



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1432 – Magnetic resonance imaging (MRI) of patients with suspected non-ischaemic cardiomyopathy

Applicant: The Cardiac Society of Australia and New Zealand (CSANZ)

Date of MSAC consideration: MSAC 69th Meeting, 6-7 April 2017

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application

An application requesting four new Medicare Benefits Schedule (MBS) listings of cardiac MRI for the diagnosis and treatment planning of patients with suspected non-ischaemic cardiomyopathies (NICM) – excluding dilated NICM was received from CSANZ by the Department of Health (the Department).

2. MSAC's advice to the Minister

MSAC noted that six separate populations who may benefit from cardiac magnetic resonance imaging (CMR) were proposed in the current application.

After considering the strength of the available evidence in relation to safety, clinical effectiveness and cost-effectiveness, MSAC supported the use of CMR in patients in whom arrhythmogenic right ventricular cardiomyopathy (ARVC) is suspected on the basis of other International Task Force Criteria (population 3) and in asymptomatic patients with a family history of ARVC in a first-degree relative (population 4). MSAC noted that CMR could change diagnoses, avoid the inappropriate implantation of an implantable cardioverter defibrillator (ICD) device and had acceptable safety and clinical effectiveness in populations 3 and 4. MSAC noted that there are a number of complex implementation issues that will need to be addressed prior to the listing of CMR in these populations including further consultation with the applicant with regards to guidelines and training programs.

Due to the limited evidence presented to the committee, MSAC was unable to determine the benefit of CMR in population 1 (patients in whom echocardiography suggests increased left ventricular [LV] wall thickness, a hypertrophic or restrictive cardiomyopathy [HCM or RCM] is suspected, and further diagnostic clarification is required) and population 2 (asymptomatic individuals with a first-degree relative with HCM/RCM with increased or indeterminate left ventricular wall thickness on echocardiography). MSAC noted that evidence to support the use of CMR in these populations may have been missed and suggested a new application to identify additional evidence to support the comparative safety, effectiveness and cost-effectiveness of CMR in these patients be undertaken.

Due to the limited evidence presented to the committee, MSAC was unable to determine the benefit of CMR in population 5 (patients with troponin-positive chest pain, electrocardiographic changes suspicious of acute coronary syndrome, and no culprit lesion identified on coronary angiography). MSAC noted that the result of the cost-effectiveness analysis in population 5 was highly uncertain, difficult to interpret and may not capture all relevant patient outcomes. MSAC noted that a more comprehensive cost-effectiveness analysis (more inputs and longer time horizon) would be needed to value cardiac MRI.

No evidence on the use of CMR was identified in population 6 (asymptomatic individuals with a family history of sudden cardiac death [SCD], excluding channelopathies and arrhythmia, or aborted SCD), and so population 6 was not further considered by the committee.

Any resubmission for populations not supported would need to be considered by ESC.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that the application had initially been for cardiac magnetic resonance imaging (CMR) for patients with suspected non-ischæmic cardiomyopathies. MSAC noted that due to the large number of patient populations the Contracted Assessment Group and the Department agreed that the application would be split into two parts, of which this was Part B. MSAC noted that this application covered hypertrophic cardiomyopathies (HCM), restrictive cardiomyopathies (RCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) and cardiomyopathies that may be due to acute coronary syndrome (ACS), myocarditis or Takotsubo cardiomyopathy (TTC). MSAC noted that Part A which was the application for patients with dilated cardiomyopathies (DCM) was considered at the July 2016 meeting ([MSAC Public Summary Document \(PSD\) Application 1393, July 2016](#)).

MSAC noted that cardiomyopathies are diseases of the heart muscle (myocardium) that are not caused by coronary artery disease (CAD), hypertension, valvular disease or congenital heart disease. While the Australian prevalence of the various cardiomyopathies considered in this application is uncertain, it has been estimated that approximately 36,000 Australians have an HCM, approximately 3,500 have an ARVC and approximately 1,400 have a TTC. The prevalence of RCM and acute myocarditis in Australia are unknown.

MSAC noted that six separate populations who may benefit from CMR were proposed in the current application. No evidence on the use of CMR was identified in population 6 — asymptomatic individuals with a family history of sudden cardiac death (SCD), excluding channelopathies and arrhythmia, or aborted SCD — and as a consequence, MSAC dismissed the use of CMR in these patients without further consideration.

The remaining patient populations proposed to benefit from the use of CMR were:

- Population 1: patients in whom echocardiography suggests increased left ventricular (LV) wall thickness, a hypertrophic or restrictive cardiomyopathy (HCM or RCM) is suspected, and further diagnostic clarification is required;
- Population 2: asymptomatic individuals with a first-degree relative with HCM/RCM with increased or indeterminate LV wall thickness on echocardiography;
- Population 3: patients in whom arrhythmogenic right ventricular cardiomyopathy (ARVC) is suspected on the basis of other International Task Force Criteria (TFC);
- Population 4: asymptomatic patients with a family history of ARVC in a first-degree relative; and
- Population 5: patients with troponin-positive chest pain, electrocardiogram (ECG) changes suspicious of acute coronary syndrome (ACS), and no culprit lesion

identified on coronary angiography. The three main diagnoses that can be suspected are ACS, myocarditis or TTC.

MSAC noted that CMR is a non-invasive imaging technique used to visualise soft tissues. MSAC noted that all patients in populations 1–4 would receive echocardiography and an ECG during workup. Patients in population 5 would also have had invasive coronary angiography (ICA) or computed tomography coronary angiography (CTCA) to rule out coronary stenoses as part of work up. Therefore, MSAC noted that the comparator for CMR for all populations was prior testing alone (i.e. without CMR).

MSAC noted the absence of direct evidence of the safety and effectiveness of CMR compared with prior testing alone in any of the populations, resulting in the need for a linked evidence approach.

MSAC accepted that CMR had a good safety profile, although it noted that rare adverse events may occur as a result of use of contrast agents.

Populations 1 and 2

MSAC was unable to determine the benefit of CMR in populations 1 and 2 due to the limited evidence base presented to the committee. There was a lack of studies on the diagnostic accuracy of CMR and no evidence that CMR changed treatment in these patients. MSAC noted that as a result, the effectiveness and cost-effectiveness of CMR compared with prior testing alone in these patients was unknown.

MSAC noted the applicant's concerns that evidence to support the use of CMR in these populations may have been missed by the literature search. MSAC suggested that a new application, with a new literature search that included terms for diseases and conditions that result in HCM/RCM (e.g. amyloidosis, sarcoidosis, iron overload), be undertaken to identify if additional evidence to support the comparative safety, effectiveness and cost-effectiveness of CMR in these patients is available.

Populations 3 and 4

MSAC noted that the reference standard for diagnosis of ARVC in populations 3 and 4 is diagnosis using the International TFC. MSAC noted that as the International TFC incorporates CMR findings, the diagnostic accuracy of CMR against this reference standard could not be determined. However, MSAC noted that in a study that modelled the relative contribution of the different criteria included in the 2010 International TFC, removal of CMR led to the greatest decline in diagnostic accuracy (Etoom Y et al 2015).

MSAC noted that although the quality of evidence was low, CMR could change diagnoses and management in populations 3 and 4. MSAC noted that among patients with a suspected ARVC prior to CMR, 9–28% received an alternative non-ARVC diagnosis after the CMR. There was also evidence from an Australian study that CMR changed decisions about implantation of an implantable cardioverter defibrillator (ICD) device for some patients (Taylor AJ et al 2013). Among 107 Australian patients with suspected ARVC, use of CMR changed decisions regarding ICD implantation in 11 (10%) patients. Seven of the 25 patients scheduled for ICD implantation were able to avoid this following CMR and one received a cardiac resynchronisation therapy device. Three of the remaining 82 patients had an ICD implanted despite there being no original plan to do so. MSAC noted that avoiding the harms associated with inappropriate ICD implantation in patients who do not require an ICD was an important patient outcome.

MSAC accepted that while it was limited, there was evidence that CMR had superior safety and non-inferior effectiveness compared with prior testing alone. In light of this, MSAC

noted that use of CMR in populations 3 and 4 was dominant (less costly and more effective) when compared with prior testing without CMR. This was driven by an increase in the appropriate implantation of ICD devices. MSAC noted that the base case assumed that the CMR was 100% accurate while prior testing alone was not. However, in sensitivity analyses use of CMR remained dominant as long as CMR led to correct management in at least 69% of patients who had discordant results on prior testing alone and CMR.

MSAC noted that the net cost to the MBS for CMR would be approximately \$20.7 million over five years for populations 3 and 4. Costs were based upon approximately 4,600 CMRs being undertaken at an MBS cost of \$4.0 million in the first year rising to just under 5,000 CMRs at a cost of \$4.3 million in year five. MSAC noted that the financial cost of listing CMR in populations 3 and 4 was most sensitive to changes in the estimated prevalence of ARVC. If the prevalence rate was estimated to be 1 in 2,000 (instead of 1 in 5,000) the net MBS cost of providing CMR in these populations increased to approximately \$10 million per year.

After considering this evidence, MSAC supported MBS funding for populations 3 and 4 based on acceptable safety, clinical effectiveness and cost-effectiveness.

