for guiding treatment pathways in patients with known CAD. The applicant has requested the addition of two new MBS items for cardiac MRI (CMRI) in the following populations:

1. Patients presenting with symptoms consistent with stable ischaemic heart disease, with an intermediate pre-test probability of CAD.
2. Adult patients with an existing diagnosis of significant CAD, who have a history of ischaemic heart disease, impaired left ventricular function, and are being considered for revascularisation.

Intervention

Description

MRI utilises strong, uniform magnetic fields to investigate the anatomy, perfusion, tissue characterisation and function of different organs and systems within the human body. When hydrogen protons present in human cells are exposed to this magnetic field, they align along its rotational axis in a uniform plane. In order to generate an image, a sequence of smaller magnetic pulses is targeted towards the area of interest, exciting the protons, which then release radiofrequency signals upon relaxation (Hundley et al 2010). These signals are then converted into an image, which represents the concentration of hydrogen protons in different tissue, making MRI particularly useful for imaging soft tissues with a high concentration of water.

CMRI uses a standard magnetic resonance scanner, with or without specialised cardiac coils, and specialised software for quantitative analysis. The latter may be incorporated within the scanner by the scanner vendor. Third party software that is external to the scanner is also available, and is more commonly applied in clinical practice as the scanners are occupied during analysis.

During the examination, patients are required to lie in either a prone or supine position within the MRI machine, with as little movement as possible. Movement during the imaging procedure will misalign the hydrogen protons on the plane being imaged, and blur the picture. The magnetic field strength within conventional MRI scanners are either 1.0T (Teslas), 1.5T or 3.0T; however, the majority of scanners utilise 1.5T fields for CMRI (Bruder et al 2009). In cardiac imaging the use of higher strength fields allows for images with higher spatial resolution, but also increases the chance of imaging artefacts that can obscure the image (Hundley et al 2010). Cardiac images obtained by MRI are interpreted by either a qualified cardiologist or radiologist.

The applicant has indicated that CMRI has potential applications in the diagnosis and management of all cardiology disease processes, including ischaemic heart disease, valvular heart disease, cardiomyopathy, heart failure, congenital heart disease, and other vascular disease (Hundley et al 2010). For the purposes of this protocol, the applicant has indicated that only patients with suspected or existing stable CAD are considered.

Administration, dose, frequency of administration, duration of treatment

The proposed medical service will be provided as either an inpatient or outpatient service. A CMRI study requires approximately 45-60 minutes of image acquisition time, plus 15-30 minutes of software analysis time, and 15-30 minutes of expert reporting time. As CMRI utilises magnetic fields to image anatomy and function, patients are not exposed to ionizing radiation. Images of the heart at rest are acquired in each type of CMRI test (i.e. myocardial perfusion and viability). For perfusion testing, images are also acquired at peak pharmacological stress.

Although general practitioners may refer patients for limited MRI procedures, it is intended that specialist referral be required for CMRI procedures due to the complexity of the test, specialist understanding of its uses and limitations, and interpretation of image scans. Current legislative requirements stipulate that Medicare eligible MRI items must be reported on by a trained and credentialed specialist in diagnostic radiology. In order to satisfy the Chief Executive of Medicare, the specialist must be a participant in the Royal Australian and New Zealand College of Radiologist's (RANZCR) Quality and Accreditation Program (Health Insurance Regulation 2013 – 2.5.4 – Eligible Providers) (Australian Government 2013). Legislative changes would be required to allow cardiologists to report on CMR scans, and there would need to be support from the sector for this change to occur. It is the intention of the applicant that the radiologist or cardiologist trained in CMRI be personally available to attend all CMRI examinations.

The level of specialist accreditation recommended for CMRI procedures by the applicant is equivalent to at least Society for Cardiovascular Magnetic Resonance (SCMR) level 2 training. These guidelines are broadly applicable, and are consistent with Australian practice. However, a specific training document for the provision of CMRI services has been developed for Australia by the Cardiac Society of Australia and New Zealand's Imaging Council. The requirement for a minimum level of training for radiologists is encouraged by the Department; however, this will have an impact on the initial availability of CMRI services as it is presumed that few Australian radiologists have attained these qualifications to date. The applicant estimates that 20 to 25 sites around Australia currently have the workforce capacity to conduct CMRI. The applicant suggests that the proposed service should not be considered a standard radiological procedure due to the additional complexity of the test in terms of defining cardiac pathologies. Although sufficiently accredited radiologists or cardiologists may report on CMR images, the proposed services is primarily intended to be utilised by cardiologists.

The applicant has suggested that for the initial diagnosis of CAD, the proposed medical service would initially be utilised as a single, once-off test for viability and perfusion. In the vast majority of these patients, limiting the use of CMRI to one service per 12 month period would be sufficient. An exception to this recommendation would include cases of new diagnosis of left ventricular thrombus in the setting of CAD, in which a follow-up scan (e.g. 3 or 6 months) would be necessary to determine the success, and necessity for continuing, anticoagulant treatment.

Background

Current arrangements for public reimbursement

There are currently five items related to CMRI listed on the MBS listed in Appendix A. These items relate to the investigation of vascular abnormalities in patients with a previous anaphylactic reaction to an iodinated contrast medium, the investigation and diagnosis of congenital heart or great vessel defects, the investigation of heart or great vessel tumours, and co-administered contrast agents for use with CMRI.

For the investigation of CAD, there is currently limited funding provided by the Victorian Government to The Alfred Hospital for CMRI investigation. There may be other State-based public hospital arrangements for CMRI; however, these arrangements are currently limited to public hospital inpatients. The applicant suggests that CMRI for CAD is not currently covered by private health insurance. Private patients who utilize CMRI services are therefore required to pay the full cost of the procedure out-of-pocket. This is a dominant factor in the current state of utilisation of CMRI services beyond the current MBS items.

Regulatory status

The proposed medical service can be used on standard whole body MRI systems that use specialised cardiac software, and either abdominal coils, body coils, thoracic coils or specialised cardiac coils. The use of specialised cardiac coils offers certain advantages, but should not necessarily preclude the use of CMRI on MRI systems that utilise other types of coil.

There are a large number of MRI devices included on the ARTG, some examples of which are provided in Table 1. For the purposes of ARTG classification MRI machines are considered active medical devices for diagnosis; meaning that the device is intended by the manufacturer to be used on a human being, either alone or in combination with another medical device, to supply information for the purpose of detecting, diagnosing, monitoring or treating physiological conditions, states of health, illness or congenital deformities (Therapeutic Goods Administration 2011). The classification of devices in this category varies according to the intended purpose of the device. MRI machines are Class IIa (low-medium risk) or Class IIb (medium-high risk) medical devices.

MRI systems would be included as Class IIa devices under rule 4.3(2)(a) where it is considered that the device will supply energy that will be absorbed by a patient's body and Class IIb devices if the intended purpose of the device is:

- to monitor vital physiological parameters of a patient, and the nature of variations monitored could result in immediate danger to the patient [rule 4.3(3)(a)]; or,
- to control, monitor or directly influence the performance of another device [rule 4.3(3)(c)] (Therapeutic Goods Administration 2011).

Conventional MRI is available in private and public facilities across Australia and there are 349 (171 full and 178 partial) Medicare-eligible MRI units in Australia, however the capacity for CMRI is currently unknown as there are no mechanisms for registering the number of MRI machines equipped with specialised cardiac software (The Department of Health 2013). Based on the limited use of CMRI

in State-based and private hospitals, the applicant estimates that there are between 20 and 25 sites in Australia which have specialised cardiac coils, dedicated cardiac software, and technologists and physicians with the requisite experience to conduct CMR scans. This is likely to be a limiting factor in the initial uptake of the proposed service.

