Remote monitoring systems for patients with implanted cardiac devices

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The Secretary
Medical Services Advisory Committee
Department of Health and Ageing
Mail Drop 106
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee with the assistance of John Gillespie, Alasdair Godfrey, Marianne Chau, Georgie Kovacs, Miranda Bailey, and Adam Gordois from IMS Health Australia. The report was edited by Ann Jones. The report was endorsed by the Minister for Health and Ageing on 28 August 2008.

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Glossary

ACMA	Australian Communications and Media Authority
AF	atrial fibrillation
AHMAC	Australian Health Ministers' Advisory Council
AIHW	Australian Institute of Health and Welfare
AR-DRG	Australian Refined Diagnosis Related Groups
AV	atrioventricular
bpm	beats per minute
CRT	cardiac resynchronisation therapy
CRT-D	cardiac resynchronisation therapy-defibrillator
ECG	electrocardiogram/electrocardiograph
FN	false negative
FP	false positive
GSM	global system mobile (communication)
HADS	Hospital Anxiety and Depression Scale
HAS	Haute Autorité de Santé
HM	home monitoring
HTA	health technology assessment
ICD	implantable cardioverter defibrillator
ICD-10	International Statistical Classification of Diseases and Health Related Problems, Tenth Revision
IHD	ischaemic heart disease
LVEF	left ventricular ejection fraction
LV-T	left ventricular tachycardia
MBS	Medicare Benefits Scheme
MICS	Medical Implant Communications Service
MIT	medical implant telecommunications

MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
NR	not reported
NYHA	New York Heart Association
PM	pacemaker
QALY	quality-adjusted life year
QUADAS	quality assessment of studies of diagnostic accuracy included in systematic reviews
QUOROM	quality of reporting of meta-analyses
RCT	randomised controlled trial
RF	radio frequency
SF	short form
SMS	short messaging system
TGA	Therapeutic Goods Administration
TTM	trans-telephonic monitoring

Executive summary

The procedure

Patients with implanted devices visit clinics regularly to check that the devices function correctly and monitor occurrences of cardiac arrhythmia. Additional clinic visits are required if patients experience new cardiac symptoms or device dysfunctions that could result in delay to medication changes or device adjustment. Remote monitoring of patients with implanted cardiac devices enables supervision and diagnostic testing to be conducted over distance. This may enable earlier detection of arrhythmias, deterioration in clinical status, and defects in device functioning. Reading, interpreting, and if necessary acting on, periodic and event triggered data enables patient cardiac health and functioning of implanted cardiac devices to be managed remotely. The medical service of remote monitoring comprises remote data analysis performed by clinicians to evaluate cardiac health and device functioning.

Remote monitoring systems comprise four common components—an implanted cardiac device, a remote sensor device, remote monitoring service centre, and a data transfer system. All are necessary to enable remote data transfer and to subsequently review patients' cardiac status and device integrity data.

Implanted cardiac devices include pacemakers, implantable cardioverter defibrillators (ICD) and cardiac resynchronisation therapy (CRT). These devices can store and transmit cardiac status and data about the device's functions.

All monitoring systems include a remote sensor device. Remote sensors are located in patients' homes to facilitate transfer of stored data from the cardiac implant to a remote monitoring service centre. Some data transfer systems are automated and others require patient initiation.

All systems require remote monitoring service centres which are central facilities operated by device manufacturers in collaboration with mobile phone and internet service providers. Remote monitoring service centres receive, store and translate transmitted data into patient-specific reports.

A means for clinicians to access patient data or to receive alerts is also required. Data transfer methods vary among remote monitoring systems, but generally, patient reports are accessed via secure websites, e-mail, fax or short-message service (SMS).

Medical Services Advisory Committee–role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing 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.

A rigorous assessment of evidence is thus the basis of decision making when funding is sought under Medicare. A team from IMS Health was engaged to conduct a systematic

review of literature on remote monitoring systems for patients with implanted cardiac devices. An advisory panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of remote monitoring systems for patients with implanted cardiac devices

Clinical need

Patients require implantable cardiac devices to treat a number of conditions. These devices include permanent pacemakers to treat or prevent symptomatic bradyarrhythmias, implantable cardioverter defibrillators (ICDs) to decrease the risk of sudden cardiac death among high risk patients, and cardiac resynchronisation therapy (CRT) to alleviate symptoms and decrease mortality for patients with severe heart failure associated with dyssynchronous ventricular contraction. Medicare billing data (from January to October 2007) indicated that at least 43,108 patients in Australia have pacemakers, and 5156 patients have implantable cardioverter defibrillators.

Patients who have implanted cardiac devices attend scheduled cardiac device clinics for regular follow-up to monitor and optimise device function and to troubleshoot patient or device related problems. Additional clinic visits are required for patients who experience new symptoms, in the event of device or lead related product recalls, and when the device is approaching end-of-life. Remote monitoring provides a way to monitor patients that can decrease numbers of clinic visits and enables earlier detection of device dysfunction or changes in patients' clinical status.

Research questions

The research questions addressed were:

Pacemakers

To what extent is remote monitoring of pacemakers safe, effective and cost-effective in the management of patients relative to current clinical practice?

Implantable cardioverter defibrillators

To what extent is remote monitoring of implantable cardioverter defibrillators safe, effective and cost-effective in the management of patients relative to current clinical practice?

Cardiac resynchronisation therapy devices

To what extent is remote monitoring of cardiac resynchronisation therapy safe, effective and cost-effective in the management of patients relative to current clinical practice?

Safety and effectiveness

The limited body of evidence concerning devices listed by the Therapeutic Goods Administration (TGA) meant that the review classified evidence according to whether or not devices were listed.

No direct safety issues associated with remote monitoring of implanted cardiac devices were identified.

Several literature reviews performed in 2005 by the Haute Autorité de Santé, a French health technology assessment group that evaluated remote monitoring use, were identified. The key findings indicated that the trialled pacemaker, Biotronik BA03 DR, provided sufficient transmission success evidence and clinically relevant data for the Biotronik Home Monitoring® system. These studies were limited by a lack of comparative data, inadequate patient management reporting, and limited information to indicate the impact of remote monitoring on patient outcomes.

Ellery et al (2006) and Varma et al (Study B 2005) conducted studies that examined TGA listed devices. Both were non-comparative studies that were subsequently classified as providing low quality (level IV) evidence. Ellery et al (2006) investigated remote monitoring of the Kronos® LV-T (a device for CRT) and Stratos® LV-T (an ICD) using the Biotronik Home Monitoring® system. The study's aim was to determine if this home monitoring system could be used to predict patient cardiac events that require admission to hospital. Retrospective review of home monitoring data detected an increase in mean heart rate (both at rest and over a 24 hour period) among 70 per cent of patients who were admitted to hospital. A decreased need for CRT was observed in 43 per cent of patients admitted to hospital in this study. The validity of remote monitoring as a predictive test was not adequately demonstrated by this study because of the limited follow-up period and inadequate outcomes reporting.

Varma et al (Study B 2005) aimed to determine the usefulness of remote monitoring as a tool for early detection of atrial fibrillation events. Biotronik's Home Monitoring® system was used to measure output from the Biotronik Philos® DR-T pacemaker. The authors reported three patients in whom silent atrial events were detected by remote monitoring which lead to change in anticoagulation therapy. This study was limited by unclear patient follow-up and ill-defined outcomes. 'Atrial fibrillation days' were used as a surrogate measure, but inadequate data reporting meant that determining how the measure corresponded to clinical outcomes could not be achieved.

The literature review identified eight other studies that provided supporting evidence for the use of remote monitoring of implantable cardiac devices (Elsner et al 2005, Brugada et al 2006, Clementy et al 2003, Lazarus et al 2007, Varma et al 2005, Wallbruck et al 2002, Schoenfeld et al 2004, Joseph et al 2004). These studies investigated implanted cardiac devices that are not TGA listed, which limited applicability to Australian clinical settings.

Elsner et al (2005) conducted a randomised controlled trial (RCT) that aimed to demonstrate the impact of remote monitoring on clinical management and patient follow-up. The study's key finding indicated that there was no difference in mortality or hospitalisation rates in either the 3 or 12 month remote monitoring arms. Inadequate data reporting and lack of comparison to clinical follow-up contributed to this study

being evaluated as providing low quality and limited evidence to inform this assessment's conclusions.