Population 5

MSAC was unable to determine the benefit of CMR compared with prior testing alone in population 5 due to the limited evidence base presented to the committee. There was a lack of studies on the diagnostic accuracy of CMR compared with prior testing alone in population 5. While there was some evidence that CMR could clarify diagnoses and change management, largely by ruling out an ACS with a subsequent reduction or cessation of medicines (anti-platelets or statins) to treat ACS, MSAC noted that this was based upon very low quality case series evidence (n = 660 from seven studies for change in diagnosis; n = 238 from two studies for change in management).

MSAC noted considerable uncertainty in the economic modelling of the use of CMR in population 5. Due to the limited information on long-term health outcomes, the economic model was restricted to the incremental cost of CMR per change in management and incremental cost per change in diagnosis over a one year time horizon. MSAC noted that if CMR is able to accurately diagnose ACS in this population, a negative CMR will result in patients being able to stop or reduce their dose of anti-platelets or statins. MSAC noted that the model, which assumed that use of CMR would lead to non-inferior health outcomes and superior safety outcomes, indicated that the direct cost of the CMR (\$1,106) would be slightly offset by changes in medicine use (-\$61) if the CMR identified that the patient had not had a myocardial infarction. In the base case, the incremental cost of CMR per appropriate change in management was \$3,235 and the incremental cost per change in diagnosis was \$3,673. MSAC noted that this result was highly uncertain, difficult to interpret in terms of cost-effectiveness and may not capture all relevant patient outcomes.

After considering the evidence, MSAC did not support MBS funding for population 5 due to cost-effectiveness concerns in this population.

Policy and implementation considerations

MSAC noted that there were a number of policy and implementation issues that needed to be addressed before CMR could be listed in the MBS for populations 3 and 4.

MSAC agreed that the providing specialist should personally attend patients during the examination and noted that the Cardiac Society of Australia and New Zealand (CSANZ) had recommended that the reporting specialist personally attend patients.

MSAC agreed that the registered medical radiation practitioners undertaking the CMR do so under the supervision of a specialist trained in CMR.

MSAC noted that there would need to be legislative changes to allow cardiologists to provide and report on CMR.

MSAC noted that radiologists and cardiologists would need appropriate training before reporting on CMR. MSAC noted that CSANZ has recommended training be at least equivalent to Society for Cardiovascular Magnetic Resonance (SCMR) Level 2 training. MSAC encouraged CSANZ and the Royal Australian and New Zealand College of Radiologists (RANZCR) work together to develop the training program.

MSAC agreed that centres undertaking CMR would be required to have Medicare eligibility, be a comprehensive practice, and be accredited under the Diagnostic Imaging Accreditation Scheme. MSAC noted these requirements would limit uptake by private MRI providers.

4. Background

CSANZ's original application was reviewed by the Protocol Advisory Sub-committee (PASC) in April 2014. PASC advised that the initial application should be split into three applications:

- Application 1237 – Cardiac MRI for myocardial stress-perfusion and viability imaging in patients with known or suspected CAD.
- Application 1393 – Cardiac MRI for non-ischaemic dilated cardiomyopathies (NIDCM) – Cardiac MRI (Part A)
- Application 1432 – Cardiac MRI of patients with suspected non-ischaemic cardiomyopathy (excluding dilated cardiomyopathy) – Cardiac MRI (Part B).

MSAC considered Application 1237 at its July 2016 meeting. MSAC did not support public funding for either indication as the clinical need was not established and the modelled economic evaluation showed that, at the fee proposed, cardiac magnetic resonance imaging (CMR) is less cost effective in the management of coronary artery disease than current funded options within the MBS, including CT coronary angiography and stress echocardiography. Further information can be found in the [Public Summary Document](#) on the MSAC website.

MSAC also considered Application 1393 at its July 2016 meeting. MSAC did not support the use of CMR in patients with suspected dilated cardiomyopathies (DCMs) due to a lack of evidence and high uncertainty around the clinical effectiveness and cost effectiveness. Further information can be found in the Public Summary Document on the MSAC website.

5. Prerequisites to implementation of any funding advice

Currently an MRI can be performed by anyone who is under the professional supervision of an eligible provider who is available to monitor and influence the conduct and diagnostic quality of the examination, including, if necessary, by personal attendance on the patient. CSANZ indicated that it is the intention to require the reporting specialist to attend in-person during the examination.

Cardiac MRI Reporting Services

It is the intention of CSANZ that radiologists and cardiologists trained in cardiac MRI will be able to report CMR services. The level of specialist accreditation recommended for cardiac MRI procedures by the CSANZ is equivalent to at least the Society for Cardiovascular Magnetic Resonance (SCMR) Level 2 training.

The Royal Australian and New Zealand College of Radiologists (RANZCR) and the CSANZ continue to develop the training requirements for specialists supervising and reporting cardiac MRI.

Current legislative requirements stipulate that Medicare eligible MRI items must be reported by a specialist in diagnostic radiology who satisfies the Chief Executive Medicare that the specialist is a participant in the RANZCR Quality and Accreditation Program (Health Insurance (Diagnostic Imaging Services Table) Regulations – 2.5.4 – Eligible Providers).

Accreditation and MRI Medicare Eligibility Requirements

All sites providing cardiac MRI will need to have Medicare eligibility (either full or partial), be considered a comprehensive practice (which requires a practice to provide x-ray, ultrasound, CT and MRI services at the one location), and be accredited under the Diagnostic Imaging Accreditation Scheme (DIAS).

6. Proposal for public funding

The four proposed MBS item descriptors are shown in Table 1. These were modified slightly from those ratified by PASC; to clarify that echocardiography is to be used to determine which patients are eligible to proceed to CMR.

Table 1 Proposed MBS Item for the investigation of suspected CMs with CMR

Category 5 – Diagnostic Imaging Services
<p>MBS [item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>NOTE: Benefits are payable for each service included by Subgroup ## on one occasion only in any 12 month period</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where the request for the scan specifically identifies the clinical indication for the scan - scan of cardiovascular system for:</p> <p>(a) assessment of myocardial structure and function, including tissue characterisation (Contrast); and</p> <p>(b) the request for the scan identifies that the patient presents with echocardiography results suggesting increased left ventricular wall thickness, a hypertrophic or restrictive cardiomyopathy is suspected, and in whom further diagnostic clarification is required.</p> <p>Fee: \$855.20 Benefit: 75% = \$641.40 85% = \$726.90</p>
<p>MBS [item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>NOTE: Benefits are payable for each service included by Subgroup ## on one occasion only in any 12 month period</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where the request for the scan specifically identifies the clinical indication for the scan - scan of cardiovascular system (Contrast):</p> <p>(a) assessment of myocardial structure and function (Contrast); and</p> <p>(b) the request for the scan identifies that the patient presents with signs or symptoms consistent with arrhythmic right ventricular cardiomyopathy on the basis of task force criteria.</p> <p>Fee: \$855.20 Benefit: 75% = \$641.40 85% = \$726.90</p>
<p>MBS [item number (Note: this will be assigned by the Department if listed on the MBS)]</p> <p>NOTE: Benefits are payable for each service included by Subgroup ## on one occasion only in any 12 month period</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider</p>

Category 5 – Diagnostic Imaging Services

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:

- (a) assessment of myocardial structure and function, including tissue characterisation (Contrast); and
- (b) the request for the scan identifies that the patient presents with troponin-positive chest pain, electrocardiography changes suspicious of acute coronary syndrome, and no culprit lesion identified on coronary angiography; and
- (c) the request for the scan identifies that the patient has a negative or indeterminate result on echocardiography.

Fee: \$855.20 Benefit: 75% = \$641.40 85% = \$726.90

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 ## 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 consultant physician and where the request for the scan specifically identifies the clinical indication for the scan - scan of cardiovascular system for:

- (a) assessment of myocardial structure and function, including tissue characterisation (Contrast); and
- (b) the request for the scan identifies that the patient presents with a family history of sudden cardiac death or aborted sudden cardiac death in a first-degree relative, excluding channelopathies and arrhythmia; and
- (c) the request for the scan identifies that the patient has inconclusive results on echocardiography.

Fee: \$855.20 Benefit: 75% = \$641.40 85% = \$726.90

7. Summary of Public Consultation Feedback/Consumer Issues

The Protocol Advisory Sub-Committee (PASC) received two responses from peak bodies, two responses from organisations and one response from a specialist. Consultation feedback for the protocol was positive.

Issues raised in the responses were:

- Current procedure image acquisition time is 60-80 minutes instead of the proposed 45-60 minutes.
- Graded MBS Items could be used to account for varying image acquisition time.
- The protocol states that the procedure can be performed using abdominal, body, thoracic or specialised cardiac coils. Concerns were raised about the image quality of specialised cardiac coils compared to body and thoracic coils.
- The protocol states that specialist referral is required for the procedure due to its complexity, specialist understanding of its uses and limitations, and the interpretation of image scans. The inclusion of General Practitioner referral for the procedure would ease diagnosis of normal heart function or minor abnormalities.
- Transesophageal echocardiography should be included in the proposed invasive tests performed for population three: patients with suspected arrhythmogenic right ventricular cardiomyopathy.
- Patient access to the procedure may be limited due to difficulty in accessing Medicare licenced MRIs.

8. Proposed intervention's place in clinical management

The primary use of CMR in all six populations is as an adjunct diagnostic tool in conjunction with echocardiography, ECG and clinical examination.

The clinical management algorithms developed by another assessment group and agreed to by PASC may be found on the MSAC website. These algorithms were slightly amended by the Adelaide Health Technology Assessment (AHTA) on the basis of further clinical input, to provide more clarity around what follow-up monitoring is used. The revised flowcharts for all populations are shown in Figure 1 to Figure 6.