Table 1   Examples of TGA approved full-body MRI devices included on the ARTG

ARTG no.	Sponsor	Item Description	Device Class
98887	Philips Electronics Australia Ltd	Digital Imaging and diagnosis of patients.	IIb
212690	Philips Electronics Australia Ltd	Digital Imaging and diagnosis of patients. It can produce cross-sectional images, spectroscopic images and/or spectra in any orientation of the internal structure of the head, body or extremities.	IIa
98319	Siemens Ltd	Whole body imaging techniques including functional imaging.	IIb
126911	Toshiba Australia Pty Ltd	The MRI system is indicated for use as a diagnostic imaging modality that produces cross- sectional transaxial, coronal, sagittal and oblique images that display anatomic structures of the head and body.	IIa

Proposed MBS listing

The proposed MBS item descriptors were developed by the assessment group in consultation with the applicant. The applicant has suggested that CMR stress myocardial perfusion imaging requires a more complicated technique to myocardial viability sequences, and should attract a higher fee to cover the additional time and resources required to perform the scan. Feedback from HESP indicates that MR stress myocardial perfusion imaging requires a similar or greater amount contrast agent compared to myocardial viability sequences, as well as an infusion of the pharmacological stress agent. These factors are reflected in the proposed fee for each item. The original application requested that new MBS items be made available via specialist referral only. PASC guidance indicates that as evidence emerges the first proposed MBS item may need to be revised to allow for GP referral, as CMRI may act as a replacement for current GP-ordered tests for CAD.

Table 2   Proposed MBS item descriptors for cardiac magnetic resonance imaging procedures

Category 5 – Diagnostic Imaging Services
MBS [item number (Note: this will be assigned by the Department if listed on the MBS)]
NOTE: Benefits are payable for each service included by Subgroup 15 on one occasion only in any 12 month period
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 the request for the scan specifically identifies the clinical indication for the scan - scan of the heart for:
(a) myocardial viability using delayed gadolinium enhancement (Contrast); and
(b) stress myocardial perfusion (Contrast); and
(c) the request for the scan identifies that the patient presents with:
(i) symptoms consistent with stable ischaemic heart disease, with an intermediate pre-test probability of coronary artery disease.
Fee: $900 Benefit: 75% = $675 85% = $765

MBS [item number (Note: this will be assigned by the Department if listed on the MBS)]

NOTE: Benefits are payable for each service included by Subgroup 15 on one occasion only in any 12 month period

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 the request for the scan specifically identifies the clinical indication for the scan - scan of the heart for:

(a) myocardial viability using delayed gadolinium enhancement (Contrast); and

(b) the request for the scan identifies that an adult patient being considered for revascularisation presents with:

    (i) an existing diagnosis of significant CAD, a history of ischaemic heart disease and impaired left ventricular function.

Fee: $700 Benefit: 75% = $525 85% = $595

Patient Population

Coronary artery disease is the leading cause of death in Australia, responsible for 12,047 male and 10,476 female deaths in 2009 (Australian Insitute of Health and Welfare 2011). In 2010, CAD accounted for 15 per cent of all registered deaths in Australia. In 2007-2008, it was estimated that three per cent of the Australian population was affected by CAD (Australian Insitute of Health and Welfare 2011). Although the true incidence of CAD in Australia is unknown, an estimate from 2007, derived from the number of major coronary events or myocardial infarction in a year, was around 49,000 events per year for people aged between 40 and 90 years. Of those events, 40 per cent were fatal.

In 2003, CAD (including secondary heart failure) was estimated to be the leading specific cause of overall disease burden for males, accounting for 11 per cent of the burden of disease (Australian Insitute of Health and Welfare 2011), and was the second leading specific cause for females, accounting for nine per cent of disease burden. In 2007-2008, two per cent of hospitalizations were attributed to CAD, representing 34 per cent of hospitalizations for cardiovascular disease in general. Of the hospitalizations for CAD, 44 per cent were due to angina (myocardial ischaemia), and 35 per cent for acute myocardial infarction (heart attack)(Australian Insitute of Health and Welfare 2011). The rate of hospitalization was double for males compared to females in each age group, and was more common (about 60 per cent) in those aged 65 years and above.

As mentioned previously, the current application requests two MBS items to cover the use of CMRI in symptomatic patients with suspected stable CAD, and patients with known CAD who are being considered for surgical revascularisation. The relevant PICO criteria to guide the assessment of CMRI for each population are discussed in the following sections.

Population 1

The first proposed population includes patients presenting with symptoms consistent with stable ischaemic heart disease, with an intermediate pre-test probability (PTP) of CAD. An intermediate risk probability of CAD is defined by the European Society of Cardiology as patients with a PTP ranging between 15 and 85 per cent (Montalescot et al 2013). A patient's PTP of CAD can be determined

using a number of criteria, including age, gender, family history, and the nature of chest pain. An example of a clinical decision matrix used to determine the PTP of a patient with chest pain symptoms is presented in Table 3 (Genders et al 2011).

Table 3   Pre-test probability of CAD, stratified by age, gender, and nature of chest pain symptoms

	Typical chest pain		Atypical chest pain		Non-anginal chest pain	
Age	Men	Women	Men	Women	Men	Women
30-39	59.1	27.5	28.9	9.6	17.7	5.3
40-49	68.9	36.7	38.4	14.0	24.8	8.0
50-59	77.3	47.1	48.9	20.0	33.6	11.7
60-69	83.9	57.7	59.4	27.7	43.7	16.9
70-79	88.9	67.7	69.2	37.0	54.4	23.8
>80	92.5	76.3	77.5	47.4	64.6	32.3

Table source: Genders et al. 2011.

The applicant recommends that the condition of "exercise and/or electrocardiogram (ECG) stress testing unfeasible" not be used to limit this population for two reasons: first, there are patients in whom ECG will report a high proportion of false positive results, and in whom CMRI is superior regardless of the feasibility of exercise or ECG stress testing. Second, the MBS items for comparator tests (i.e. SPECT or stress echocardiography) are not limited in this way.

Intervention

The proposed use of CMRI for the first population is reflected in the first proposed MBS item, which incorporates both myocardial stress perfusion and myocardial viability MRI sequences.

Stress myocardial perfusion CMRI is used to assess the contractile reserve of myocardium through the application of pharmacological stress. Change to myocardial perfusion is one of the earliest manifestations of CAD. When coronary arteries become narrowed due to atherosclerotic processes, the resistance of distal perfusion beds is reduced in an attempt to normalise myocardial blood flow and maintain myocardial oxygen supply. In order for perfusion changes at resting blood flow to be detectable, a stenosis must be greater than 85 per cent of the lumen diameter (Fihn et al 2012; Salerno and Beller 2009). However, less severe stenoses may be detected by reduced maximal coronary flow in response to vasodilator stimulus. Stress perfusion testing aims to induce coronary vasodilation, either through pharmacological means or exercise (Fihn et al 2012). Perfusion abnormalities can be indicative of underlying CAD and may provide both diagnostic and prognostic information (Schwitter et al 2008). Delayed and functional contrast-enhanced viability CMRI are also used in this population to determine the presence of necrotic or scarred myocardium (Woodard et al 2006). HESP feedback suggests that viability imaging is used in conjunction with stress perfusion imaging sequences to provide the most accurate diagnosis of CAD.

Co-administered interventions

CMRI procedures involving stress perfusion require the additional use of a gadolinium chelate contrast agent, currently listed on the MBS as item number 63491 (see Table 9). Delayed contrast-enhanced MRI uses gadolinium-based contrast agents to define the extent of irreversibly damaged myocardium (Medical Advisory Secretariat 2010). The total dose of contrast required is dependent on the type of gadolinium used, and the weight of the patient. The applicant has suggested that the volume of contrast agent required for myocardial stress perfusion testing is greater than for non-cardiac applications, and that the current item for the use of contrast agents with magnetic resonance angiography (MBS Item 63491) is unlikely to offset the additional cost of the proposed service. In contraindicated patients, the sensitivity for detecting diseases through tissue characterisation and viability would be significantly decreased.

During stress perfusion testing, a pharmacological agent (either adenosine or dobutamine) will be administered intravenously to induce increased myocardial oxygen demand and inotropy. Pharmacological stress agents are also used for stress nuclear or stress echocardiography imaging, with the dose dependent on the agent used and patient weight. In MRI stress perfusion, first-pass perfusion imaging would typically be performed under peak pharmacological stress induced by dobutamine or adenosine.