Brugada et al (2006) compared clinician judgement of remote monitoring data with information obtained during regular clinical follow-up to measure the accuracy of remote monitoring. This study tested the Biotronik Home Monitoring® component of the Biotronik ICD Belos® VR-T. The authors estimated that 81 per cent of clinician visits could be avoided by using remote monitoring, but they also described a false negative rate of 14 per cent associated with remote monitoring. This study was limited by inconsistency in reporting, minimal applicability to the Australian setting, non-consecutive patient enrolment, and indications that blinding may have been incomplete.

The Biotronik Home Monitoring® system was trialled by Clementy et al (2003), Lazarus et al (2007), Varma et al (2005) and Wallbruck et al (2002). The Medtronic CareLink® system was trialled by Schoenfeld et al (2004). Joseph et al (2004) reviewed the St Jude Housecall® system.

These studies provided limited evidence to support remote monitoring. The studies by Joseph et al (2004), Schoenfeld et al (2004) and Wallbruck et al (2002) were non-comparative and lacked clarity in reporting clinical follow-up schedules. Lazarus et al (2007), Varma et al (Study A 2005) and Clementy et al (2003) used unblinded comparisons to the reference standard, and overall clinical follow-up was short (three months in Study A by Varma et al 2005).

Although no direct safety implications associated with remote monitoring were identified, successful and complete transmission of data by remote monitoring was regarded as a significant indirect safety outcome in this assessment. The potential for failure of data transmission presents a safety issue of which treating clinicians need to be aware—consistent data transmission failure may indicate that remote monitoring is unsuitable for a particular patient. The studies presenting transmission data indicated that during the study periods remote monitoring coverage was maintained for between 88 and 100 per cent of patients. Inadequate data reporting meant that it was not clear whether patients who maintained remote monitoring during the study were the same throughout, or this status applied to different patients at different times during follow-up. These studies also reported that 89 to 100 per cent of scheduled reports were successfully transmitted by remote monitoring systems. Transmissions outcomes were insufficiently reported. Brugada et al (2006) and Schoenfeld et al (2004) did not report the number of successfully transmitted scheduled reports; Varma et al (Study A 2005) did not indicate the number of patients who were able to maintain remote monitoring. Furthermore, unclear reporting meant that it was uncertain whether standard clinical practice was applied at regular scheduled clinical follow-up visits.

Cost-effectiveness

There is a lack of clinical evidence regarding patient outcomes and resource cost savings associated with remote monitoring systems. Therefore, an economic analysis of remote monitoring systems for patients with implanted cardiac devices is not presented in this assessment. There were three economic evaluations of remote monitoring identified in the literature (Chan and Chun 2002, Elsner et al 2006, Fauchier et al 2005). These studies have significant limitations and their results are not generalisable to an Australian setting.

It is proposed that the MBS fee for data analysis by remote monitoring should account for the opportunity cost of cardiologists' time in analysing results of remote monitoring devices. The fee could also account for capital costs incurred by cardiologists, for example, the amortised cost of equipment used to analyse data. An annual fee per patient is likely to be most appropriate solution and would avoid incentive to over-service patients.

In addition to the proposed fee, a future cost-effectiveness study of data analysis by remote monitoring should, at a minimum, include the costs of clinical follow-up visits and hospitalisations for cardiac events. These events are expected to be reduced by use of remote monitoring compared with regular clinical follow-up. The analysis should also include all capital costs attributable to the remote monitoring system (such as patient device, service centre, cardiologist equipment). An analysis from the societal perspective should also include productivity costs (time away from work due to clinic visits and cardiac events) and transportation costs, which are expected to be lower with remote monitoring systems.

More data are required to determine whether cost savings derived from use of remote monitoring systems exceed the cost of data analysis, or whether the net cost of remote monitoring is value for money in terms of the benefits provided by the service (such as cardiac events and deaths avoided).

Recommendation

MSAC has considered the safety, effectiveness and cost-effectiveness for the use of remote monitoring systems for patients with implanted cardiac devices including standard pacemakers, implanted cardioverter defibrillators and cardiac resynchronisation therapy compared with standard clinic-based follow-up alone.

MSAC finds that the procedure is safe.

MSAC finds that clinical effectiveness is not demonstrated.

A formal economic assessment was therefore not performed.

MSAC does not support public funding for the use of remote monitoring systems for patients with implanted cardiac devices.

–The Minister for Health and Ageing accepted this recommendation on 28 August 2008–

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of remote monitoring systems for patients with implanted cardiac devices. This is a diagnostic technology for patients with abnormal heart rhythms. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are at Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for remote monitoring systems for patients with implanted cardiac devices.

Background

Implanted cardiac devices

Cardiac electrical impulses, generated by the sinus node in the right atrium, coordinate synchronised contractions of the heart's four chambers and are transmitted by a specialised conduction system. Cardiac arrhythmia occurs when the regular heart beat is disrupted. Bradyarrhythmia (dangerously slow heart rate) is caused by the deterioration of the sinus node or the conduction system. This results in slow or no signals coming from the sinus node (sick sinus syndrome), or prevents signals from the atria reaching the ventricles (heart block). Tachyarrhythmia (abnormally fast heart rate) is caused by extra and abnormal electrical impulses that can arise in the atria, ventricles, conduction system, or from abnormal connections between the atria and the ventricles.

Cardiac arrhythmias that are not transient or reversible require constant clinical monitoring. Diagnosis delays occurring from lapses in providing medical assistance may increase risks of adverse outcomes such as heart failure, stroke or sudden cardiac death among people with certain arrhythmias. This is particularly relevant among high risk patients, such as those with structural heart disease, in whom early detection of arrhythmia is important to enable interventions to decrease risks of adverse outcomes. Hence, implantable cardiac devices, including standard permanent pacemakers, implantable cardioverter defibrillators (ICD) and cardiac resynchronisation therapy (CRT), have become increasingly important devices in the management of cardiac arrhythmia.

Pacemakers are implantable devices that transmit electrical impulses via a lead to the heart to maintain appropriate heart rate. They are used to treat both bradycardia and tachycardia. The basic architecture of pacemakers includes a pulse generator that houses a microcomputer and a long-lasting battery. Implantable cardioverter defibrillators (ICDs) apply the same basic function and design as pacemakers but also provide interventions for both bradycardia and tachycardia. ICDs are calibrated to respond to only life-threatening deviations from the natural heart rhythm. When the ICD detects a life-threatening tachyarrhythmia, such as ventricular tachycardia or fibrillation, an electrical shock is emitted to arrest the arrhythmia and avoid sudden cardiac death.

Cardiac resynchronisation therapy (CRT), also known as biventricular pacing, treats ventricular dyssynchrony for patients with severe heart failure (Peters and Gold 2000). The objective of treatment is to restore synchronous contraction of both ventricles. CRT involves implanting a device that has functions similar to either a pacemaker, ICD, or a combination of both. The lead from the pacing device delivers electrical current directly to both ventricles and the right atrium to induce synchronous contractions (Peters and Gold 2000).

ICD technology has been proven as providing the most effective means of preventing sudden cardiac death and reducing total mortality for patients with life-threatening ventricular tachyarrhythmia (Moss et al 1996, AVID investigators 1997, Winkle et al 1989). Studies by Bardy et al (2005) and Moss et al (2002) demonstrate the clinical effectiveness of ICDs for primary prevention of sudden cardiac death among high risk patients. This therapy also appears to be cost-effective (Zwanziger et al 2006, MSAC

reference 32). Hence, real time monitoring for high risk patients has potential for inclusion as a preventive tool in the management of cardiac arrhythmia.

Remote monitoring

Patients with implanted devices visit clinics regularly to check that the devices function correctly and monitor occurrences of cardiac arrhythmia. Additional clinic visits are required if patients experience new cardiac symptoms or device dysfunctions that could result in delay to medication changes or device adjustment. Remote monitoring of patients with implanted cardiac devices enables supervision and diagnostic testing to be conducted over distance. Reading, interpreting, and if necessary, acting on, periodic and event triggered data allows patient cardiac health and functioning of implanted cardiac devices to be managed remotely. The medical service of remote monitoring comprises the remote data analysis performed by clinicians to evaluate cardiac health and device functioning. Remote monitoring may enable earlier detection of arrhythmias such as atrial fibrillation, deterioration in clinical status, and device functioning (Furman et al 1975, Griffin et al 1986, Vallario et al 1988).