Populations 1 and 2

- Population 1** Patients presenting with chest pain, shortness of breath, fatigue, arrhythmia or syncope, and in whom echocardiography suggests increased wall thickness, an HCM or RCM is suspected, and further diagnostic clarification is required.
- Population 2** Asymptomatic individuals with a family history of HCM or RCM in a first-degree relative, in whom echocardiography suggests increased LV wall thickness, an HCM or RCM is suspected, and further diagnostic clarification is required.

The revised clinical management algorithms for populations 1 and 2 are shown in Figure 1 and Figure 2. The diagnosis of HCM in symptomatic patients is often established on the basis of family history, clinical assessment, biochemistry and non-invasive testing (including ECG and echocardiography). The primary use of CMR in this population is as an adjunct diagnostic tool in conjunction with echocardiography, ECG and clinical examination.

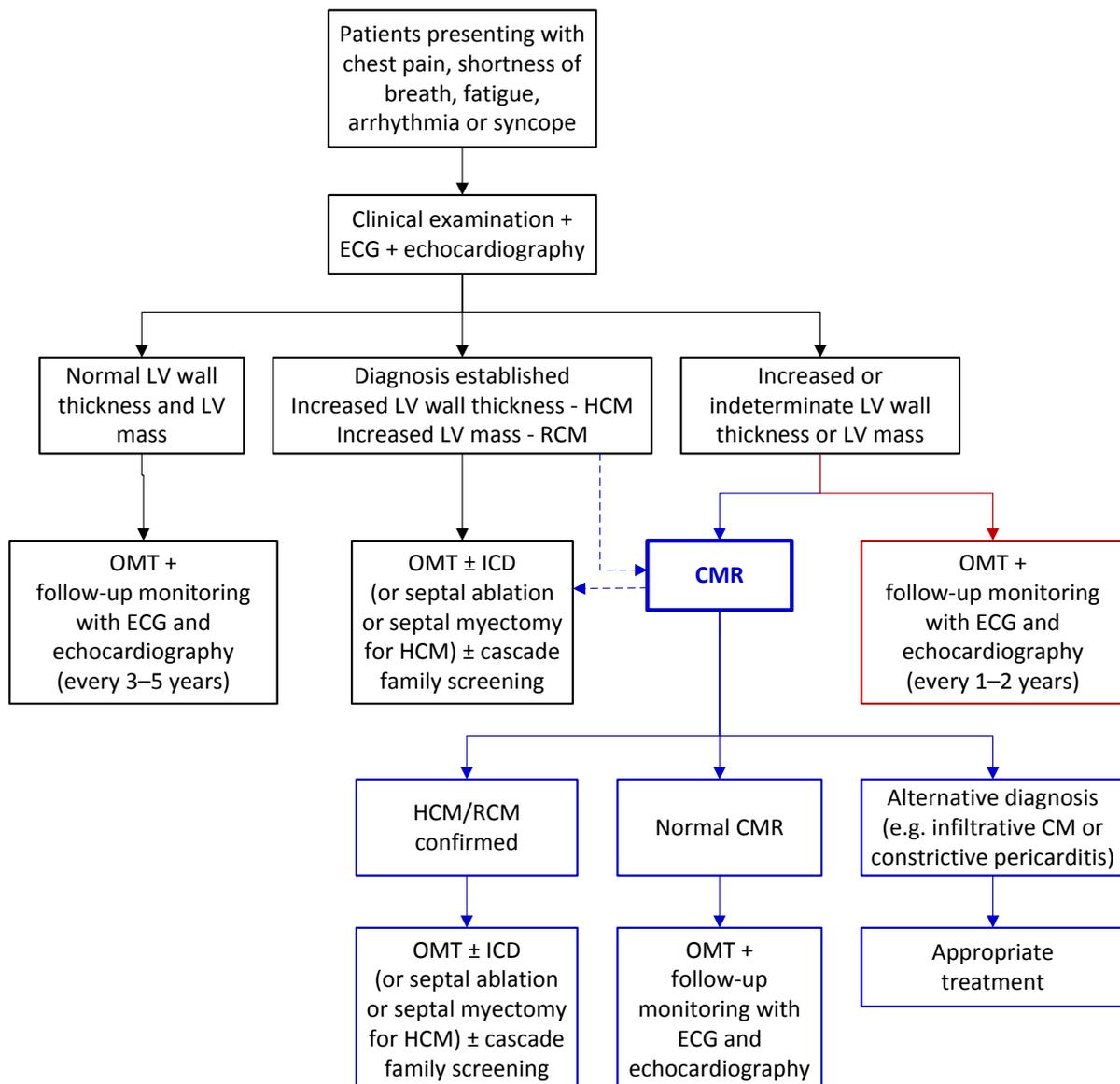


Figure 1 Revised current and proposed clinical management algorithms for the diagnosis of patients with suspected HCM/RCM

Source: Figure 3 from the Final Protocol for MSAC application 1393, which was informed by the European Society of Cardiology’s clinical practice guidelines for the diagnosis and treatment of HCM.

The possibility of leakage occurring so that all patients diagnosed with HCM have a CMR in order to inform patient management is indicated by dashed blue lines. The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

CM = cardiomyopathy; CMR = cardiac magnetic resonance (imaging); ECG = electrocardiography; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter defibrillator; LV = left ventricle; OMT = optimal medical therapy; RCM = restrictive cardiomyopathy

In asymptomatic individuals with a family history of HCM or RCM, CMR is primarily intended to be used as an adjunct to conventional testing (including clinical assessment, ECG and echocardiography). In individuals with a suspected pathology based on conventional testing, CMR will provide additional information on the aetiology of the disease, leading to potential changes to therapeutic management. In the absence of CMR, asymptomatic individuals are typically managed with follow-up monitoring.

Further clinical input has also indicated that it is likely that leakage will occur; all patients diagnosed with HCM are likely to have a CMR in order to inform prognosis.

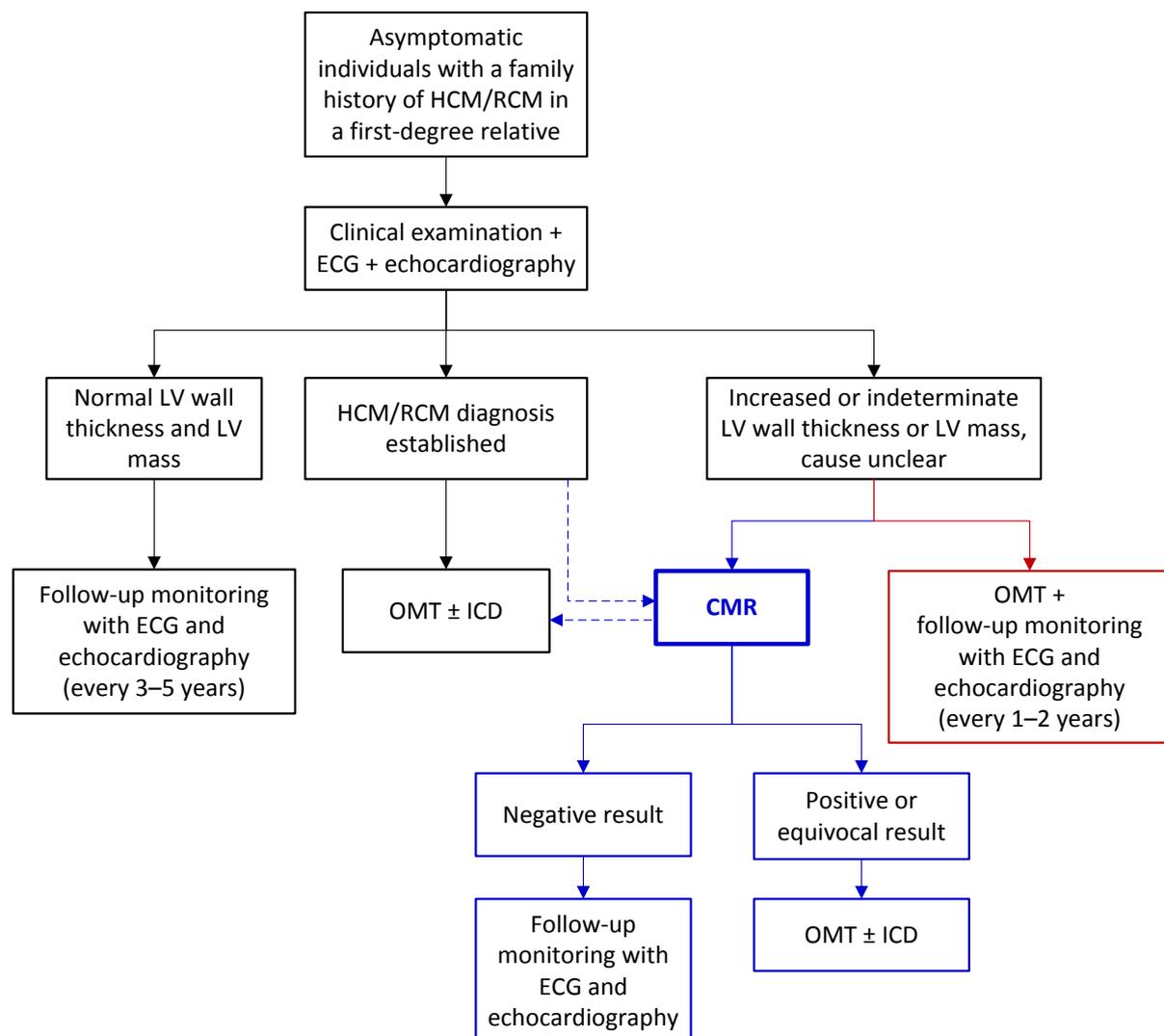


Figure 2 Revised current and proposed clinical management algorithm for the investigation of asymptomatic patients with a family history of HCM/RCM in a first-degree relative

Source: Figure 4 from the Final Protocol for MSAC application 1393, which was informed by the European Society of Cardiology’s clinical practice guidelines for the diagnosis and treatment of hypertrophic cardiomyopathy.