Clinical place for proposed intervention

The natural history of CAD is progression from a mild to a severe stenosis within a coronary artery. The ischaemic cascade hypothesis indicates that the coronary stenosis first causes a reduction in perfusion, then inducible wall motion abnormalities, then ECG changes and finally angina. The reduction in blood supply first leads to myocardial ischaemia during stress (or exertion) and can progress to ischaemia occurring at rest. This coronary stenosis can lead to myocardial infarction and subsequently to heart failure and death. While there may be no presenting symptoms prior to an acute ischaemic event, common symptoms include angina (chest pain) and shortness of breath.

The clinical pathway for patients with suspected CAD, shown in Figure 1, has been informed by the European Society of Cardiology's guidelines for the diagnosis of stable CAD (Montalescot et al 2013). CMRI is intended to be used in patients with suspected CAD, who are not at immediate or high risk of death, and following clinical assessment, troponin testing and resting ECG and echocardiography. CMRI is posed as an alternative to existing stress testing modalities and computed tomography coronary angiography (CTCA). It is possible that CTCA or invasive coronary angiography (ICA) may be conducted following CMRI to confirm the presence of significant CAD; however, patients imaged with CMRI may avoid CTCA if perfusion imaging detects significant inducible ischaemia. The applicant suggests CMRI may be used in addition to existing stress testing methods in a minority of cases (~1%). PASC notes that justification of this estimate must be presented in the assessment.

Figure 1 Clinical pathway for the diagnosis of patients with suspected ischaemic heart disease who do not have suspected high risk lesions
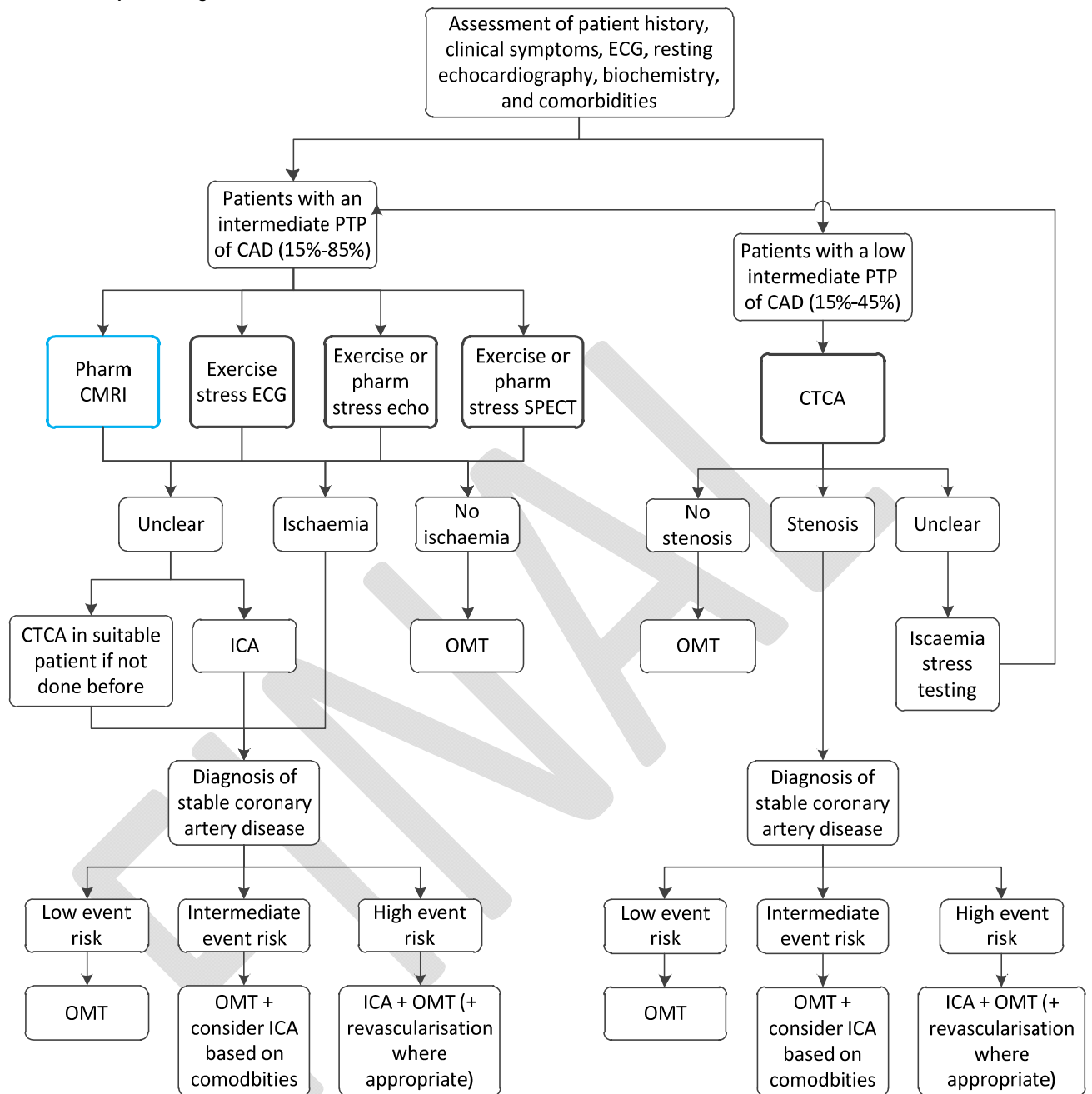
CAD: coronary artery disease. CMRI: cardiac magnetic resonance imaging. CTCA: computed tomography coronary angiography. ECG: electrocardiography. Echo: echocardiography. ICA: invasive coronary angiography. OMT: optimal medical therapy. PTP: pre-test probability. SPECT: single photon emission computed tomography.

Comparator(s)

1. <u>Exercise electrocardiography (ECG) in patients with an interpretable ECG able to complete a treadmill test (MBS Item 11712)</u>

Exercise stress testing with 12-lead ECG is a simple, affordable and widespread modality for detecting inducible ischaemia in patients with suspected CAD. An ECG examination records the electrical conduction of the heart to determine the presence of myocardial damage caused by ischaemia. The primary diagnostic indicator for myocardial ischaemia is ≥1mm horizontal or down-sloping ST-segment depression 0.08 seconds after the J-point, in one or more leads during peak stress (Fihn et al 2012). The diagnostic utility of exercise ECG is affected by resting ECG abnormalities, inability to reach peak exercise stress, inability to exercise, and the use of anti-ischaemic medication (Montalescot et al 2013).

2. <u>Exercise or dobutamine stress echocardiography (MBS Items 55116, 55117, 55122, 55123)</u>

Stress echocardiography can be used to define regional or global left ventricular dysfunction caused be inducible ischaemia. Wall motion abnormalities induced by exercise or pharmacological stress are diagnostic markers for the presence of myocardial ischaemia (Fihn et al 2012). Exercise is the primary method of stress where possible, with pharmacological agents typically reserved for patients who are unable to exercise. Pharmacological stress agents are recommended in patients with resting wall motion abnormalities (Montalescot et al 2013).

3. <u>Exercise or pharmacologic (adenosine or dobutamine) single-photon emission computed tomography (SPECT) (MBS Items 61302, 61303, 1306, 61307, 61651, 61652, 61653, 61654)</u>

SPECT utilises technetium-99m or thallium-201 radiopharmaceutical tracers to visualise regional myocardial blood flow and perfusion (Montalescot et al 2013). Regional areas affected by myocardial ischaemia are identified by monitoring tracer uptake under peak stress (either pharmacological or exercise) compared to baseline uptake during rest. As with the previously mentioned comparator tests, the use of pharmacological stress agents is only preferred for patients who are unable to otherwise exercise, or in whom an exercise stress test has returned an equivocal result.

4. <u>Computed tomography coronary angiography (CTCA) (MBS Items 57360, 57361)</u>

CTCA utilises intravenous contrast to visualise the lumen of coronary arteries, and is therefore able to diagnose myocardial ischaemia due to coronary artery stenosis. The use of CT to image coronary arteries where possible may avoid the use of invasive coronary catheterisation. However, the use of CTCA is contraindicated in patients who are obese, cannot hold a breath, have high calcium scores (e.g. Agatston score > 400), an irregular heart rate (e.g. atrial fibrillation) or a regular heart rate greater than 65 beats per minute (Montalescot et al 2013). CTCA is primarily indicated for patients who have a low intermediate PTP of CAD (15-45%) (Paech and Weston 2011).