The concept of trans-telephonic monitoring (TTM) to examine pacemaker longevity was introduced in the early 1970s (Gessman et al 1995). TTM was further developed during the late 1970s and 1980s to provide sensing, data capture, and to enable detection of lead defects and arrhythmias (Igidbashian et al 2002, Dressing et al 2002). The clinical utility of TTM was established in the 1990s (Chan and Chun 2002). Patient participation is an issue in remote monitoring. TTM interrogation requires considerable patient participation which is not feasible in many instances. Automated methods using computer and communication technologies have been developed to alleviate reliance on patient reporting. These developments offer benefits in detecting supraventricular arrhythmia and atrioventricular (AV) conduction monitoring (Israel et al 2004). Data transmission has improved to achieve a success rate of approximately 92 per cent; patient acceptance and reliability of home monitoring systems ranged from 93 to 97 per cent (Glotzer et al 2003).

Currently available remote monitoring systems offer the benefits of integrated telecommunication and information technology with cardiology and device therapy for optimum patient management.

The four common components of remote monitoring systems enable remote data transfer and subsequent review of patient cardiac status and device integrity. The principal component is the implanted cardiac device, which can be a pacemaker, implantable cardioverter defibrillator (ICD) or cardiac resynchronisation therapy (CRT) device. These devices can store and transmit cardiac status and device function data. Remote sensor devices are located in patients' homes to transfer stored data from the cardiac implant to a remote monitoring service centre. Systems differ regarding data transfer which can be automated or require patient initiation. Each system maintains central remote monitoring service centres operated by device manufacturers in collaboration with mobile phone and internet service providers. Remote monitoring service centres receive, store and translate transmitted data into patient-specific reports. Remote monitoring systems also incorporate means for clinicians to access patient data or to receive alerts. Methods differ, but generally, patient reports are accessed via secure websites, e-mail, fax or short-message service (SMS).

The components required for remote monitoring are illustrated schematically in Figure 1.

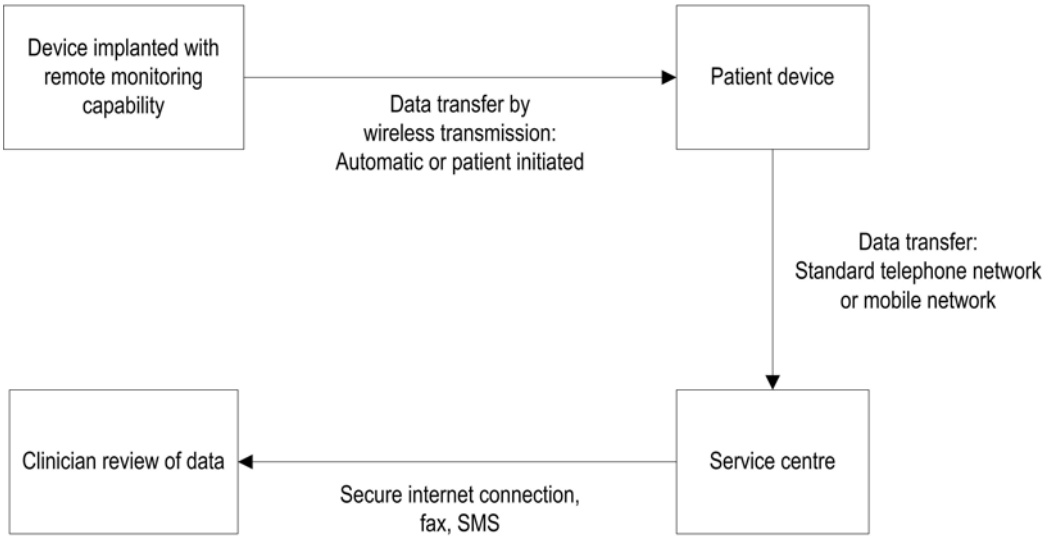

Figure 1 Schematic illustration of remote monitoring systems

Remote monitoring system components are compatible within manufacturers' ranges of products only.

Remote monitoring systems developed and maintained by Biotronik and Medtronic have been approved by the Therapeutic Goods Administration (TGA) and are currently available in Australia.

Biotronik Home Monitoring®

Cardiac health and technical data (electrocardiograph [ECG] of actual rhythm, heart rate, heart rate variability, number of mode switches, atrial fibrillation episodes, battery status and voltage, autocapture thresholds and so forth) stored in the memory of the implanted device are transmitted to the patient device (CardioMessenger®) daily at a scheduled time, or can be patient-initiated by applying a reader device over the implanted pacemaker. The CardioMessenger® device must be placed within 2.5 m of the patient (Vallario et al 1988, Biotronik product information).

Communication between the implant and the patient device is initiated by the implant's proprietary radio frequency (RF) circuit. In the USA, RF transmission uses a frequency band (402–405 MHz) dedicated by the US Federal Communications Commission for medical implantable devices. The Australian Communications and Media Authority (ACMA) authorises the use of radio frequencies for medical implant telecommunications.

Data are then transmitted from the patient device to the Biotronik Service Centre. Transmission is made by one of two methods; choice is dependent on availability of:

1. standard global system for mobile communications (GSM) cellular telephone technology to transmit digital data to send and receive messages by SMS; or

2. using the standard telephone system.

Messages received at the service centre are translated into a cardio report. This report is accessed by clinicians using internet access, fax, e-mail or SMS.

Data transferred by e-mail or the internet are encrypted before dispatch to safeguard patient confidentiality. New data are added to a database as they are received.

Medtronic CareLink®

Medtronic's CareLink® Network comprises implant, monitor and service centre components. CareLink® Network remote monitoring applies a similar three step methodology as described for Biotronik Home Monitoring.

The patient holds the mouse-like antenna of the Medtronic CareLink® Network monitor over the cardiac device implant to initiate data transfer from the implant to the monitor. The monitor, connected to a standard telephone line, automatically dials a toll-free, pre-programmed telephone number and sends the patient's device data to a secure server.

Data are then translated into a format similar to the information gathered during a typical clinic follow-up visit. Clinicians receive messages to view patient data at the secure Medtronic CareLink® website. A secure internet website for patients to access personalised information about their device and condition is also provided.

In the event that the implant device detects a problem, such as atrial fibrillation or a device integrity issue, and if the patient's device is programmed to notify the clinician, the device automatically establishes wireless communication with the Medtronic CareLink® Monitor. The message is sent automatically to the secure server via the phone line. The clinician receives a Medtronic CareAlert® notification via pager or voice message.

Medtronic markets cardiac implants (Concerto™ CRT-D and Virtuoso™ ICD) that are compatible with Conexus Telemetry. This system allows automatic transfer of stored data from the implant to the CareLink® Network. Conexus Telemetry uses the Medical Implant Communications Service (MICS), a radio frequency band designated for implantable medical devices. The MICS band protects Medtronic's wireless transmissions (402–405 MHz) from interference caused by mobile phones or other common electronic devices (Medtronic product information, Schoenfeld et al 2003). Clinicians can schedule up to six automatic device checks for each patient. The device automatically sends data following the described methodology at the scheduled times.

Intended purpose

This review evaluates the use of remote monitoring of patients with permanent pacemakers, implantable cardioverter defibrillators (ICD) and patients receiving cardiac resynchronisation therapy (CRT)

Clinical need

Sudden cardiac death is a major cause of fatality in developed countries (Trappe 2006). Most sudden cardiac deaths are caused by acute, fatal cardiac arrhythmia (abnormal heart rhythm). Death due to cardiac arrhythmia is most commonly associated with ventricular tachyarrhythmia (rapid heart rhythm), and is believed to account for over half of all deaths attributable to cardiovascular disease in Australia annually (Subbiah et al 2003). Bradycardia and heart block are also potentially fatal especially among people with advanced heart failure (Bubien et al 2004). Cardiac arrhythmia occurs most often in structurally abnormal hearts. Structural abnormalities may result from damage sustained following myocardial infarction or caused by cardiomyopathies. Sudden cardiac death can be the initial presentation of disease for many patients (Bubien et al 2004).