The possibility of leakage occurring so that all patients diagnosed with HCM have a CMR in order to inform patient management is indicated by dashed blue lines. The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

CMR = cardiac magnetic resonance (imaging); ECG = electrocardiography; HCM = hypertrophic cardiomyopathy; ICD = implantable

Populations 3 and 4

Population 3 Patients in whom ARVC is suspected on the basis of other International TFC, without the use of CMR.

Population 4 Asymptomatic people with a family history of ARVC in a first-degree relative, and in whom ARVC is suspected on the basis of the International TFC, without the use of CMR.

The revised clinical management algorithms for populations 3 and 4 are shown in Figure 3 and Figure 4. CMR is an established tool used in the workup for establishing a diagnosis of ARVC. Further clinical input has indicated that all symptomatic patients in whom ARVC is suspected but cannot be definitively diagnosed would have a management plan to treat their symptoms (ventricular tachycardia (VT) or fibrillation (VF)), which would include optimal medical therapy (OMT), continued monitoring and possibly an ICD, depending on the severity of their symptoms and their family history. It should also be noted that, as the presenting symptoms are VT/VF, patients who receive an alternative diagnosis by CMR may still require an ICD as part of their treatment plan.

Alternative diagnoses by CMR may occur in approximately 9% of patients, including cardiac sarcoidosis, congenital heart disease, RV volume overload conditions and other CMs.

Asymptomatic family members in whom ARVC is suspected but cannot be definitively diagnosed would likely be monitored every 3–5 years in the absence of CMR. Invasive testing would occur very rarely, if at all.

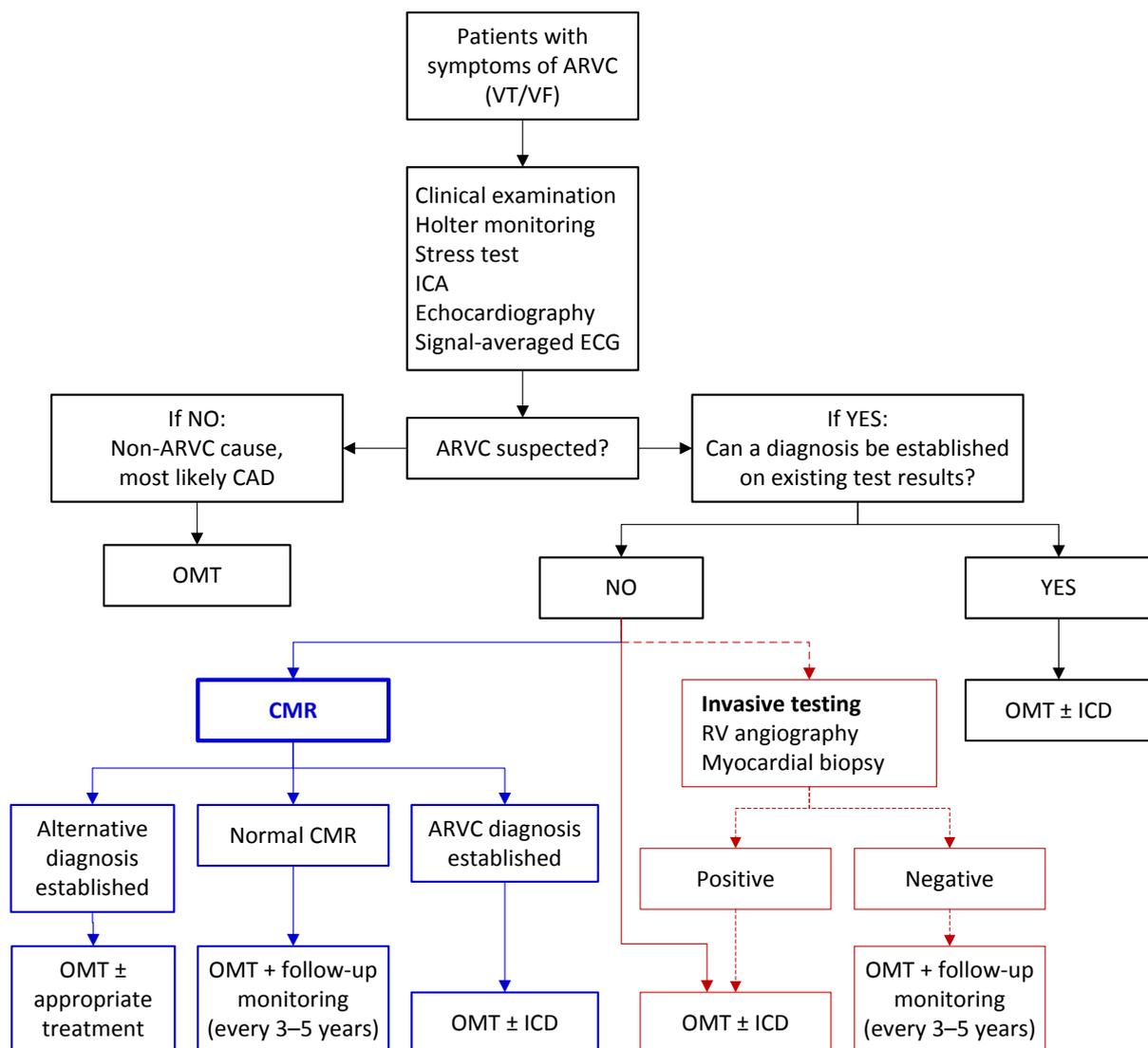


Figure 3 Revised current and proposed clinical management algorithm for the diagnosis of suspected ARVC

Source: Figure 5 from the Final Protocol for MSAC application 1393, which was informed by the International TFC, and a published diagnostic algorithm by Anderson (2006).

Further clinical advice has indicated that patients only rarely have invasive testing due to its poor diagnostic accuracy in these patients. Thus, this pathway has been shown with dashed lines. The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

ARVC = arrhythmogenic right ventricular cardiomyopathy; CAD = coronary artery disease; CMR = cardiac magnetic resonance (imaging); ECG = electrocardiography; ICA = invasive coronary angiography; ICD = implantable cardioverter defibrillator; OMT = optimal medical therapy; RV = right ventricle; VF = ventricular fibrillation; VT = ventricular tachycardia