Reference standard

Invasive coronary angiography (ICA) is currently the gold standard used to confirm or rule out a diagnosis of CAD. Due to its invasiveness, ICA is only recommended in stable patients with suspected CAD if non-invasive testing provides inadequate information to determine the likelihood of a cardiac event (Montalescot et al 2013).

Outcomes

Effectiveness

Health outcomes

Cardiac disease specific mortality rate

Survival rate

Adverse cardiac event over defined period

Cardiac hospitalisation

Quality of life scores

Diagnostic accuracy (for detecting myocardial ischaemia)

Sensitivity, specificity (confirmed by reference standard)

Positive likelihood ratio, negative likelihood ratio (confirmed by reference standard)

Positive predictive value, negative predictive value (confirmed by reference standard)

ROC curves

Unsatisfactory or uninterpretable test results

Patient management

Change in clinical diagnosis

Change in treatment pathway (initiated, ceased, modified, avoided)

Patient compliance/preference for with imaging

Time to initial diagnosis

Time from diagnosis to treatment

Safety

Gadolinium contrast adverse reaction

Claustrophobia

Physical harms from follow-up testing

Other adverse events arising from CMRI

Cost-effectiveness

Cost

Cost per quality adjusted life year or disability adjusted life year

Incremental cost-effectiveness ratio

Clinical claim

As stated previously, CMRI is posed as an alternative to CTCA and existing ischaemia stress testing modalities. The applicant claims that the proposed medical service has superior diagnostic accuracy compared to existing stress testing modalities. This claim is made on the basis that CMRI for CAD

provides more detailed information, and more reliable data with reduced inter- and intra-observer variability (Greenwood et al 2012). These improvements are proposed to have the following benefits for patient health outcomes compared to existing stress testing modalities:

  i.   Reduced test failure rate, leading to earlier diagnosis and management of CAD, or earlier exclusion of CAD.
  ii.   Improved sensitivity, which will lead to additional/earlier case detection and management, with fewer false negatives.
  iii.   Improves specificity, which will lead to fewer false positives, reducing the need for further invasive testing.

CMRI is also posed as an alternative to CTCA for patients with a low intermediate risk of CAD (15-45%), therefore avoiding patient exposure to ionising radiation. It is possible that CTCA may be conducted following an equivocal CMRI result to confirm the presence of significant CAD; however, patients imaged with CMRI may avoid CTCA if perfusion imaging detects significant inducible ischaemia.

Appropriate therapy choices are contingent upon the correct diagnosis of disease and underlying pathologies. It is suggested that the use of CMRI instead of comparator imaging modalities will reduce the need for CTCA, ICA and myocardial biopsy in eligible patients. The use of CMRI would replace echocardiography, nuclear SPECT imaging in the one single examination thereby reducing downstream costs due to layered testing. A HESP member has suggested that it would require a major shift in referral patterns to fully replace echocardiography and nuclear cardiac testing, as they are firmly entrenched in the standard workup of cardiac patients.

Table 4   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

Summary of PICO for Population 1

Table 5 Summary of extended PICO to define research question that assessment will investigate for population 1

Patients	Intervention	Comparator(s)	Reference test(s)	Outcomes to be assessed
Patients presenting with symptoms consistent with ischaemic heart disease, with an intermediate pre-test probability of CAD	Cardiac MRI of myocardial stress perfusion, and viability using delayed gadolinium enhancement	1. Exercise ECG in patients with an interpretable resting ECG, who are able to complete a treadmill test; for others: 2. Exercise or dobutamine stress echo 3. Exercise or pharmacologic (adenosine or dobutamine) SPECT 4. CTCA	1. Coronary angiography	**Effectiveness** _Health outcomes_ Cardiac disease specific mortality rate Survival rate Adverse cardiac event over defined period Cardiac hospitalisation Quality of life scores _Diagnostic accuracy (for detecting myocardial ischaemia)_ Sensitivity, specificity (confirmed by reference standard) Positive likelihood ratio, negative likelihood ratio (confirmed by reference standard) Positive predictive value, negative predictive value (confirmed by reference standard) ROC curves Unsatisfactory or uninterpretable test results _Patient management_ Change in clinical diagnosis Change in treatment pathway (initiated, ceased, modified, avoided) Patient compliance/preference for with imaging Time to initial diagnosis Time from diagnosis to treatment **Safety** Gadolinium contrast adverse reaction Claustrophobia Physical harms from follow-up testing Other adverse events arising from CMRI **Cost-effectiveness** Cost Cost per quality adjusted life year or disability adjusted life year Incremental cost-effectiveness ratio

Research question for review: In patients presenting with symptoms consistent with ischaemic heart disease, with an intermediate pre-test probability of CAD, what are the safety, effectiveness and cost-effectiveness of CMRI in establishing a diagnosis of CAD compared to exercise ECG, stress echocardiography, SPECT, and CTCA?

Population 2

The second proposed population includes adult patients with an existing diagnosis of significant CAD, who have a history of ischaemic heart disease, impaired left ventricular (LV) function, and are being considered for revascularisation.

Intervention

The proposed use of CMRI in this population is reflected in the second proposed MBS item, which includes a myocardial viability MRI sequence only. The purpose of CMRI in this population is to determine the severity of myocardial injury in patients with LV systolic dysfunction after myocardial infarction, the extent of residual viable myocardium, and therefore the likelihood of improvement following revascularisation. Delayed contrast-enhanced viability imaging is used to determine the steady-state concentration of a gadolinium contrast agent in myocardium, allowing necrotic or scarred tissue to be visualised (Woodard et al 2006).

LV dysfunction is a frequent cause of heart failure in patients with CAD. Myocardial ischemia that is severe and prolonged can cause loss of contractile function and tissue infarction (Bhola 2013). The extent and nature of damage to the myocardium may predict a patient's response to revascularisation. LV dysfunction is considered reversible when dysfunction is caused by adaptive down-regulation of myocardial contractibility without necrosis (Bhola 2013; Medical Advisory Secretariat 2010). There are various pathophysiological processes implicated in impaired myocardial contractibility, and myocardial tissue may be hibernating myocardium (chronically dysfunctional but viable) or stunned myocardium (short periods of dysfunctional myocardium).

Reversible dysfunction is characterised by impaired contractile function of the myocardium but maintained cell viability. LV dysfunction is considered permanent when it is the result of myocardial scarring (non-viable cells). Revascularisation procedures offer limited value in patients with permanent LV dysfunction (Bhola 2013; Medical Advisory Secretariat 2010). As such, the identification and quantification of viable myocardium is considered an important component of patient selection for appropriate treatments. CMRI in this setting would be used to determine the viability of myocardium, to inform the suitability of revascularisation surgery.

Co-administered interventions

As discussed earlier, CMRI procedures involving myocardial viability require the additional use of a gadolinium chelate contrast agent, currently listed on the MBS as item number 63491 (see Table 9). There are no diagnostic tests considered to be co-administered with CMRI in this population.

Clinical place for proposed intervention

Revascularisation surgery is considered in patients who are at high risk of suffering a hard cardiovascular event (including death or MI) due to the presence of significant CAD and LV dysfunction (Montalescot et al 2013). In the setting of known CAD, it is likely that patients will have had a prior angiogram to define the extent and significance of coronary stenoses. Stress echocardiography and myocardial perfusion imaging are also used to define inducible ischaemia that is predictive of future cardiac events (Montalescot et al 2013). Patients with normal LV function, or

with LV dysfunction but with no baseline wall motion abnormalities or inducible ischaemia are deemed to be at low risk of a hard event, and may not be considered for revascularisation (Montalescot et al 2013).

The use of CMRI for myocardial viability imaging is intended to replace existing methods of viability imaging, including low-dose dobutamine echocardiography, SPECT, (F-18)-fludeoxyglucose positron emission tomography (FDG PET) and CT perfusion imaging with delayed contrast enhancement. Currently, FDG PET has limited uptake and availability in Australia, and CT imaging with delayed contrast enhancement is an emerging technique for determining viability. Therefore, CMRI may have the greatest impact on the utilisation of low-dose dobutamine stress echocardiography and SPECT.