Arrhythmia

Cardiac arrhythmia is caused by malfunctions in the heart's electrical system that prevents uniform, regular contraction of the atria and ventricles and consequently compromises cardiac blood flow. Cardiac arrhythmia can be classified into two broad groups according to underlying heart rate: bradyarrhythmia and tachyarrhythmia. These can be further divided into subgroups relating to their atrial or ventricular origins (Subbiah et al 2003).

Cardiac arrhythmias are associated with significant morbidity and mortality and can result in syncope (a transient loss of consciousness resulting from insufficient cerebral blood supply) or lead to sudden cardiac death (Subbiah et al 2003).

Bradyarrhythmia

Symptomatic bradycardia is defined as a heart rate of less than 60 beats per minute (bpm) that is directly responsible for development of syncope or near syncope, transient vertigo, dysequilibrium, fatigue, exercise intolerance, confusion from cerebral hypoperfusion, or congestive heart failure (Dresing and Wilkoff 2007). Bradyarrhythmia results from disorders of impulse formation due to sinus node dysfunction, and impulse propagation from atrioventricular (AV) block. Sinus node dysfunction and AV block are the most common reasons for implantation of cardiac devices (Toogood 2007).

Sinus node dysfunction (sick sinus syndrome) is a frequent cause of bradycardia, generally precipitated by impaired impulse formation. Damage to the sinus node can result in reduced electrical impulse conduction to the chambers. Sinus node dysfunction also encompasses more widespread atrial abnormalities that form the basis for development of atrial tachyarrhythmia (Vardas et al 2007).

The most severe symptom of sinus node dysfunction is syncope, or near syncope, which occurs among about half of the affected patient population. Syncope is generally caused by sinus arrest or sinoatrial block (Vardas et al 2007). Most sinus node dysfunction symptoms result from decreased cerebral perfusion caused by reduced cardiac output.

A common manifestation of sinus node dysfunction is bradycardia-tachycardia syndrome where episodes of paroxysmal atrial fibrillation, flutter, or tachycardia are followed by severe sinus bradycardia, sinoatrial block, or sinus arrest (Durham and Worthley 2002). Patients who have frequent, repetitive, long-lasting episodes of sinus node dysfunction or

atrial fibrillation have potential for the atrial myocardium, including the sinoatrial region, to be altered both structurally and electrically, and are prone to systemic embolism (Cox 2003, Vardas et al 2007).

Causes of dysfunction can be intrinsic or extrinsic to the sinus node; idiopathic degeneration is the most common cause (Dresing 2001). Degenerative fibrosis of nodal tissue is the most common cause of intrinsic changes. Certain coronary artery conditions can cause these intrinsic changes. Up to 30 per cent of patients who present with acute coronary syndromes, especially those with inferior and posterior infarction, have bradycardia symptoms (Dresing 2001).

Atrioventricular (AV) block is characterised by a delay or failure of impulse conduction from the atria to the ventricles, despite that the atrioventricular node is not refractory to conduction (Dresing 2001). Atrioventricular block can be further classified into three degrees based on severity. First and second degree AV block are not commonly associated with symptoms, although syncope may occur with Mobitz type II second degree AV block (Toogood 2007). Third degree AV block occurs when no atrial stimulus is conducted to the ventricles, resulting in independent atrial and ventricular activity, and an atrial rate faster than the ventricular rate (Toogood 2007).

Third degree AV block may contribute to the progression of heart failure (Bubien et al 2004). Expected survival rates of patients with third degree heart block (without a permanent pacemaker) are 60 per cent at 12 months and 30 per cent at five years. Third degree AV block may be an underlying condition in sudden cardiac death. Death is sudden in 30 per cent of patients with third degree AV blocks (Toogood 2007).

Third degree AV block can be congenital or acquired through damage sustained from myocardial infarction, cardiomyopathy or metabolic disturbances such as severe hyperkalaemia (Durham and Worthley 2002). Slightly less than 10 per cent of people experiencing acute inferior myocardial infarction will develop third degree AV block (Levine and Brown 2006). Many of these are temporary, but when AV block occurs as a result of anterior myocardial infarction, prognosis is poor (Dresing 2001).

Ventricular tachyarrhythmia and ventricular fibrillation

Ventricular tachycardia originates from ventricular ectopic pacemaker cells that cause premature heart beats in addition to the standard rhythm generated from the sinus nodes or other atrial tissue. Ventricular tachycardia is characterised by heart rates typically in the range of 150 to 250 bpm with consistent rhythm (Ernoehazy 2006). Ventricular tachycardia can be well tolerated, but is also associated with grave, life-threatening haemodynamic compromise especially if ventricular fibrillation results.

Ventricular tachycardia is usually the consequence of structural heart disease. Mechanisms include normal conduction pattern breakdown, increased automaticity, and activation of re-entrant pathways in the ventricular conduction system (Ernoehazy 2006). In patients with coronary artery disease who have a history of myocardial infarction, ventricular tachycardia may be related to re-entry in the areas bordering the infarction. These regions exhibit varying impairment of impulse conduction, as well as recovery from excitability, potentially resulting in areas of slow conduction and unidirectional block that predispose to re-entry (Bubien et al 2004). The mechanism is less well understood among patients with dilated non-ischaemic cardiomyopathy, or idiopathic ventricular tachycardia.

Tachycardia symptoms include palpitations, vertigo or dysequilibrium, dyspnoea, chest pain or angina, and syncope. Morbidity and mortality principally results from spontaneous degeneration into ventricular fibrillation, a more malignant condition. Even in the absence of such degeneration, ventricular tachyarrhythmia can produce congestive heart failure and haemodynamic compromise, with subsequent morbidity and mortality. The consequences depend largely on the presence or absence of myocardial dysfunction (such as may result from ischaemia or infarction) and on the rate of ventricular tachyarrhythmia (Ernoehazy 2006).

Ventricular fibrillation occurs when the heart muscle begins a quivering motion caused by disunity in contractile cell function. Clinical features of ventricular fibrillation include heart rates of greater than 250 bpm with no discernible rhythmic pattern. Effective blood circulation ceases. Ventricular fibrillation is considered to be a form of cardiac arrest, and people experiencing the condition do not survive without immediate provision of cardiopulmonary resuscitation and defibrillation. The mechanisms of ventricular fibrillation are likely to be complex and can involve ischaemia, degeneration from ventricular tachyarrhythmia, triggered activity from Purkinje fibres, and myocardial stretch. Maladaptive neuro-hormonal responses and hyper-adrenergic state, as well as electrolyte abnormalities, may also predispose patients to fibrillation. Patients who survive ventricular fibrillation have a high risk of recurrence (Bubien et al 2004).

Structural anatomic cardiac abnormalities are the basis for the development of tachyarrhythmia and ventricular fibrillation. Abnormalities can be caused by myocardial infarction, hypertrophy resulting from hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy, or valvular heart disease (Bubien et al 2004).

Implantable cardiac devices are used for both primary and secondary prevention of sudden cardiac death from ventricular tachyarrhythmia or fibrillation. Implantable cardiac devices are provided for patients who have experienced an episode of aborted sudden cardiac death, or who carry heightened risk of an event, to detect and treat ventricular tachyarrhythmia or fibrillation. Primary prophylactic ICD indications include people with chronic stable heart failure and severe left ventricular dysfunction.

Heart failure

Heart failure is a complex clinical syndrome. The initial manifestation among most patients is dyspnoea, which is usually progressive, and pulmonary oedema may follow (Duncan et al 1996). Patients with heart failure often have limited exercise capacity, frequent need for hospitalisation, high mortality rates, and impaired quality of life (Dubin et al 2003). Heart failure is characterised by evidence of an underlying structural abnormality or cardiac dysfunction that impairs the ability of the heart to fill or eject blood (Krum et al 2004). It is often associated with coronary heart disease (AIHW 2003). Heart failure can occur suddenly, although it usually develops slowly, often over many years.

Up to half of patients with significant heart failure have advanced conduction abnormalities (Toogood 2007). These patients often have dyssynchronous contractions of the cardiac chambers due to either ineffective synchronisation between the atria and ventricles (AV dyssynchrony) or lack of ventricular synchronisation (ventricular dyssynchrony) (Conti 2001). Intraventricular and interventricular delays can result leading to inefficient ventricular contraction.