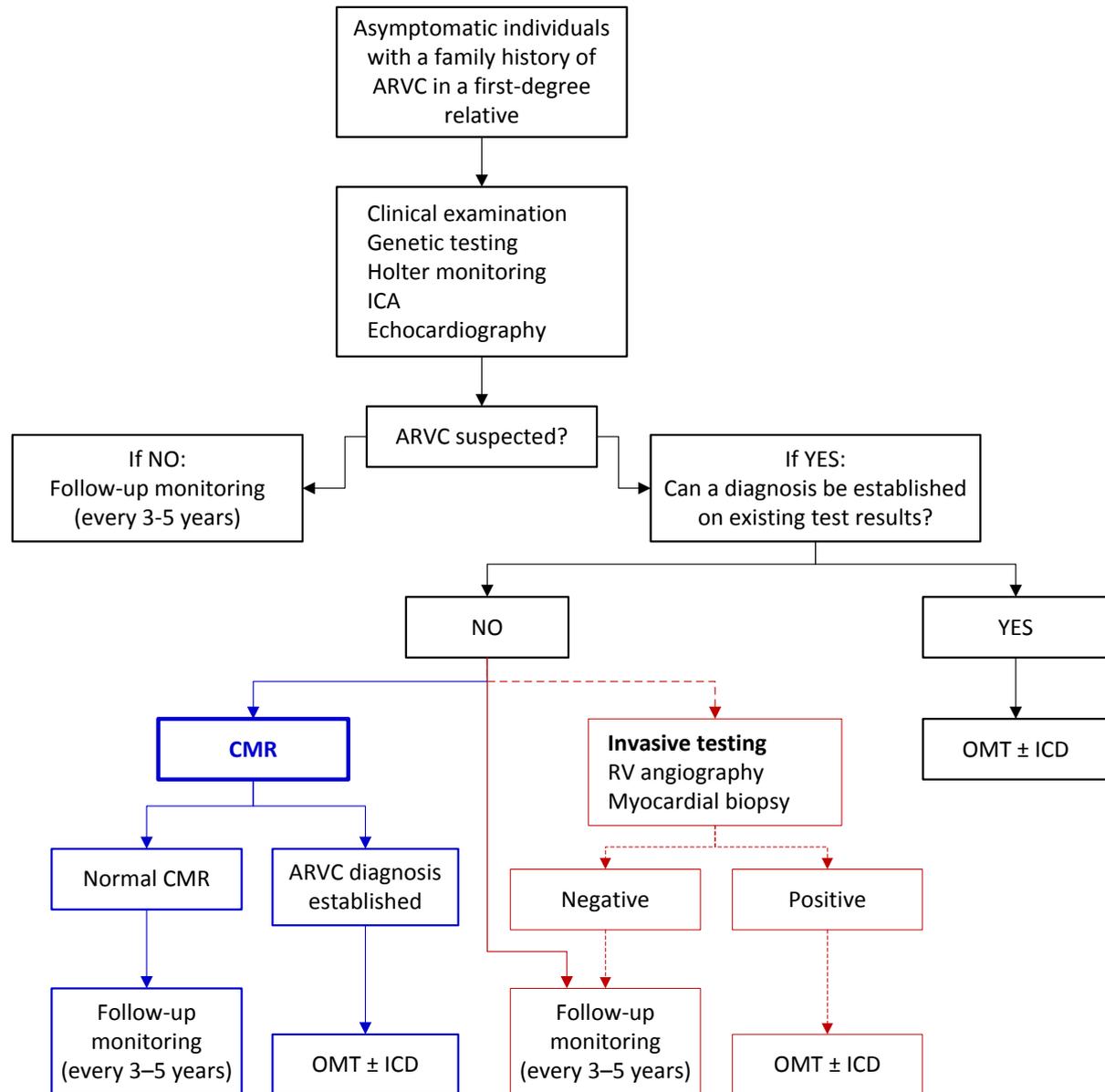


Figure 4 Revised current and proposed clinical management algorithm for investigating patients with a family history of ARVC in a first-degree relative

Source: Figure 6 from the Final Protocol for MSAC application 1393, which was informed by the International TFC, and a published diagnostic algorithm by Anderson (2006).

The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

ARVC = arrhythmogenic right ventricular cardiomyopathy; CMR = cardiac magnetic resonance (imaging); ECG = electrocardiography; ICD = implantable cardioverter defibrillator; OMT = optimal medical therapy; RV = right ventricle

Population 5

The revised clinical management algorithm for patients with troponin-positive chest pain, ECG changes suspicious of ACS, and no culprit lesion identified on ICA or CTCA, and an indeterminate or a negative result on echocardiography is shown below in Figure 5. The primary use of CMR is as an adjunct diagnostic tool in conjunction with ECG, biochemistry,

angiography and echocardiography. In these patients the diagnosis is often unclear, but primarily includes an AMI/ACS (a subcategory of CAD), acute myocarditis or TTC.

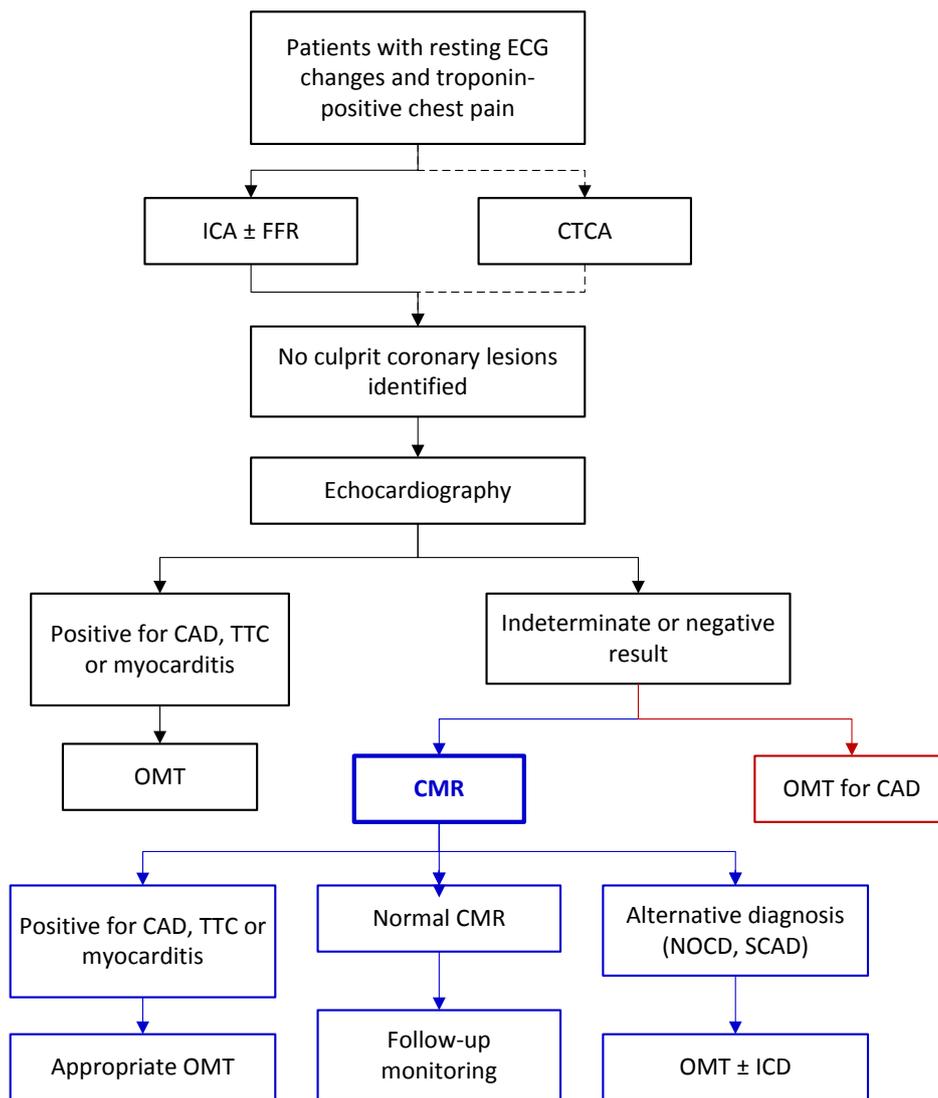


Figure 5 Revised current and proposed clinical practice algorithm for the diagnosis of patients with troponin-positive chest pain, ECG changes suspicious of ACS, and no culprit lesion identified on angiogram

Source: Figure 7 from the Final Protocol for MSAC application 1393, which was established by the Group contracted to write the protocol in consultation with the applicant.

Further clinical advice has indicated that most cardiovascular centres in Australia do not have easy access to CTCA testing for these patients; therefore, this testing option has been shown with dashed lines. The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

CAD = coronary artery disease; CMR = cardiac magnetic resonance (imaging); CTCA = computed tomography coronary angiography; ECG = electrocardiography; FFR = fractional flow rate; ICA = invasive coronary angiography; ICD = implantable cardioverter defibrillator; LV = left ventricular; NOCD = non-occlusive coronary disease; OMT = optimal medical therapy; SCAD = spontaneous coronary artery dissection; TTC = Takotsubo cardiomyopathy

Without CMR, the default diagnosis for patients with indeterminate or negative echocardiography results would mostly be ACS, even though non-obstructive or normal coronary arteries had been found with either ICA or CTCA, and these patients would receive lifelong medical therapy and follow-up for CAD.

Population 6

The revised clinical management algorithm for asymptomatic patients with a family history of SCD or aborted SCD in a first-degree relative, excluding channelopathies and arrhythmia, and in whom prior tests were inconclusive is shown in Figure 6.

In asymptomatic individuals with a family history of SCD, CMR is intended to be used as an adjunct diagnostic test to clinical evaluation, ECG and transthoracic echocardiography. Other

tests may depend upon the exact type of pathology being investigated. For example, Holter monitors may also be applied. In the absence of clinical practice guidelines, the proposed clinical management algorithm for patients with a family history of SCD is as in Figure 6.

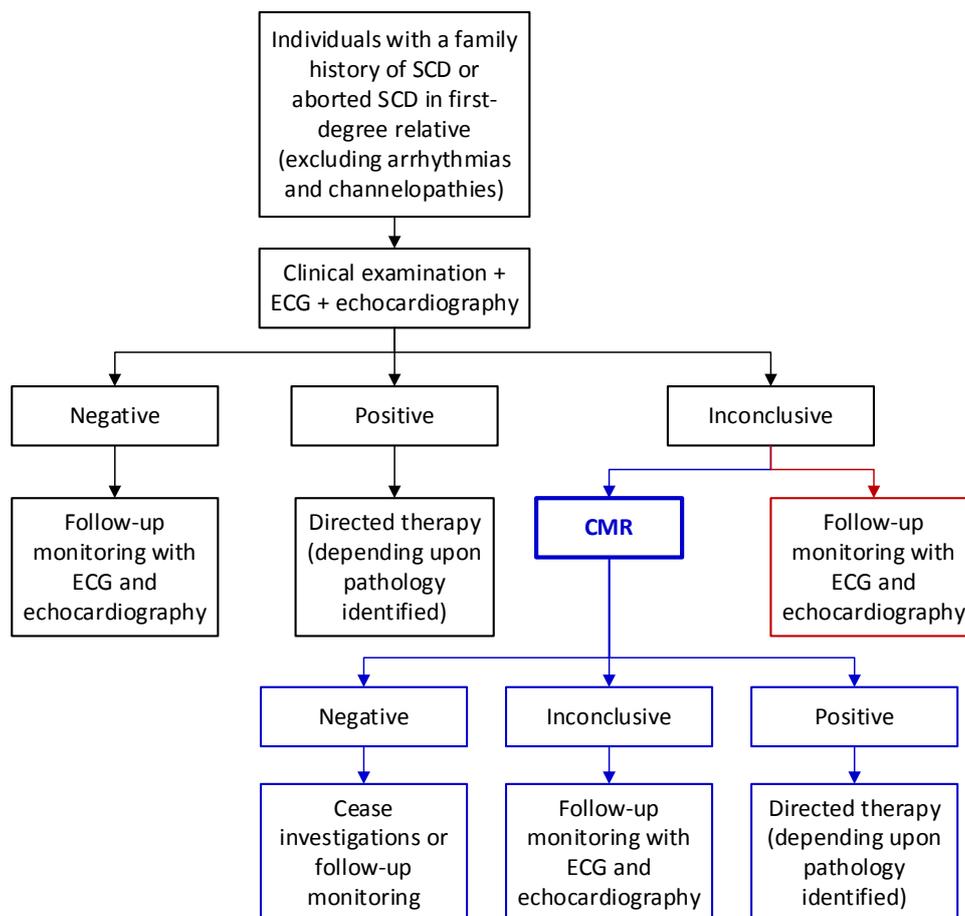


Figure 6 Revised current and proposed clinical management algorithm for asymptomatic individuals with a family history of SCD or aborted SCD in a first-degree relative

Source: Figure 8 from the Final Protocol for MSAC application 1393, which was developed by the Group contracted to write the protocol in consultation with the applicant.