The current clinical pathway for patients in whom surgical revascularisation is contemplated is shown in Figure 2. The proposed service, representing a change to current practice, is highlighted in blue. The current clinical pathway for the investigation of established CAD has been informed by The American College of Cardiology's guidelines for the diagnosis and management of stable ischaemic heart disease (Fihn et al 2012).

Figure 2 Clinical pathway for the use of viability imaging with MRI in patients with an existing diagnosis of significant CAD, who have a history of ischaemic heart disease and impaired left ventricular function
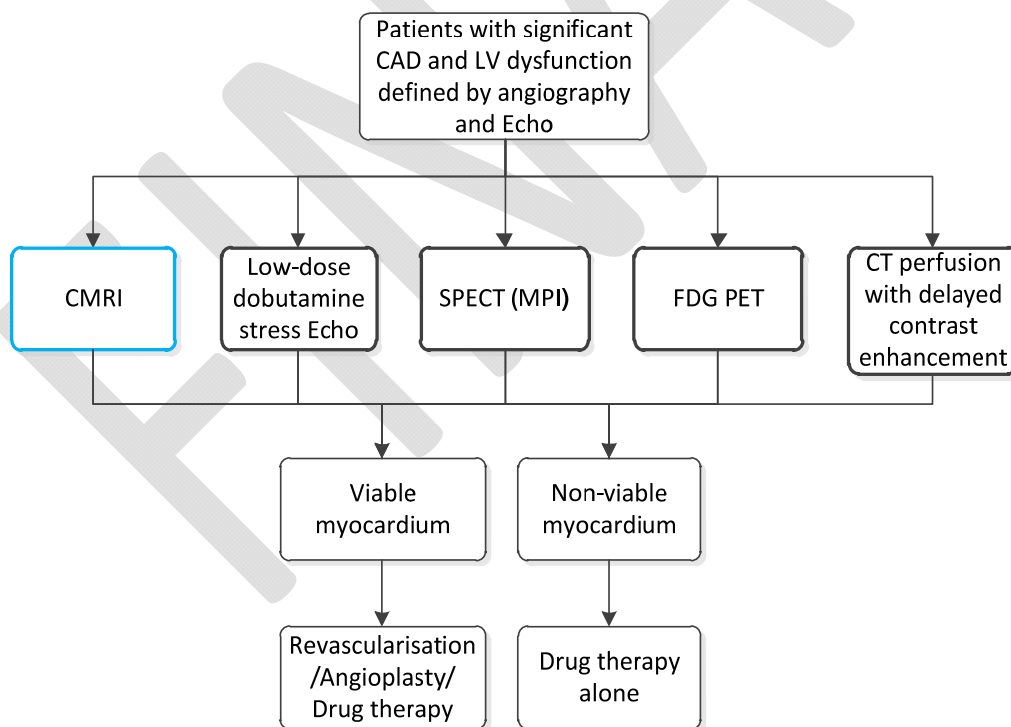
CAD: coronary artery disease. CMRI: cardiac magnetic resonance imaging. CT: computed tomography. Echo: echocardiography. FDG PET: 18-fludeoxyglucose positron emission tomography. LV: left ventricular. SPECT: single-photon emission computed tomography.

Comparator

1. <u>Low-dose dobutamine stress echocardiography (MBS Items 55116, 55117, 55122, 55123)</u>

Myocardium that has been damaged by an acute ischaemic event will often present with dysfunctional contractility, but may still be viable for revascularisation. The administration of a dobutamine stress agent can be used to increase contractility in dysfunctional segments. During echocardiography, areas of myocardium that show improved contractility under stress may be viable for revascularisation, whereas myocardium that does not improve is likely to be scarred (Camici et al 2008). Areas affected by dysfunctional contractility and scarring are less unlikely to respond to revascularisation.

2. <u>SPECT using thallium/sestamibi/tetrofosmin (MBS Items 61302, 61303, 1306, 61307, 61651, 61652, 61653, 61654)</u>

Various SPECT protocols can be used to determine the viability of myocardium, including stress-redistribution-reinjection and rest-redistribution. In either protocol, a radiopharmaceutical tracer (e.g. thallium-201, or technetium-99m tracers such as sestamibi or tetrofosmin) is intravenously administered, and the uptake in myocardial cells is monitored over a period of time. The presence of thallium-201 uptake after a prolonged period is a predictor of viable myocardium (Camici et al 2008). In contrast, the use of technetium-99m tracers requires uptake imaging at rest only. SPECT can also measure regional wall thickening as a predictor of myocardial viability (Maruyama et al 2002).

3. <u>Positron Emission Tomography (PET) using (F-18)-FDG (No current MBS items)</u>

Measuring the myocardial uptake of FDG tracers on PET is a non-invasive method of determining the viability of myocardium (Maruyama et al 2002). There is ongoing debate as to whether FDG-PET or CMRI should be considered the gold standard for assessment of myocardial viability. Unlike CMRI, PET exposes the patient to radiation and is limited by the need for access to (F-18)-FDG. The applicant suggests CMRI compares favourably to PET in clinical research studies performed over last 10 years.

4. <u>CT Perfusion Imaging with Delayed Contrast Enhancement (No current MBS items)</u>

CT perfusion imaging with delayed contrast enhancement is an emerging technique for characterising myocardial scar. This technique follows similar principles to CMR viability imaging (Bettencourt et al 2013). In CT delayed contrast enhancement imaging an iodinated contrast agent, such as iopromide, is administered. Repeat imaging occurs between six to ten minutes post-contrast administration in order to determine the steady-state concentration of contrast in myocardium after the wash out period. Areas of myocardial scar retain a higher concentration of contrast compared to healthy myocardium after the wash out period, allowing them to be visualised with CT (Bettencourt et al 2013).

Reference standard

There is currently no reference test for determining myocardial viability. In the absence of an accepted gold standard, PASC suggests an assessment of the accuracy of MRI at determining myocardial viability be based on patient health outcomes (e.g. survival, hospitalisation, quality of life)

following treatment, rather than surrogate outcomes (e.g. global LV function). PASC noted that the relative effectiveness of revascularisation versus medical management for patients with impaired LV function 'with' versus those 'without' viable myocardium should ideally be assessed in randomised controlled trials, and compared using a statistical test for interaction.

Additional relevant evidence, in the absence of a reference standard, may include the prognostic value of myocardial viability determined by cardiac MRI versus comparator tests. This would include studies that compare the prognosis for CAD patients with and without viable myocardium (measured with CMRI and at least one comparator test) who have been treated with revascularisation or medical management. This evidence should be provided during the assessment phase.

Outcomes

Effectiveness

<u>Health outcomes</u>

Cardiac disease specific mortality rate

Survival rate

Adverse cardiac event over defined period

Quality of life scores

Cardiac hospitalisation

<u>Diagnostic accuracy (for detecting viable myocardium or regional functional recovery)</u>

Sensitivity, specificity (confirmed by reference standard)

Positive likelihood ratio, negative likelihood ratio (confirmed by reference standard)

Positive predictive value, negative predictive value (confirmed by reference standard)

ROC curves

Unsatisfactory or uninterpretable test results

<u>Patient management</u>

Change in treatment pathway (initiated, ceased, modified, avoided)

Patient compliance/preference for imaging

Safety

Gadolinium contrast adverse reaction

Claustrophobia

Physical harms from follow-up testing

Other adverse events arising from CMRI

Cost-effectiveness

Cost

Cost per quality adjusted life year or disability adjusted life year

Incremental cost-effectiveness ratio

Clinical claim

The application suggests CMRI has non-inferior effectiveness compared to other non-invasive imaging modalities. In this regard, CMRI is proposed to be non-inferior to existing modalities for selecting patients who may respond to revascularisation, coronary artery bypass grafting and implantable cardioverter-defibrillators. In order to substantiate these claims, PASC suggests that the assessment will need to present evidence of whether a patient's myocardial viability status is correlated to improved outcomes following revascularisation surgery or not. This evidence should include any randomised controlled trials that compare revascularisation and medical management for patients with impaired viability.