Mechanical abnormalities contribute to chronic myocardial stretch and cardiac remodelling. Left bundle branch block can alter the sequence of contraction, causing wall segments to contract prematurely or belatedly. Intraventricular dyssynchrony can cause mitral valve incompetence and shortening of left ventricular filling. Delays in AV timing can also influence mechanical function of the chambers (Vardas et al 2007). Consequences include change in ventricular end diastolic filling pressure which directly impacts systolic performance (Bubien et al 2004).

Ventricular dyssynchrony has been shown to be an independent risk factor for increased mortality among patients with heart failure (Xiao et al 1996) and is an indication for cardiac resynchronisation therapy.

Heart failure is commonly assessed according to the New York Heart Association (NYHA) functional classification system. This system assigns patients to one of four functional classes depending on the degree of effort needed to elicit symptoms to everyday activities and quality of life (see Table 1).

Table 1 New York Heart Association functional classification system

Class I	No limitation of physical activity; ordinary physical activity does not cause undue fatigue or dyspnoea
Class II	Slight limitation of physical activity; comfortable at rest, but ordinary physical activity results in fatigue or dyspnoea
Class III	Limitation of physical activity; comfortable at rest but less than ordinary activity causes fatigue or dyspnoea
Class IV	Unable to perform physical activity without symptoms; symptoms are present even at rest; symptoms increase if any physical activity is undertaken

Owing to the chronic and progressive nature of heart failure, functional class tends to deteriorate over time, although most patients with heart failure do not typically experience an uninterrupted worsening of symptoms (Gregoratos 2002).

Heart failure is classified to ICD-10 code I50 *Heart failure* in Australian hospital morbidity and mortality data collections. Heart failure includes congestive heart failure (I50.0), left ventricular failure (I50.1) and unspecified heart failure (I50.9) (AIHW 2003). Congestive symptoms are the leading cause of admissions for acute heart failure in most cases (Braunschweig 2007). The main risk factors for congestive heart failure are long standing hypertension and coronary artery disease (Duncan et al 2006). Ischaemic heart disease is present in more than half of newly diagnosed patients; hypertension occurs in about two thirds; and idiopathic dilated cardiomyopathy in found in 5 to 10 per cent (Krum et al 2004).

Patients with heart failure face substantial risk of death from the disease. Sudden cardiac death is responsible for the deaths of between 25 and 50 per cent of patients with heart failure. The risk among patients with mild to moderate heart failure is relatively higher, as opposed to those with advanced forms of the condition, where pump failure death is more common (Braunschweig 2007). Ho et al (1993) published results from an international study based on long term follow-up of 5000 people who participated in the Framingham Heart Study. The authors concluded that congestive heart failure was associated with five-year survival rates of 25 per cent and 48 per cent in males and females respectively (AIHW 2003). This finding was supported by Massad (2004) who estimated that about 60 per cent of affected patients died within five years of diagnosis.

Burden of disease

On the whole, instances of sudden cardiac death are caused by acute, fatal cardiac arrhythmia. Most people who die from sudden cardiac death have coronary artery disease or ischaemic heart disease. About three-quarters of these patients have evidence of prior myocardial infarction (Kannel et al 1975).

In Australia, cardiovascular disease is the largest single cause of mortality and morbidity. The National Heart Survey indicated that 19.4 per cent of the population self-reported some form of cardiovascular disease in 2001; of these, 9.6 per cent had cardiac rhythm disorders (AIHW 2004). Cardiovascular disease caused 47,637 deaths in 2004 and affected 3.5 million Australians in 2004–2005 (AIHW 2006). Coronary artery disease accounted for the largest proportion of cardiovascular deaths in Australia (51% in 2004) (AIHW 2004).

Heart failure claimed 2279 lives in 2004 (1.7% of all deaths). There are no national data indicating heart failure incidence in Australia, but results from the 2004–2005 National Health Survey indicated that 263,000 Australians had chronic heart failure (about 1.3% of the population). Because clinical diagnosis is challenging in patients with mild heart failure, this may underestimate actual rates (AIHW 2006). Heart failure is estimated to account for 0.6 per cent (41,425) of all hospital admissions in Australia and 9.5 per cent of all admissions for cardiovascular disease (Krum et al 2006). Up to half of all patients who present with heart failure have evidence of cardiac rhythm disturbances (Toogood 2004).

Marketing status of the device

Remote monitoring components are available from Biotronik®, Medtronic, St Jude Medical and Guidant (merged with Boston Scientific, April 2008). These manufacturers offer a range of devices (pacemakers, ICDs, CRT) that enable remote monitoring.

The Therapeutic Goods Administration (TGA) lists remote monitoring components on the Australian Register of Therapeutic Goods (ARTG). The ARTG listing numbers for remote monitoring components are listed in Table 2.

Table 2 ARTG listing numbers for remote monitoring devices and components in Australia

ARTG #	Manufacturer	Description
116038	Medtronic Australasia Pty Ltd	CareLink programmer, model 2090–Pacemaker programmer
119153	St Jude Medical Australia Pty Ltd	Model #3830 Rapid Programmer–Unclassified
123599	Guidant Australia Pty Ltd	ZOOM LATITUDE Programming System–Pacemaker programmer
127469	Biotronik Australia Pty Ltd	Stratos LV-T Three Chamber, Biventricular, Rate Adaptive, Home Monitoring Implantable Cardiac Pulse Generator
131834	St Jude Medical Australia Pty Ltd	3850, 1232 (wand)–Unclassified
140355	Biotronik Australia Pty Ltd	CardioMessenger II–Telemetry transmitter, instrument data
142199	St Jude Medical Australia Pty Ltd	Rapid Programmer model 3831–Active implantable device communicator

Current reimbursement arrangement

Data analysis by remote monitoring is not currently reimbursed on the MBS. Testing implanted pacemakers or ICDs at regular clinical follow-up visits (face-to-face patient-physician contacts) is currently funded under MBS item codes 11721 and 11727, at fees of $62.95 and $85.65 per service, respectively.

Approach to assessment

Clinical pathway

A clinical flowchart (Figure 2) was developed based on published literature and clinical advice to define the role of remote monitoring in the clinical management of patients with implanted cardiac devices.