The proposed pathway is shown in blue, and the resultant changes to the current pathway are shown in red.

CMR = cardiac magnetic resonance (imaging); ECG = electrocardiography; SCD = sudden cardiac death

9. Comparator

Prior to CMR, all patients would first undergo ECG and echocardiography. In all population groups the appropriate comparator to the intervention (CMR plus prior tests) is prior tests alone, without CMR. For population 5, patients would also have had coronary stenoses ruled out by either invasive coronary angiography (ICA) or computed tomography coronary angiography (CTCA); therefore, these were also considered to be prior tests, in addition to ECG and echocardiography.

10. Comparative safety

Being a non-invasive test without any associated radiation, CMR has a good safety profile.

The harms from CMR testing relate mainly to the gadolinium contrast agent, used for the purposes of early or late gadolinium enhancement. Rare acute allergy-like reactions may occur with the use of intravenous gadolinium-based contrast agents in 0.03–0.2% of patients. In patients with poor kidney function, gadolinium chelate injections can cause nephrogenic

systemic fibrosis. Poor kidney function is a contraindication for CMR to avoid the risk of nephrotic toxicity.

11. Comparative effectiveness

Populations 1 and 2 - HCM/RCM patients

Accuracy

According to the one study reporting on the sensitivity of CMR in patients suspected of HCM using clinical diagnosis as the reference standard, the sensitivity of both echocardiography and CMR was 100% (k=1; n=48) in symptomatic patients. Both echocardiography and CMR were diagnostic in 45/48 patients, CMR alone in three asymptomatic patients, and echocardiography alone in none. CMR was also used to diagnose fibrosis/scarring in HCM patients, with EMB as the reference standard (k=1; n=21). CMR had good sensitivity (76–100%) but low specificity (27–50%) for diagnosing fibrosis.

The diagnostic evidence in the RCM population was aimed at diagnosing fibrosis as a cause of RCM. CMR diagnosed fibrosis in 7/28 patients, of whom five were initially diagnosed with a different aetiology according to their echocardiography results.

Eight studies compared echocardiography with CMR and reported concordance data (without a valid reference standard). Five studies showed good correlation in wall/septum thickness measurements between echocardiography and CMR. CMR measured a significantly lower myocardial/LV mass compared with echocardiography, according to 2 studies. Diagnosing LV wall hypertrophy in both measurement methods was compared in 3 studies; the proportion of echocardiography-positive subjects in whom CMR was also positive (i.e. positive percent agreement) was 100% in all studies. However, one study reported that in 12% of HCM patients segmental LV hypertrophy was underestimated or undetected by echocardiography.

CMR may be useful in diagnosing patients with echocardiography-negative/indeterminate CMR results.

HCM mutation carriers / first-degree family members of HCM patients

Two studies were identified that investigated the diagnostic yield of CMR in HCM mutation carriers. The first study identified hypertrophy in 2/16 (12.5%) carriers, which was not picked up by echocardiography. In the second study CMR detected mild focal hypertrophy in 3/40 (7.5%) mutation carriers who were classified as normal on echocardiography.

Clinical validity (prognosis)

Fifteen studies were identified that reported prognostic data on LGE-CMR in patients with HCM. The presence of LGE on CMR was a significant prognostic marker for (aborted) SCD, all-cause mortality, cardiac death, and major adverse effects (AEs), with relative risks (RRs) of 2.2, 1.7, 2.5 and 3.7, respectively. It did not significantly predict heart failure (HF) deaths (RR 2.04; 95%CI 0.78, 5.24). No prognostic studies were identified including RCM patients. One study found that the presence of LGE was a predictor for exercise-related arrhythmias in HCM mutation carriers. However, the study was limited in its sample size (n=31).

Therapeutic efficacy (change in management)

One study was identified that investigated whether the incremental value of CMR leads to a change in patient management in patients suspected of HCM. In 51% (55/107) of patients suspected of HCM, CMR allowed the clinician to make a definitive diagnosis. Patient management was changed due to CMR in 51% of cases. The most common changes were (1) further prognostic workup and genetic screening and (2) discharges from follow-up that was

no longer considered necessary. It was not reported whether CMR had an impact on treatment changes in HCM patients.

Therapeutic effectiveness (health benefit from change in management)

As there was no evidence on change in treatment of patients with HCM after CMR, the therapeutic effectiveness of CMR has not been considered. However, even though no impact on treatment was explicitly reported, CMR may still have clinical utility, due to its impact on further tests ordered or on the screening of patients and/or family members.

Populations 3 and 4 - ARVC

Accuracy

Of all the patients who were suspected of having ARVC at presentation, 17–22% had CMR scans showing any RV abnormality that could be related to ARVC, but only 2–4% had abnormalities that met the 2010 major TFC and 1–11% met minor TFC.

Only 53% (median, range 40–63%; k=4) of patients diagnosed with ARVC met a major CMR TFC, and an additional 9% (median, range 0–27%; k=4) met a minor CMR TFC. Among family members, 20% (median; range 8–32%; k=2) had a major CMR TFC and 5% (median; range 0–10%; k=2) had a minor CMR TFC. Thus, not all patients who are diagnosed with ARVC have RV structural or functional changes that can be detected by CMR. Consequently, the results suggest that although CMR is not useful as a stand-alone test for the diagnosis of ARVC, it could be beneficial for some patients when used in conjunction with other tests undertaken to establish a diagnosis according to the 2010 TFC, which is considered to be the reference standard. This approach is in line with the clinical algorithm proposed for populations 3 and 4.

Three studies compared CMR and echocardiography and found that the kappa coefficient for agreement between the two varied between 0 (i.e. no better than chance) and 0.16 (i.e. slight agreement). In these studies approximately half of the abnormalities detected by CMR were also detected by echocardiography. However, according to the clinical algorithm, echocardiography would be performed before CMR, and patients who are negative by echocardiography would not be eligible for CMR. Among patients already diagnosed with ARVC, 80–100%, and 50% among first-degree relatives who have abnormalities associated with ARVC detected by echocardiography, would also be detected by CMR. It should be noted that it cannot be determined whether patients with disparate results for CMR and echocardiography are falsely negative or falsely positive.

One study compared CMR with a Holter ECG and 12-lead ECG composite outcome, and found moderate agreement between CMR and ECG (kappa = 0.43; 95%CI 0.23, 0.64) among family members who harboured a mutation associated with ARVC. Nearly all people who had abnormalities related to ARVC detectable by CMR also had ECG changes. Conversely, only about half (52%) of individuals with ECG changes would have abnormalities associated with ARVC that are detectable by CMR.

Clinical validity (prognosis)

Five cohort studies reported on the prognosis of patients who were diagnosed as having abnormalities relevant to ARVC by CMR compared with those who had normal CMR scans. Patients with CMR abnormalities had 6-times more chance of having an arrhythmic event than those with normal CMR scans. Most of the arrhythmic events were episodes of sustained ventricular tachycardia (VT) / ventricular fibrillation (VF) or appropriate implantable cardioverter-defibrillator (ICD) discharges, but SCD or aborted SCD also occurred. The difference in the number of cardiac deaths in patients with or without CMR abnormalities did not reach statistical significance.

Two studies reported on the adverse health outcomes in patients diagnosed with ARVC or their mutation-positive relatives who had LGE associated with the RV and/or LV, compared with those that did not. Although it is likely that the presence of LGE may predict worse health outcomes for patients diagnosed with ARVC and for their at-risk relatives, the results should be viewed with caution. As the evidence base is extremely limited, the extent of its clinical value remains uncertain.

Two studies with a low risk of bias reported on the ability of LV involvement to predict health outcomes in patients diagnosed with ARVC. Due to the limited evidence base and the contradictory results from the 2 studies providing this evidence, the result is unclear; however, there may be little prognostic value in determining LV involvement in ARVC, except in at-risk family members.

Therapeutic efficacy (change in management)

Of those patients who were suspected of having ARVC, the majority (65%) had normal CMR scans, and 19% had RV abnormalities associated with ARVC but were only severe enough to either be strongly suggestive of or meet the TFC in 4% of cases. An alternative diagnosis after CMR occurred in 14% of patients.