In terms of safety, it is suggested that CMRI has superior safety compared to nuclear imaging technologies as patients are not exposed to ionising radiation. The application also claims that CMRI has a significant impact on therapy planning, and patients' preferred choice of therapy (Taylor et al 2013).

Table 6   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

Summary of PICO for Population 2

Table 7 Summary of extended PICO to define research question that assessment will investigate for population 2

Patients	Intervention	Comparator(s)	Reference test(s)	Outcomes to be assessed
Adult patients with an existing diagnosis of significant CAD, who have a history of ischaemic heart disease, impaired left ventricular function, and are being considered for revascularisation	Cardiac MRI of myocardial viability using delayed gadolinium enhancement	1. Low-dose dobutamine stress echo. 2. SPECT using thallium/sestamibi/ tetrofosmin. 3. PET using (F-18)-FDG (available but rarely used in Australia). 4. CT perfusion imaging with delayed contrast enhancement.	No valid reference test was identified. The assessment of CMRI accuracy should be based on a comparison of health outcomes between patients treated with and without prior viability imaging.	**Effectiveness** Health outcomes Cardiac disease specific mortality rate Survival rate Adverse cardiac event over defined period Quality of life scores Cardiac hospitalisation Diagnostic accuracy (for detecting viable myocardium or regional functional recovery) Sensitivity, specificity (confirmed by reference standard) Positive likelihood ratio, negative likelihood ratio (confirmed by reference standard) Positive predictive value, negative predictive value (confirmed by reference standard) ROC curves Unsatisfactory or uninterpretable test results Patient management Change in treatment pathway (initiated, ceased, modified, avoided) Patient compliance/preference for imaging **Safety** Gadolinium contrast adverse reaction Claustrophobia Physical harms from follow-up testing Other adverse events arising from CMRI **Cost-effectiveness** Cost Cost per quality adjusted life year or disability adjusted life year Incremental cost-effectiveness ratio

Research question for review: In adult patients with an existing diagnosis of significant CAD, who have a history of ischaemic heart disease, impaired left ventricular function, and are being considered for revascularisation, what are the safety, effectiveness and cost-effectiveness of CMRI in determining viable myocardium compared to stress echocardiography, SPECT, FDG PET and CT perfusion imaging with delayed contrast enhancement?

Health care resources affected by introduction of proposed intervention

More information regarding the resources to be considered in the economic analysis is required. Particularly with reference to the investigative resources used to identify the eligible population and the resource utilisation associated with the comparators for the proposed service. The applicant has provided a comprehensive list of direct practice cost components of the proposed medical service; these are provided in Appendix C.

The proposed medical service is likely to change the utilisation of echocardiography and nuclear medicine as MRI would form a substitute test for one or a combination of these services. The applicant states that by avoiding layered testing, healthcare expenditure will be reduced. The applicant also states that the use of MRI may also avoid the need for coronary angiography in cases of suspected coronary artery disease.

The applicant proposes that there is no substitute medical service for the use of MRI in myocardial tissue characterisation. Therefore MRI for tissue characterisation constitutes an additional diagnostic service and considerations of any additional costs to the healthcare system should be considered.

The assessment phase will also need to consider the impact of the proposed service on the downstream costs to the health system. The application states that MRI offers more accurate diagnoses than current reference standards and additionally provides information that may be used to select patients who are more likely to respond to certain treatments. This may result in changed costs to the healthcare system as patients may be more likely to receive appropriate treatment, or different therapeutic options, than they were prior to receiving CMRI.

Table 8   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
Resources provided to identify eligible population										
- Diagnostic procedures	Appropriately trained Cardiologist or Radiologist	At private rooms/radiology practice; or in a private or public hospital								TBD
Resources provided to deliver comparator 1 (Nuclear medicine)										
- Nuclear Medicine	Specialist	Outpatient or inpatient								TBD
Resources provided in association with comparator 1 (e.g., pre-treatments, co-administered interventions, resources used to monitor or in follow-up, resources used in management of adverse events, resources used for treatment of down-stream conditions)										
										TBD
Resources provided to deliver comparator 2 (echocardiography)										
- Echocardiography	Specialist	Outpatient or inpatient								TBD
Resources provided in association with comparator 2, etc										
										TBD
Resources provided to deliver comparator 3 (coronary angiography)										
- Coronary angiography	Specialist	Outpatient or inpatient								TBD
Resources provided to deliver proposed intervention										
- CMR	Appropriately trained Cardiologist or Radiologist	Location with appropriate equipment (MRI) and personnel								TBD
- Stress perfusion	Suitably trained	Location with								TBD

	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
	Physician/Cardiologist/Radiologist	appropriate equipment (MRI) and personnel								
Resources provided in association with proposed intervention										
- Gadolinium	Suitably trained personnel	Outpatient or inpatient								TBD
- Linen	Suitably trained personnel	Outpatient or inpatient								TBD
- ECG electrodes including cannula and connecting tube (viability and tissue characterisation, stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD
- Dual Syringe (viability and tissue characterisation, stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD
- Adenosine (stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD
- 150 cm connecting tubing (stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD
- 50 ml syringe (stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD
- 2nd cannula (stress perfusion)	Suitably trained personnel	Outpatient or inpatient								TBD

TBD: to be determined.

References

Australian Insitute of Health and Welfare 2011, *Cardiovascular disease: Australian facts 2011*, Canberra, Australia, viewed

Bettencourt, N, Ferreira, ND, Leite, D, Carvalho, M, Ferreira Wda, S, Schuster, A, Chiribiri, A, Leite-Moreira, A, Silva-Cardoso, J, Nagel, E & Gama, V. 2013, 'CAD detection in patients with intermediate-high pre-test probability: low-dose CT delayed enhancement detects ischemic myocardial scar with moderate accuracy but does not improve performance of a stress-rest CT perfusion protocol', *JACC Cardiovasc Imaging*, vol.6(10), pp. 1062-71.

Bhola, R 2013, *Hibernating and Stunned Myocardium Imaging*, Medscape, viewed 12 March 2014, <http://emedicine.medscape.com/article/352588-overview#aw2aab6b3>.

Bruder, O, Schneider, S, Nothnagel, D, Dill, T, Hombach, V, Schulz-Menger, J, Nagel, E, Lombardi, M, van Rossum, AC, Wagner, A, Schwitter, J, Senges, J, Sabin, GV, Sechtem, U & Mahrholdt, H. 2009, 'EuroCMR (European Cardiovascular Magnetic Resonance) registry: results of the German pilot phase', *J Am Coll Cardiol*, vol.54(15), pp. 1457-66.

Camici, PG, Prasad, SK & Rimoldi, OE. 2008, 'Stunning, hibernation, and assessment of myocardial viability', *Circulation*, vol.117(1), pp. 103-14.

Fihn, SD, Gardin, JM, Abrams, J, Berra, K, Blankenship, JC, Dallas, AP, Douglas, PS, Foody, JM, Gerber, TC, Hinderliter, AL, King, SB, 3rd, Kligfield, PD, Krumholz, HM, Kwong, RY, Lim, MJ, Linderbaum, JA, Mack, MJ, Munger, MA, Prager, RL, Sabik, JF, Shaw, LJ, Sikkema, JD, Smith, CR, Jr., Smith, SC, Jr., Spertus, JA & Williams, SV. 2012, '2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: executive summary: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons', *Circulation*, vol.126(25), pp. 3097-137.

Genders, TS, Steyerberg, EW, Alkadhi, H, Leschka, S, Desbiolles, L, Nieman, K, Galema, TW, Meijboom, WB, Mollet, NR, de Feyter, PJ, Cademartiri, F, Maffei, E, Dewey, M, Zimmermann, E, Laule, M, Pugliese, F, Barbagallo, R, Sinitsyn, V, Bogaert, J, Goetschalckx, K, Schoepf, UJ, Rowe, GW, Schuijf, JD, Bax, JJ, de Graaf, FR, Knuuti, J, Kajander, S, van Mieghem, CA, Meijs, MF, Cramer, MJ, Gopalan, D, Feuchtner, G, Friedrich, G, Krestin, GP & Hunink, MG. 2011, 'A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension', *Eur Heart J*, vol.32(11), pp. 1316-30.