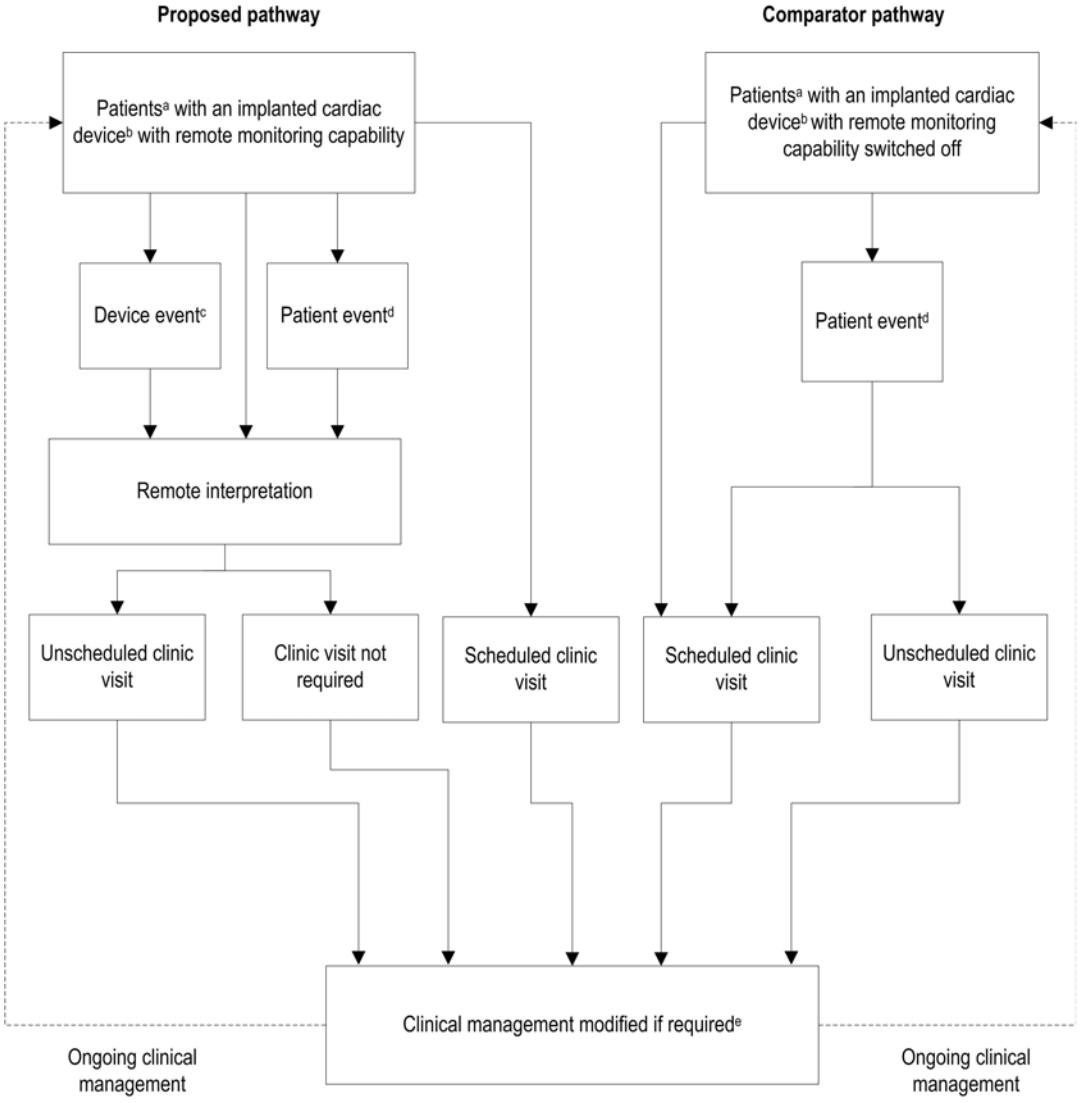

Figure 2 Clinical pathway for management of patients with implanted cardiac devices with and without remote monitoring function

[a] Patients monitored remotely require routine clinic visits. Patients with pacemakers currently visit clinics every 6 months; patients with ICDs visit every 3 months and CRT patients visit clinics every 3 months
[b] Pacemaker; ICD; CRT
[c] Patients may be unaware of device events. Device events can be related to device functioning and/or the patient's cardiovascular system
[d] Symptoms occur in patient events. Patient events can be related to device functioning and/or the patient's cardiovascular system
[e] Clinical management modifications may include change in anti-arrhythmia drugs, device reprogramming to achieve improved arrhythmia outcomes; warfarin therapy for documented atrial fibrillation, device reprogramming to reduce right ventricular pacing and possible left ventricular dysfunction

Research questions

Pacemakers

The PPICO criteria (target population, prior tests, index test, comparator, outcomes) developed *a priori* to evaluate the use of remote monitoring in the management of patients with pacemakers are presented in Table 3.

Table 3 PPICO criteria for the use of remote monitoring in the management of patients with pacemakers

Population	Prior tests	Intervention/test	Comparator	Reference standard	Outcomes
Patients [a] who have pacemakers with remote monitoring capability	Not applicable	Remote monitoring of pacemakers plus regular scheduled clinic follow-up	Current clinical practice Regular clinic follow-up [b] of patients with implanted pacemaker (with remote monitoring capability switched off)	Current clinical practice Regular clinic follow-up [b] of patients with implanted pacemaker (with remote monitoring capability switched off)	Change in clinical management [c] Change in clinical outcomes [d] Diagnostic accuracy [e] Safety outcomes [f]

[a] Patients with bradycardia, tachycardia or congestive heart failure. This patient population will be subdivided into high risk patients with heart failure, left ventricular dysfunction, pacemaker dependency (no escape rhythm), past history of serious arrhythmias, devices nearing end of life, devices on hazard alert, and low-risk patients

[b] Regular biannual clinician visits

[c] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device reprogramming to achieve improved arrhythmia outcomes, warfarin therapy for documented atrial fibrillation, device reprogramming to reduce right ventricular pacing and possible left ventricular dysfunction)

[d] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient comfort and convenience), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, unnecessary pacing, ventricular arrhythmia); adverse event reports; adverse events known to be associated with pacemakers (abnormal lead impedance, displaced leads; sudden death, inappropriate pacing)

[e] Sensitivity, specificity

[f] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review

The research question for this indication, based on these criteria, was as follows.

To what extent is remote monitoring of pacemakers:

- safe, and
- effective (including diagnostic performance and the impact of diagnosis on changes in clinical management and changes in clinical outcomes), and
- cost-effective

in the management of patients with pacemakers relative to current clinical practice?

Implantable cardioverter defibrillators

The PPICO criteria developed *a priori* to evaluate remote monitoring in the management of patients with implantable cardioverter defibrillators are presented in Table 4.

Table 4 PPICO criteria for the use of remote monitoring in the management of patients with implantable cardioverter defibrillators

Population	Prior tests	Intervention/test	Comparator	Reference standard	Outcomes
Patients who have implantable cardioverter defibrillators with remote monitoring capability	Not applicable	Remote monitoring of implantable cardioverter defibrillators plus regular scheduled clinic follow-up	Current clinical practice Regular clinic follow-up [a] of implantable cardioverter defibrillators (with remote monitoring capability switched off)	Current clinical practice Regular clinic follow-up [a] of implanted cardioverter defibrillators (with remote monitoring capability switched off)	Change in clinical management [b] Change in clinical outcomes [c] Diagnostic accuracy [d] Safety outcomes [e]

[a] Regular 3 monthly clinician visits
[b] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device programming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, reprogramming device to reduce right ventricular pacing and possible left ventricular dysfunction)
[c] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience, admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, ventricular arrhythmia); unnecessary shock from device, adverse event reports; adverse events known to be associated with ICD (abnormal lead impedance, displaced leads; sudden death)
[d] Sensitivity, specificity
[e] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review

The research question for this indication, based on these criteria, was as follows.

To what extent is remote monitoring of implantable cardioverter defibrillators:

- safe, and
- effective (including diagnostic performance and the impact of diagnosis on changes in clinical management and changes in clinical outcomes), and
- cost-effective

in the management of patients with implantable cardioverter defibrillators relative to current clinical practice?

Cardiac resynchronisation therapy

The PPICO criteria developed *a priori* to evaluate the use of remote monitoring in the management of patients receiving cardiac resynchronisation therapy are presented in Table 5.

Table 5 PPICO criteria for the use of remote monitoring in the management of patients receiving cardiac resynchronisation therapy

Population	Prior tests	Intervention/test	Comparator	Reference standard	Outcomes
Patients who have cardiac resynchronisation therapy [a] with remote monitoring capability	Not applicable	Remote monitoring of cardiac resynchronisation therapy plus regular clinic scheduled follow-up	Current clinical practice Regular clinic follow-up [b] of implanted cardiac devices for cardiac resynchronisation therapy (with remote monitoring capability switched off)	Current clinical practice Regular clinic follow-up [b] of implanted cardiac devices for cardiac resynchronisation therapy (with remote monitoring capability switched off)	Change in clinical management [c] Change in clinical outcomes [d] Diagnostic accuracy [e] Safety outcomes [f]

[a] All cardiac resynchronisation devices are pacemakers, but most also provide implantable cardioverter defibrillator facility
[b] Regular 3 monthly clinician visits
[c] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device programming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, device programming to ensure biventricular pacing)
[d] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience and comfort), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, ventricular arrhythmia); adverse event reports; adverse events known to be associated with cardiac resynchronisation therapy
[e] Sensitivity, specificity
[f] Safety Outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review

The research question for this indication, based on these criteria, was as follows.

To what extent is remote monitoring of cardiac re-synchronisation therapy:

- safe, and
- effective (including diagnostic performance and the impact of diagnosis on changes in clinical management and changes in clinical outcomes), and
- cost-effective

in the remote management of patients with cardiac resynchronisation therapy relative to current clinical practice?

Assessment framework

Types of evidence

A systematic review of the medical literature was undertaken to identify relevant studies that examined the value of remote monitoring in the clinical management of patients with implanted cardiac devices. Direct evidence indicating the impact of remote monitoring on health outcomes was sought. The literature search was not limited by outcomes or comparators. In the absence of studies providing direct evidence, indirect evidence indicating the impact of remote monitoring on clinical management and diagnostic accuracy was assessed.