The patient group of interest, according to the proposed clinical pathway, comprises those who are suspected of having ARVC on the basis of other TFC. It can therefore be assumed that the majority of these patients, in the absence of CMR, would be treated as if they had ARVC, and their family members would receive screening and surveillance as if they were at risk of ARVC. However, the evidence base suggests that between 7% and 27% of patients will receive a non-ARVC diagnosis, most likely requiring a different management plan. The proportion of these patients that would have been correctly diagnosed with their condition using current tests such as echocardiography cannot be determined from the available data. Nevertheless, a large number of patients could potentially receive inappropriate treatment leading to serious long-term adverse effects.

One study from the United Kingdom found that management decisions, mainly to initiate or terminate further clinical surveillance or genetic/familial assessment, were influenced by CMR results in 40% of cases. CMR provided no incremental utility towards either diagnosis or management in only 12% of cases.

An Australian study found that, following CMR, 10% of patients had a change in their management plan for ICD implantation. However, the author of this study said that this result was conservative, as many participating clinicians referring patients for CMR did not commit to a treatment plan (i.e. device implantation or not) until after the CMR results were obtained. The main change was that, in the absence of CMR, clinicians were more likely to refer patients for an ICD, whereas with CMR they felt more confident that patients did not have ARVC and did not require an ICD. If ARVC is excluded in a symptomatic patient, this would also have the flow-on effect of ruling out the requirement for cascade screening of family members.

Therapeutic effectiveness (health benefit from change in management)

Ruling out ongoing surveillance in patients or family members who do not require it is unlikely to impact patients' health. CMR is unlikely to result in more patients being treated for ARVC, as the target population comprises those suspected of having ARVC, they would likely receive treatment for it, unless ruled out by CMR. The key impact to health, therefore, is in those who are ruled out by CMR.

In patients who have ARVC ruled out by CMR, the avoidance of an ICD implantation may result in the avoidance of harms associated with ICDs, or a risk of higher mortality if ruled

out incorrectly. In those who are correctly ruled out, it is expected that receiving optimal medical therapy (OMT) alone would result in non-inferior effectiveness outcomes compared with receiving OMT in combination with an ICD.

There is evidence that in those with ARVC, having an ICD may be beneficial at reducing the risk of SCD. In those who are incorrectly identified as not having ARVC (i.e. false negatives), the absence of an ICD would therefore result in inferior effectiveness. However, it is unknown how many patients are incorrectly ruled out from having ARVC.

Two meta-analyses estimated the annualised rate of inappropriate ICD shocks to be 3.7% and 3.9% per year. It should be noted that ARVC patients are generally younger than other patients receiving an ICD implantation, and are likely to suffer from more AEs due to having the ICD implantation for a longer period of time. Consequently, any indication for ICD implantation in ARVC should weigh the potential benefit against the risk of complications.

From the diagnostic yield data, it was reported that up to 28% of patients initially suspected of ARVC received an alternative diagnosis due to CMR results. Some of these diagnoses, such as Brugada syndrome and long QT syndrome, may be treated in a similar manner to ARVC, so the health impact on these patients of having a correct diagnosis may not be significant. However, other alternative diagnoses included ischaemic heart disease (IHD), myocarditis, HCM, dilated CM (DCM), congenital heart disease, valvular diseases, sarcoidosis and amyloidosis. Identification of these diseases may allow appropriate treatment, such as revascularisation for those with ischaemia, or treatment of the cause of myocarditis, if able to be identified. Although this contracted assessment could not assess the effectiveness of treatments for all these diseases, it is assumed that a correct diagnosis would result in more-appropriate treatment and better health outcomes.

Population 5 - myocarditis / acute myocardial infarction (AMI) / Takotsubo CM (TTC)

Accuracy

No data were found providing information on the accuracy of diagnoses made without the use of CMR in patients suspected of having ACS but without coronary stenosis. The population of interest comprises those who are considered to have an indeterminate diagnosis based on prior tests, so the accuracy of these prior tests is therefore expected to be low.

No studies reported on the accuracy of CMR in the specific population of those in whom prior tests were indeterminate.

In patients suspected of having myocarditis, the accuracy of CMR was determined using the reference standard EMB in 8 articles. Different criteria were used to interpret the CMR information, to determine whether patients had myocarditis. The most applicable evidence was considered to be from 1 study of 37 patients, which used the Lake Louise Criteria for determining myocarditis based on CMR in patients with infarct-like suspected myocarditis. The sensitivity and specificity of CMR were 86% (95%CI 74, 99) and 75% (95%CI 45, 100), respectively. However, EMB is an imperfect reference standard that is susceptible to sampling bias.

To determine the accuracy of diagnosing TTC, 2 studies compared CMR against follow-up clinical examinations using the Mayo Clinic Criteria. In these studies all patients who were diagnosed as having TTC by CMR were considered to have TTC by the clinical reference standard. However, the studies did not allow conclusions to be made on whether there were any false negatives, as follow-up data on those without TTC based on CMR were not provided.

Only one study provided an indication of the overall accuracy of CMR, for differential diagnosis between AMI, TTC, myocarditis and other cardiac conditions, compared to consensus clinical diagnosis (incorporating CMR) at follow-up. CMR was considered to have provided a correct diagnosis in 90% of patients, misdiagnosing 8% and providing no diagnosis in 2%. In those considered misdiagnosed, CMR did not adequately distinguish between tachycardia-induced CM and DCM, hypertrophic heart disease, and myocarditis. One patient with no structural heart disease was misdiagnosed as having ARVC.

Therapeutic efficacy (change in management)

Although the evidence regarding the analytical validity of CMR was not strong, there is evidence that clinicians trust the information gained by CMR, and that it has a large impact on both the diagnosis and treatment that patients receive.

In 3 studies that specifically reported on patients without a clear diagnosis based on prior tests, CMR was able to provide a definitive diagnosis (of myocarditis, AMI, TTC, DCM or HCM) in 63–72% of patients, and rule out a cardiac condition in the remaining patients. A negative CMR triggered investigations for non-cardiac diagnoses such as pulmonary embolism, sepsis and renal failure.

Seven studies reported on the impact that CMR had on diagnoses when clinicians had trusted the prior tests enough to allocate a diagnosis. Overall, 37% (120/328) of patients in this population had their diagnosis changed as a result of CMR. Those classified as having had an AMI on the basis of the prior tests were the most likely to have a change in diagnosis based on CMR (50–69%; k=2). One retrospective case review in the United Kingdom (n=108) reported that CMR provided a new definitive diagnosis in 44% of cases, and additional diagnostic information in a further 47%.

Change in diagnosis was followed by a change in management. Two studies reported that 32–55% of patients had their management changed as a result of undergoing CMR. The changes that occurred were predominantly discontinuation or reduction of treatment for ACS (i.e. anti-platelet therapy, aspirin, clopidogrel, high-dose statins), with a small proportion of patients having treatment targeted to myocarditis (i.e. anti-inflammatory treatment) and treatment for otherwise missed cases of AMI.

Therapeutic effectiveness (health benefit from change in management)

For the majority of cases who have their treatment altered due to having ACS ruled out by CMR, the impact is likely to be non-inferior health outcomes and superior safety outcomes. Medications for ACS, targeted at thinning the blood, stopping coagulation and reducing cholesterol, may have side effects such as gastrointestinal bleeding. Although the absolute risk of these side effects is low, the ability to avoid lifelong treatment for ACS is considered a clinically relevant outcome to patients.

A small number of patients were identified, based on CMR results, as having had an AMI that was unsuspected after having shown unobstructed coronary arteries on ICA. In these patients anti-platelet therapy was initiated. In patients diagnosed with ACS, anti-platelet therapy is an effective secondary prevention measure, reducing the likelihood of further cardiac events.

In those identified as having myocarditis, there is some limited evidence that treatment targeting the underlying pathology may have some benefit for improving cardiac functioning. The key benefit for most people diagnosed with myocarditis, however, is likely to be the avoidance of a lifelong diagnosis and management of ACS.

In patients diagnosed with TTC, observational studies have reported that treatments such as ACE-inhibitors, aspirin, statins, inotropics and beta-blockers are not beneficial. These patients may therefore avoid the side effects due to treatments for ACS, but it is unclear what treatments benefit them.

In patients without a cardiac condition diagnosed on CMR, further testing is likely to occur for alternative non-cardiac diagnoses such as pulmonary embolism, renal failure or sepsis. It was outside the capacity of this assessment to be able to assess the impact of the downstream consequences of alternative diagnoses, although it is assumed that having a correct diagnosis is likely to be considered important by patients.

The clinical implications of the misdiagnoses outlined in the accuracy section above are unknown.

Overall, it appears that CMR can inform the diagnosis and alter the management of a large number of patients in whom a diagnosis is otherwise difficult to make.

Clinical Claim

The applicant stated that the use of CMR may avoid the use of invasive testing, such as endomyocardial biopsy (EMB) in populations 3 and 5, and right ventricular (RV) angiography or electrophysiological studies in population 3.

12. Economic evaluation

Populations 1 and 2

The clinical evidence suggests that in patients with increased LV wall thickness who are suspected of having HCM or RCM, the incremental benefit of CMR, in terms of increased or improved diagnostic yield, could not be determined from the body of evidence presented in section B. On this basis no cost-effectiveness analyses will be presented for this population.