Greenwood, JP, Maredia, N, Younger, JF, Brown, JM, Nixon, J, Everett, CC, Bijsterveld, P, Ridgway, JP, Radjenovic, A, Dickinson, CJ, Ball, SG & Plein, S. 2012, 'Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial', *Lancet*, vol.379(9814), pp. 453-60.

Hundley, WG, Bluemke, DA, Finn, JP, Flamm, SD, Fogel, MA, Friedrich, MG, Ho, VB, Jerosch-Herold, M, Kramer, CM, Manning, WJ, Patel, M, Pohost, GM, Stillman, AE, White, RD & Woodard, PK. 2010, 'ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document on cardiovascular magnetic resonance: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents', *J Am Coll Cardiol*, vol.55(23), pp. 2614-62.

Maruyama, A, Hasegawa, S, Paul, AK, Xiuli, M, Yoshioka, J, Maruyama, K, Hori, M & Nishimura, T. 2002, 'Myocardial viability assessment with gated SPECT Tc-99m tetrofosmin % wall thickening: comparison with F-18 FDG-PET', *Ann Nucl Med*, vol.16(1), pp. 25-32.

Medical Advisory Secretariat. 2010, 'Magnetic resonance imaging (MRI) for the assessment of myocardial viability: an evidence-based analysis', *Ont Health Technol Assess Ser*, vol.10(15), pp. 1-45.

Montalescot, G, Sechtem, U, Achenbach, S, Andreotti, F, Arden, C, Budaj, A, Bugiardini, R, Crea, F, Cuisset, T, Di Mario, C, Ferreira, JR, Gersh, BJ, Gitt, AK, Hulot, JS, Marx, N, Opie, LH, Pfisterer, M, Prescott, E, Ruschitzka, F, Sabate, M, Senior, R, Taggart, DP, van der Wall, EE, Vrints, CJ, Zamorano, JL, Baumgartner, H, Bax, JJ, Bueno, H, Dean, V, Deaton, C, Erol, C, Fagard, R, Ferrari, R, Hasdai, D, Hoes, AW, Kirchhof, P, Knuuti, J, Kolh, P, Lancellotti, P, Linhart, A, Nihoyannopoulos, P, Piepoli, MF, Ponikowski, P, Sirnes, PA, Tamargo, JL, Tendera, M, Torbicki, A, Wijns, W, Windecker, S, Valgimigli, M, Claeys, MJ, Donner-Banzhoff, N, Frank,

H, Funck-Brentano, C, Gaemperli, O, Gonzalez-Juanatey, JR, Hamilos, M, Husted, S, James, SK, Kervinen, K, Kristensen, SD, Maggioni, AP, Pries, AR, Romeo, F, Ryden, L, Simoons, ML, Steg, PG, Timmis, A & Yildirir, A. 2013, '2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology', *Eur Heart J*, vol.34(38), pp. 2949-3003.

Paech, DC & Weston, AR. 2011, 'A systematic review of the clinical effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of suspected coronary artery disease', *BMC Cardiovasc Disord*, vol.11pp. 32.

Salerno, M & Beller, GA. 2009, 'Noninvasive Assessment of Myocardial Perfusion', *Circ Cardiovasc Imaging*, vol.(2), pp. 412-24.

Schwitter, J, Wacker, CM, van Rossum, AC, Lombardi, M, Al-Saadi, N, Ahlstrom, H, Dill, T, Larsson, HB, Flamm, SD, Marquardt, M & Johansson, L. 2008, 'MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial', *Eur Heart J*, vol.29(4), pp. 480-9.

Taylor, AJ, Ellims, A, Lew, PJ, Murphy, B, Pally, S & Younie, S. 2013, 'Impact of cardiac magnetic resonance imaging on cardiac device and surgical therapy: a prospective study', *Int J Cardiovasc Imaging*, vol.29(4), pp. 855-64.

The Department of Health 2013, *Magnetic Resonance Imaging (MRI)*, The Department of Health, viewed 5 March 2014, [The Department of Health 2013, 'Magnetic Resonance Imaging (MRI)](#).

Therapeutic Goods Administration 2011, *Australian Regulatory Guidelines for Medical Devices*, The Department of Health and Ageing, viewed 12 March 2014, [Therapeutic Goods Administration 2011, Australian Regulatory Guidelines for Medical Devices](#).

Woodard, PK, Bluemke, DA, Cascade, PN, Finn, JP, Stillman, AE, Higgins, CB, White, RD & Yucel, EK. 2006, 'ACR practice guideline for the performance and interpretation of cardiac magnetic resonance imaging (MRI)', *J Am Coll Radiol*, vol.3(9), pp. 665-76.

Appendix A

Table 9   Current MBS item descriptors for CMRI services

Category 5 – Diagnostic Imaging Services	Item start date	Description start date
MBS item 63401 NOTE: Benefits are payable for each service included by Subgroup 15 on three occasions only in any 12 month period MAGNETIC RESONANCE ANGIOGRAPHY 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 the request for the scan specifically identifies the clinical indication for the scan - scan of cardiovascular system for: - vascular abnormality in a patient with a previous anaphylactic reaction to an iodinated contrast medium (R) (Contrast) Bulk bill incentive (Anaes.) Fee: $403.20 Benefit: 75% = $302.40 85% = $342.75 (See para DIQ of explanatory notes to this Category)	01-Aug-2004	01-Aug-2004
MBS item 63407 NOTE: Benefits are payable for each service included by Subgroup 15 on three occasions only in any 12 month period MAGNETIC RESONANCE ANGIOGRAPHY 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 the request for the scan specifically identifies the clinical indication for the scan - scan of cardiovascular system for: - vascular abnormality in a patient with a previous anaphylactic reaction to an iodinated contrast medium (R) (NK) (Contrast) Bulk bill incentive (Anaes.) Fee: $201.60 Benefit: 75% = $151.20 85% = $171.40 (See para DIQ of explanatory notes to this Category)	01-Jul-2011	01-Jul-2011
MBS item 63385 NOTE: Benefits are payable for each service included by Subgroup 14 on two occasions only in any 12 month period MAGNETIC RESONANCE IMAGING (including Magnetic Resonance Angiography if performed), 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 - scan of cardiovascular system for: - congenital disease of the heart or a great vessel (R) (Contrast) Bulk bill incentive (Anaes.) Fee: $448.00 Benefit: 75% = $336.00 85% = $380.80 (See para DIQ of explanatory notes to this Category)	01-Aug-2004	01-Aug-2004
MBS item 63491 NOTE: Benefits in Subgroup 22 are only payable for modifying items where claimed simultaneously with MRI services. Modifiers for sedation and anaesthesia may not be claimed for the same service. Modifying items for use with MAGNETIC RESONANCE IMAGING or MAGNETIC RESONANCE ANGIOGRAPHY performed under the professional supervision of an eligible provider at an eligible location where the service requested by a medical practitioner. Scan performed: - involves the use of contrast agent for eligible Magnetic Resonance Imaging items (Note: (Contrast) denotes an item eligible for use with this item) Bulk bill incentive Fee: $44.80 Benefit: 75% = $33.60 85% = $38.10	01-Aug-2004	01-Nov-2012

(See para DIQ of explanatory notes to this Category)		
MBS item 63388 - tumour of the heart or a great vessel (R) (Contrast) Bulk bill incentive (Anaes.) Fee: $448.00 Benefit: 75% = $336.00 85% = $380.80 (See para DIQ of explanatory notes to this Category)	01-Aug-2004	01-Aug-2004

Appendix B

Table 10   Current MBS items for conventional diagnostic imaging of CAD (The applicant indicated that green highlighted items are likely to be replaced by CMRI)

Category 2 – Diagnostic Procedures and Investigations

MBS Item 11712

MULTI CHANNEL ECG MONITORING AND RECORDING during exercise (motorised treadmill or cycle ergometer capable of quantifying external workload in watts) or pharmacological stress, involving the continuous attendance of a medical practitioner for not less than 20 minutes, with resting ECG, and with or without continuous blood pressure monitoring and the recording of other parameters, on premises equipped with mechanical respirator and defibrillator