Review of the literature

The medical literature was searched to identify all relevant studies and reviews published up to 2007.

Search strategy

Primary databases

Searches were conducted in the primary databases indicated in Table 6.

Table 6 Electronic databases searched during the review of remote monitoring in the clinical management of patients with implanted cardiac devices

Database	Date searched
Medline and EMBASE [a]	16 November 2007
PreMedline [b]	16 November 2007
Cochrane Library	16 November 2007 (Issue 4, 2007)

[a] Using the EMBASE.com interface
[b] Using the PubMed interface

The search terms included the following (as determined from the PPICO criteria):

- home monitoring, home care, telemonitoring, remote monitoring, telemedicine and
- implantable cardioverter defibrillator, pacemaker, cardiac resynchronisation or
- carelink, cardiomessenger, home monitoring.

Complete details of the literature searches performed using the primary databases are presented in Appendix F.

Secondary databases

A review of databases maintained by health technology assessment (HTA) agencies was undertaken to identify existing reports regarding remote monitoring of implantable cardiac devices. The list of secondary databases searched is presented in Appendix F.

Additional searches were conducted to source quality of life, epidemiological and economic information, as required.

Citation lists

The citation lists of included studies were searched to identify any additional studies.

Selection criteria

Selection criteria presented in Table 7, Table 8 and Table 9 were applied to the citations identified in the literature search results. Studies that did not meet the specified inclusion criteria were excluded from further analysis. Studies with small patient numbers (< 10 patients) or data inadequacies were also excluded.

Table 7 Selection criteria for studies of remote monitoring in the management of patients with pacemakers

Characteristic	Inclusion criteria	Exclusion criteria
Publication type	Clinical studies	Studies with < 10 patients
Patient	Patients [a] who have pacemakers with remote monitoring capability	
Prior tests	Not specified	
Intervention/test	Remote monitoring of pacemakers	Wrong device
Comparators	Current clinical practice: Regular follow-up [b] of patients with pacemakers (with remote monitoring capability switched off)	
Reference standard	Current clinical practice: Regular follow-up [b] of patients with pacemakers (with remote monitoring capability switched off)	
Outcome	Change in clinical management [c]	Inadequate data reporting
	Change in clinical outcomes [d]	Wrong outcome
	Diagnostic accuracy [e]	
	Safety outcomes [f]	
Language	English language articles [g]	

[a] Patients with bradycardia, tachycardia or congestive heart failure. This patient population was subdivided into high risk patients with heart failure, left ventricular dysfunction, pacemaker dependency (no escape rhythm), past history of serious arrhythmias, devices nearing end of life, or devices on hazard alert, and low risk patients

[b] Regular biannual clinician visits

[c] Alterations in treatment plan (eg, change in ant-arrhythmia drugs, increased or decreased follow-up visits, device reprogramming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, device reprogramming to reduce right ventricular pacing and possible left ventricular dysfunction)

[d] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient comfort and convenience), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, unnecessary pacing, ventricular arrhythmia); adverse event reports; adverse events known to be associated with pacemakers (abnormal lead impedance, displaced leads; sudden death, inappropriate pacing)

[e] Sensitivity, specificity

[f] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for review of the data

[g] Non-English language articles were excluded unless they appeared to provide a higher level of evidence than English language articles

Table 8 Selection criteria for studies of remote monitoring in the management of patients with implantable cardioverter defibrillators

Characteristic	Inclusion criteria	Exclusion criteria
Publication type	Clinical studies	Studies with < 10 patients
Patient	Patients who have implantable cardioverter defibrillators with remote monitoring capability	
Prior tests	Not specified	
Intervention/test	Remote monitoring of implantable cardioverter defibrillators	Wrong device
Comparators	Current clinical practice: Regular follow-up [a] of patients with implantable cardioverter defibrillators (with remote monitoring capability switched off)	
Reference standard	Current clinical practice: Regular follow-up [a] of patients with implantable cardioverter defibrillators (with remote monitoring capability switched off)	
Outcome	Change in clinical management [b]	Inadequate data reporting
	Change in clinical outcomes [c]	Wrong outcome
	Diagnostic accuracy [d]	
	Safety outcomes [e]	
Language	English language articles [f]	

[a] Regular 3 monthly clinician visits
[b] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device reprogramming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, device reprogramming to reduce right ventricular pacing and possible left ventricular dysfunction)
[c] Survival (complication-free and overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience, admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, ventricular arrhythmia); unnecessary shock from device, adverse event reports; adverse events known to be associated with ICD (abnormal lead impedance, displaced leads; sudden death)
[d] Sensitivity, specificity
[e] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinicians in a timely and guaranteed method to allow for data review
[f] Non-English language articles were excluded unless they appeared to provide a higher level of evidence than English language articles

Table 9 Selection criteria for studies of remote monitoring in the management of patients receiving cardiac resynchronisation therapy

Characteristic	Inclusion criteria	Exclusion criteria
Publication type	Clinical studies	Studies with < 10 patients
Patient	Patients who have cardiac resynchronisation therapy [a] with remote monitoring capability	
Prior tests	Not specified	
Intervention/test	Remote monitoring of patients receiving cardiac resynchronisation therapy	Wrong device
Comparators	Current clinical practice: Regular follow-up [b] of patients receiving cardiac resynchronisation therapy (with remote monitoring capability switched off)	
Reference standard	Current clinical practice: Regular follow-up [b] of patients receiving cardiac resynchronisation therapy (with remote monitoring capability switched off)	
Outcome	Change in clinical management [c]	Inadequate data reporting
	Change in clinical outcomes [d]	Wrong outcome
	Diagnostic accuracy [e]	
	Safety outcomes [f]	
Language	English language articles [g]	

[a] All cardiac resynchronisation devices are pacemakers, but up to 85% will also provide cardioverter defibrillator functions
[b] Regular 3 monthly clinician visits
[c] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device reprogramming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, reprogramming device to ensure biventricular pacing)
[d] Survival (complication-free and overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience and comfort), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, unnecessary pacing, ventricular arrhythmia); adverse event reports; adverse events known to be associated with cardiac resynchronisation therapy
[e] Sensitivity, specificity
[f] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review
[g] Non-English language articles were excluded unless they appeared to provide a higher level of evidence than English language articles

Search results

The QUOROM (quality of reporting of meta-analyses) flowchart (Figure 3) summarises reasons for exclusion of studies. A total of 2285 non-duplicate references were identified from the literature searches presented in Appendix F: 60 were reviewed for safety and clinical effectiveness. Citation list searching identified an additional 13 (retrievable) studies, and review of secondary databases identified seven HTA reports [L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)]: these references were also reviewed for safety and clinical effectiveness.