Populations 3 and 4

The clinical evidence suggests that it is uncertain whether the addition of CMR to current testing for the diagnosis of ARVC will result in better or worse health outcomes, as there is no reference standard available. Cost-effectiveness analyses will be presented based on the Australian change-in-management data from patients suspected of ARVC enrolled in the Taylor et al. (2013) study. The outcomes measured include: cost per additional appropriate device implanted, cost per additional appropriate management plan and cost per inappropriate device avoided.

The results of the analysis showed that CMR is associated with a net incremental cost saving of \$366 per patient in the base-case analysis. While CMR is associated with incremental costs associated with testing and appropriate device management, these costs are offset by a reduction in the cost of inappropriate device implantation. In addition, CMR is associated with positive outcomes—an increase in the number of appropriate devices planned and a reduction in the number of inappropriate devices planned. This was due to discordant management plans observed in 9.3% of patients, and the assumption that where CMR provides additional information to change management based on prior testing alone, the management change based on CMR is correct.

Given the cost savings and improvement in effectiveness outcomes, the base-case analysis concludes that CMR is dominant (i.e. less costly and more effective) for ARVC diagnosis and management, compared with use of prior testing alone. Sensitivity analyses provide additional information on the minimum threshold levels of accuracy and/or concordance required to support this conclusion.

Population 5

The clinical evidence suggests that in this population the addition of CMR to the prior testing regimen has an impact on both the diagnosis and treatment that patients receive, compared to prior tests alone. However, no data was found on the accuracy of diagnoses made without CMR in these patients; long-term treatment outcomes of patients suspected of having ACS, but without coronary stenosis remains unclear; and treatment for alternative conditions of myocarditis and TTC are of uncertain benefit, thus modelling of patient-relevant long-term treatment outcomes was not possible.

A cost-effectiveness analysis in terms of a cost per change in clinical diagnosis is presented, with the model restricted to 12 months and cost inputs limited to CMR and ACS medication costs.

CMR is associated with an incremental cost of \$1,045 per service in the base-case; that is, the MBS listing price of CMR (\$1,106) is only slightly offset by changes in the pharmaceutical management of patients no longer receiving an inappropriate diagnosis of AMI.

The incremental cost per change in diagnosis was estimated at \$3,673; or \$3,235 in terms of cost per appropriate change in management. However, these estimates are highly uncertain and the outcomes do not capture all patient relevant concerns, such that they may not be adequate to determine cost-effectiveness.

13. Financial/budgetary impacts

The estimates of expected CMR use and associated costs are shown in Table 2.

Table 2 Total estimated services and costs to the MBS associated with proposed CMR testing (including associated services) in the proposed populations for listing, 2016–17 to 2020–21

-	2015–16	2016–17	2017–18	2018–19	2019–20
Populations 1 and 2					
Number of CMR services	52,669	55,712	58,756	61,800	64,844
Total MBS costs	\$45,208,555	\$47,821,296	\$50,434,036	\$53,046,777	\$55,659,517
Populations 3 and 4					
Number of CMR services	4,664	4,759	4,838	4,918	4,995
Total MBS costs	\$4,003,131	\$4,084,537	\$4,153,086	\$4,221,027	\$4,287,916
Population 5					
Number of CMR services	2,836	2,845	2,853	2,862	2,870
Total MBS costs	\$1,927,022	\$1,932,862	\$1,938,701	\$1,944,541	\$1,950,381
TOTAL CMR services	60,169	63,316	66,447	69,580	72,709
TOTAL MBS costs (including associated costs)	\$51,138,708	\$53,838,695	\$56,525,823	\$59,212,345	\$61,897,814

CMR = cardiac magnetic resonance; MBS = medical benefits schedule

There is considerable uncertainty in the estimates of use and the combined total estimates of services and costs may be overestimates. Patients who are being investigated for multiple possible cardiac diagnoses and may be eligible for CMR under more than one listing (including listings detailed in other MSAC reports) may be double counted. It would be expected that such patients would receive only one CMR, and only one item number would be claimed.

14. Key issues from ESC for MSAC

ESC considered the evidence supporting the safety, effectiveness and cost effectiveness of cardiac magnetic resonance imaging (CMR) for the diagnosis and treatment planning of patients with suspected non-ischaemic cardiomyopathies (NICM). This application excludes the use of CMR for dilated NICMs which was previously considered by MSAC in July 2016 ([Application 1393: Cardiac MRI — Cardiomyopathy \[Part A\]](#)).

ESC noted that there is no current MBS listing for CMR for cardiomyopathy.

ESC noted that CMR and the other non-invasive imaging tests used as comparators in this application had a good safety profile.

There are six populations included in the application. However, ESC did not consider population 6 due to the lack of evidence presented. The remaining populations are:

- Population 1: patients in whom echocardiography suggests increased left ventricular (LV) wall thickness, a hypertrophic or restrictive cardiomyopathy (HCM or RCM) is suspected, and further diagnostic clarification is required;
- Population 2: asymptomatic individuals with a first-degree relative with HCM/RCM with increased or indeterminate LV wall thickness on echocardiography;
- Population 3: patients in whom arrhythmogenic right ventricular cardiomyopathy (ARVC) is suspected on the basis of other International Task Force Criteria (TFC);
- Population 4: asymptomatic patients with a family history of ARVC in a first-degree relative; and
- Population 5: patients with troponin-positive chest pain, ECG changes suspicious of acute coronary syndrome (ACS), and no culprit lesion identified on coronary angiography.

ESC noted that the evidence base for the use of CMR in NICM was incomplete and that a broader literature search to inform the evidence base for these populations may have been warranted. ESC also noted that opportunities for interested parties to inform and refine the PICO criteria and search terms were available during the PASC process.

Population 1 and 2

ESC noted that the evidence base for the use of CMR in populations 1 and 2 was incomplete and that the literature search informing the evidence base for these populations may have been improved by the inclusion of search terms for diseases that result in HCM/RCM (e.g. amyloidosis, sarcoidosis).

ESC noted that CMR may provide additional information to allow a definitive diagnosis in these populations but the evidence presented in the application to support this was very limited. ESC noted that due to uncertainty about any additional benefits of CMR in population 1 or population 2, no economic evaluation was presented.

Population 3 and 4

ESC noted that a linked evidence approach was undertaken to investigate the effectiveness of CMR in populations 3 and 4. ESC noted that while the evidence base was limited, there was low level evidence that CMR could change diagnoses. ESC noted that CMR could also change management decisions with regards to implantation of an implantable cardioverter defibrillator (ICD) device for some patients. ESC noted that avoidance of inappropriate ICD implantation would reduce patient harm and was an important patient outcome.

ESC noted that in a study that modelled the relative contribution of the different criteria included in the 2010 TFC for the diagnosis of ARVC, removal of CMR led to the greatest decline in diagnostic accuracy.

ESC noted that, if CMR was assumed to have superior safety and non-inferior effectiveness, its use in populations 3 and 4 was dominant (less costly and more effective) when compared with prior testing without CMR. This was driven by an increase in the appropriate implantation of ICD devices. ESC noted that use of CMR remained dominant as long as CMR led to correct management in at least 69% of patients who had discordant results on prior testing and CMR.

ESC agreed that the six-month time horizon used in this economic model was acceptable.

ESC anticipated that the number of ARVC cases would remain stable with just under 5,000 patients diagnosed each year and a cost for CMR of approximately \$4.2 million per year.

Population 5

ESC noted that there was limited evidence that CMR could provide additional information to allow clinicians to make a diagnosis in population 5. There was also limited evidence that use of CMR could change management by ruling out an ACS resulting in a reduction or cessation of medicines to treat ACS.

ESC noted the considerable uncertainty surrounding the economic and financial impact of the use of CMR in population 5. ESC noted that a cost effectiveness analysis, which assumed that use of CMR would lead to non-inferior health outcomes and superior safety outcomes in this population, indicated that the direct cost of the CMR (\$1,106) would be slightly offset by changes in medicine use (-\$61) if the CMR identified that the patient had not had a myocardial infarction. In the base case the incremental cost of CMR was \$1,045 per service.

Policy and implementation

ESC agreed that there were a number of policy and implementation issues that were well described in the ESC policy document. These included issues around:

- supervision;
- legislative changes to allow cardiologists to provide and report on CMR;
- training of cardiologists and radiologists; and
- the need for the sites providing CMR to have Medicare eligibility, be a comprehensive practice and be accredited under the DIAS.

ESC agreed that the providing specialist should personally attend patients during the examination and that the registered medical radiation practitioners undertaking the CMR do so under the supervision of a specialist trained in CMR. ESC noted that these requirements could be managed through the item descriptor.

ESC noted concerns that provider training and site accreditation needs could initially limit availability of CMR for patients with an NICM. However, ESC noted that these patients are managed in tertiary care centres where CMR is already part of the standard of care and so such access issues may be minimal.

ESC noted that the cost of CMR for these patients is currently being borne by the public sector of each state or territory and so any listing is likely to result in cost shifting.

ESC noted that the site accreditation requirements would limit uptake by private MRI providers.

ESC noted that additional input from the CSANZ may be useful in scoping any future application.

ESC noted MSAC may wish to consider how any future application for these six populations fits in with any future application for the populations considered in [Application 1393: Cardiac MRI — Cardiomyopathy \(Part A\)](#).

From a consumer perspective, ESC noted that CMR was already routinely conducted in these patients and benefited some patients, but that appropriate training and accreditation of providers was important.

15. Other significant factors

Nil.

16. Applicant's comments on MSAC's Public Summary Document

The applicant had no comment.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)