Fee: $152.15 Benefit: 75% = $114.15 85% = $129.35

Category 5 – Diagnostic Imaging Services

MBS Item 61302

SINGLE STRESS OR REST MYOCARDIAL PERFUSION STUDY - planar imaging (R)

Bulk bill incentive

Fee: $448.85 Benefit: 75% = $336.65 85% = $381.55

MBS Item 61303

SINGLE STRESS OR REST MYOCARDIAL PERFUSION STUDY - with single photon emission tomography and with planar imaging when undertaken (R)

Bulk bill incentive

Fee: $565.30 Benefit: 75% = $424.00 85% = $489.10

MBS Item 61306

COMBINED STRESS AND REST, stress and re-injection or rest and redistribution myocardial perfusion study, including delayed imaging or re-injection protocol on a subsequent occasion - planar imaging (R)

Bulk bill incentive

Fee: $709.70 Benefit: 75% = $532.30 85% = $633.50

MBS Item 61307

COMBINED STRESS AND REST, stress and re-injection or rest and redistribution myocardial perfusion study, including delayed imaging or re-injection protocol on a subsequent occasion - with single photon emission tomography and with planar imaging when undertaken (R)

Bulk bill incentive

Fee: $834.90 Benefit: 75% = $626.20 85% = $758.70

MBS Item 61651

SINGLE STRESS OR REST MYOCARDIAL PERFUSION STUDY - planar imaging (R) (NK)

Bulk bill incentive

Fee: $224.45 Benefit: 75% = $168.35 85% = $190.80

MBS Item 61652

SINGLE STRESS OR REST MYOCARDIAL PERFUSION STUDY - with single photon emission tomography and with planar imaging when undertaken (R) (NK)

Bulk bill incentive

Fee: $282.65 Benefit: 75% = $212.00 85% = $240.30

MBS Item 61653

COMBINED STRESS AND REST, stress and re-injection or rest and redistribution myocardial perfusion study, including delayed imaging or re-injection protocol on a subsequent occasion - planar imaging (R) (NK)

Bulk bill incentive

Fee: $354.85 Benefit: 75% = $266.15 85% = $301.65

MBS Item 61654

COMBINED STRESS AND REST, stress and re-injection or rest and redistribution myocardial perfusion study, including delayed imaging or re-injection protocol on a subsequent occasion - with single photon emission tomography and with planar imaging when undertaken (R) (NK)

Bulk bill incentive

Fee: $417.45 Benefit: 75% = $313.10 85% = $354.85

MBS Item 55116

EXERCISE STRESS ECHOCARDIOGRAPHY performed in conjunction with item 11712, with two-dimensional recordings before exercise (baseline) from at least three acoustic windows and matching recordings from the same windows at, or immediately after, peak exercise, not being a service associated with a service to which an item in Subgroups 1 (with the exception of item 55054) or 3, or another item in this Subgroup applies (with the exception of items 55118 and 55130). Recordings must be made on digital media with equipment permitting display of baseline and matching peak images on the same screen (R)

Bulk bill incentive

Fee: $261.65 Benefit: 75% = $196.25 85% = $222.45

MBS Item 55117

PHARMACOLOGICAL STRESS ECHOCARDIOGRAPHY performed in conjunction with item 11712, with two-dimensional recordings before drug infusion (baseline) from at least three acoustic windows and matching recordings from the same windows at least twice during drug infusion, including a recording at the peak drug dose not being a service associated with a service to which an item in Subgroups 1 (with the exception of item 55054) or 3, or another item in this Subgroup, applies (with the exception of items 55118 and 55130). Recordings must be made on digital media with equipment permitting display of baseline and matching peak images on the same screen (R)

Bulk bill incentive

Fee: $261.65 Benefit: 75% = $196.25 85% = $222.45

MBS Item 55122

EXERCISE STRESS ECHOCARDIOGRAPHY performed in conjunction with item 11712, with two-dimensional recordings before exercise (baseline) from at least three acoustic windows and matching recordings from the same windows at, or immediately after, peak exercise, not being a service associated with a service to which an item in Subgroups 1 (with the exception of items 55026 and 55054) or 3, or another item in this Subgroup applies (with the exception of items 55118, 55125, 55130 and 55131). Recordings must be made on digital media with equipment permitting display of baseline and matching peak images on the same screen (R) (NK)

Bulk bill incentive

Fee: $130.85 Benefit: 75% = $98.15 85% = $111.25

MBS Item 55123

PHARMACOLOGICAL STRESS ECHOCARDIOGRAPHY performed in conjunction with item 11712, with two-dimensional recordings before drug infusion (baseline) from at least three acoustic windows and matching recordings from the same windows at least twice during drug infusion, including a recording at the peak drug dose not being a service associated with a service to which an item in Subgroups 1 (with the exception of items 55026 and 55054) or 3, or another item in this Subgroup, applies (with the exception of items 55118, 55125, 55130 and 55131). Recordings must be made on digital media with equipment permitting display of baseline and matching peak images on the same screen (R) (NK)

Bulk bill incentive

Fee: $130.85 Benefit: 75% = $98.15 85% = $111.25

MBS Item 57360

COMPUTED TOMOGRAPHY OF THE CORONARY ARTERIES performed on a minimum of a 64 slice (or equivalent) scanner, where the request is made by a specialist or consultant physician, and:

a)the patient has stable symptoms consistent with coronary ischaemia, is at low to intermediate risk of coronary artery disease and would have been considered for coronary angiography; or

b)the patient requires exclusion of coronary artery anomaly or fistula; or

c)the patient will be undergoing non-coronary cardiac surgery (R) (K)

Bulk bill incentive (Anaes.)

Fee: $700.00 Benefit: 75% = $525.00 85% = $623.80

MBS Item 57361

COMPUTED TOMOGRAPHY OF THE CORONARY ARTERIES performed on a minimum of a 64 slice (or equivalent) scanner, where the request is made by a specialist or consultant physician, and:

a)the patient has stable symptoms consistent with coronary ischaemia, is at low to intermediate risk of coronary artery disease and would have been considered for coronary angiography; or

b)the patient requires exclusion of coronary artery anomaly or fistula; or

c)the patient will be undergoing non-coronary cardiac surgery (R) (NK)

Bulk bill incentive (Anaes.)

Fee: $350.00 Benefit: 75% = $262.50 85% = $297.50

Appendix C

Direct costs of the proposed medical service

The applicant has provided the following information pertaining to the costs of the intervention.

Staff component

- Technologist - $100,000 (including on costs). It is anticipated that 1.6 FTE is needed to staff 9-5 weekday service (to account for annual and sick leave)
- Consultant (cardiologist or radiologist) - $300,000 for one FTE annually or $30,000 per session.
- Reporting (30mins) – Cardiologist/Radiologist $180-200 per hour
- Supervision for stress perfusion – Physician/Cardiologist/Radiologist (30mins). $180 per hour.

Consumable component

All patients: Gadolinium $50.00 per patient, Linen $5.00 per patient

Viability and Tissue Characterisation

- ECG electrodes $2.52, Cannula $1.52, Connecting tubing $30.50
- Dual Syringe $28, Valves x2 $5.10

Stress Perfusion (same as above and)

- Adenosine $45.14
- 150cm connecting tubingx4 $10.80
- 50ml syringe $1.00
- 2nd cannula $1.52

Equipment costs

- MRI scanner with cardiac software is about $1 to 1.5 million for a 1.5T. 3T magnet purchase $1.7 to $2.5 million
- Fit out - $150-200k, Pressure injector $40k, Syringe injector for adenosine $5k
- Monitoring equipment
- Resus equipment and drugs
- PACS/RIS Workstation $100k , 3rd party Cardiac software $20k

Other components of costs

- Wage for nurse or for helper $20-25 per hour. Changing patient and getting them into the MRI room, can partly be taken on by a helper or nurse. Currently consider 20min prep time – 10min by helper, 10min by radiographer (change, exclude contraindications, cannulate, ECG placement, position on table prior to scanning). Post procedure 10mins – helper probably sufficient but a nurse may be needed with stress perfusion.