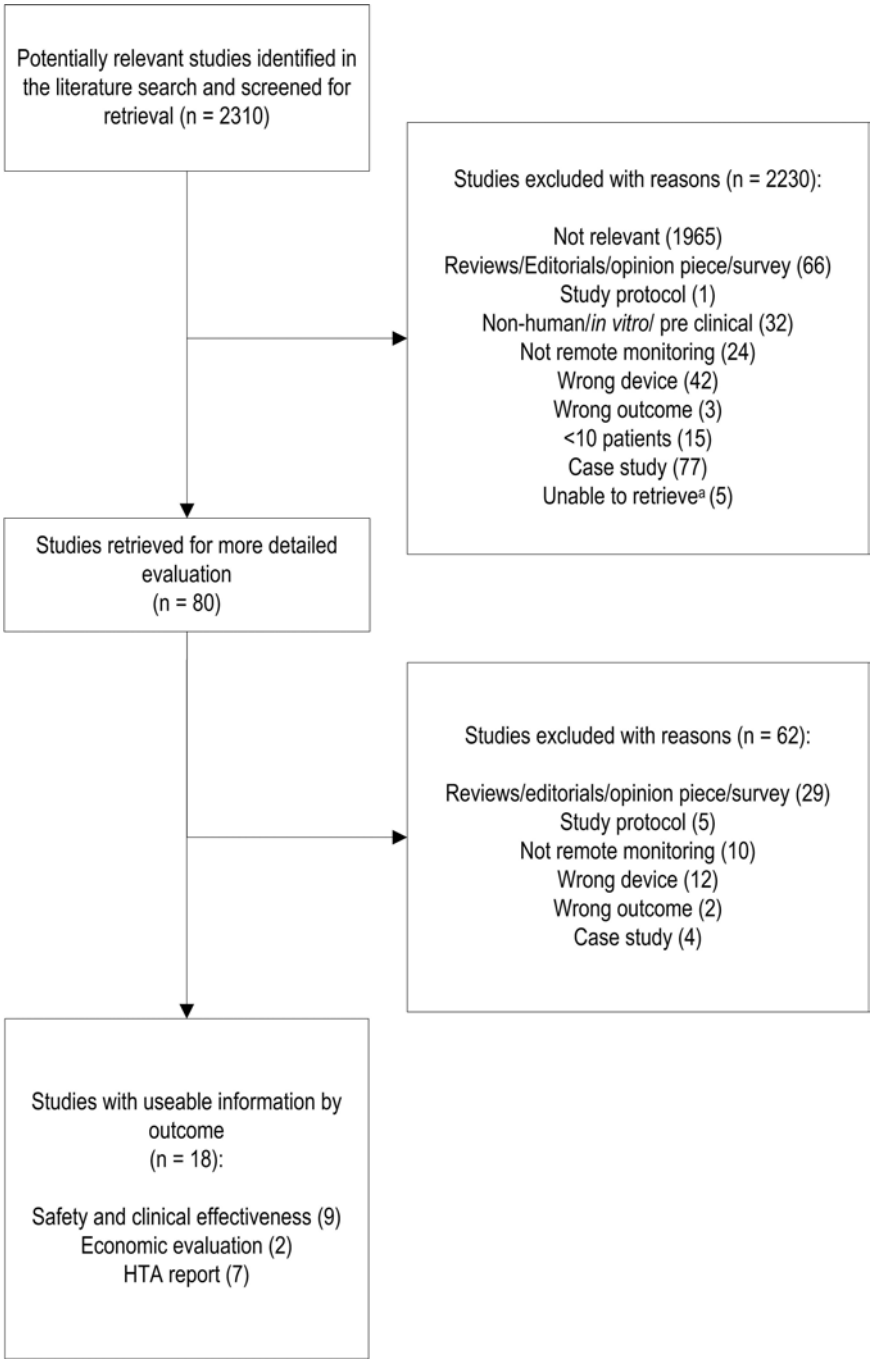

Figure 3 QUOROM flowchart used to identify and select studies for the literature review of remote monitoring of implanted cardiac devices

[a] Five studies identified by citation list checking could not be obtained
Adapted from Moher et al (1999)

Study appraisal

Direct evidence of the value of remote monitoring of implantable cardiac devices to current clinical practice, when used in the relevant patient group, is required to justify public funding. Evidence should ideally be in the form of studies reporting effects on patient-centred health outcomes. Alternatively, evidence of greater diagnostic accuracy than the comparator, along with linked evidence of change in management and verification that treatment will affect health outcomes, is required.

Where an additional diagnostic test is to be used in the clinical pathway, proof of an effect on management change is a key component of the evidence base. The most appropriate design for investigation of the effects on management change is a pre-test/ post-test case series study. Where a pre-test management plan is not reported, the outcomes of a study do not truly represent change in patient management and consequently, outcomes are likely to be biased.

The ideal design for a study of the comparative accuracy of diagnostic tests is one in which each test is performed in a population with a defined clinical presentation, in a consecutive series. The study should be an independent, blinded comparison with a valid reference standard (NHMRC 2005).

Assessment of eligible studies

Evidence retrieved from the literature searches was assessed according to the NHMRC dimensions of evidence (Table 10) where applicable. There are three main domains: strength of the evidence, size of the effect and relevance of the evidence. Strength of evidence is derived directly from the literature identified for specific diagnostic tests. Determination of the size of effect and establishing evidence relevance require input from expert clinical experts.

An aspect of the strength of the evidence domain is the level of evidence of the study. After analysis, studies were assigned NHMRC levels of evidence (Table 11). The quality and applicability of the included studies was assessed according to specified criteria (Appendix G).

Table 10 Dimensions of evidence

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design [a]
Quality	The methods used by investigators to minimise bias within a study design
Statistical precision	The *p* value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect
Size of effect	The distance of the study estimate from the null value and the inclusion of only clinically important effects in the confidence interval
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used

Source: NHMRC (2005)
[a] See Table 11

Table 11 Designations of levels of evidence according to type of research question

Level	Intervention [b]	Diagnosis [e]
I [a]	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard [f] among consecutive patients with a defined clinical presentation [g]
III-1	A pseudo-randomised controlled trial (ie, alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard [f] among non-consecutive patients with a defined clinical presentation [g]
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial [c] Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study [d] Interrupted time series without a parallel control group	Diagnostic case-control study [g]
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard) [h]

Source: NHMRC (2005)

[a] A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence

[b] Definitions of these study designs are provided in *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000) pp 7–8

[c] This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie, utilise A vs. B and B vs. C, to determine A vs. C)

[d] Comparing single arm studies ie, case series from two studies

[e] The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See MSAC (2004) Guidelines for the assessment of diagnostic technologies. Available at: www.msac.gov.au

[f] The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study. See Whiting P, Rutjes AWS, Reitsma JB, Bossuyt PMM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology* 2003, 3: 25

[g] Well-designed population based case-control studies (eg, population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice

[h] Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. These may be the only alternative when there is no reliable reference standard

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg, level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence

The quality of studies of diagnostic accuracy was ranked using the composite grading system described in the assessment of studies of diagnostic accuracy guidelines (Table 12). In accordance with MSAC guidelines, studies of diagnostic accuracy were described according to the extent that they achieve the component factors of study validity.

Table 12 Grading system for the appraisal of studies evaluating diagnostic tests

Validity criteria	Description	Grading system
Appropriate comparison	Did the study evaluate a direct comparison of the index test strategy versus the comparator test strategy?	C1 direct comparison CX other comparison
Applicable population	Did the study evaluate the index test in a population that is representative of the subject characteristics (age and sex) and clinical setting (disease prevalence, disease severity, referral filter and sequence of tests) for the clinical indication of interest?	P1 applicable P2 limited P3 different population
Quality of study	Was the study designed to avoid bias?	
	High quality = no potential for bias based on pre-defined key quality criteria	Q1: high quality
	Fair quality = some potential for bias in areas other than those pre-specified as key criteria	Q2: fair quality
	Poor quality = poor reference standard and/or potential for bias based on key pre-specified criteria	Q3: poor quality

Source: Medical Services Advisory Committee (2005). *Guidelines for the assessment of diagnostic technologies*. Canberra, Commonwealth of Australia

Data analysis

The characteristics of the study, patient population, prior tests, index test, comparator, reference standard, and outcomes measures were extracted from each study. Where appropriate, the results of eligible studies were statistically synthesised (meta-analysed) and pooled results presented.

Data extraction

A single reviewer extracted relevant information using a standardised data extraction form designed specifically for this review. Any uncertainties were resolved by discussion with another reviewer and/or clinical advisers.

Expert advice

An advisory panel with expertise in cardiology, general practice, health economics and consumer affairs was established to evaluate the evidence and provide advice to MSAC from a clinical perspective. In selecting members for advisory panels, MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the advisory panel is provided at Appendix B.

Assessment of the body of evidence

The overall body of evidence was assessed as well as individual studies. An evidence level from A (excellent) to D (poor) was assigned after considering each of the components outlined in the body of evidence matrix presented in Table 13.

Table 13 Body of evidence assessment matrix

Component	A Excellent	B Good	C Satisfactory	D Poor
Volume of evidence	Several level I or II studies with low risk of bias	One or two level II studies with low risk of bias or a systematic review/multiple level III studies with low risk of bias	Level III studies with low risk of bias, or level I or II studies with moderate risk of bias	Level IV studies, or level I to III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studies in body of evidence are the same as the target population	Population/s studies in the body of evidence are similar to the target population	Population/s studied in body of evidence different to target population but it is clinically sensible to apply this evidence to the target population	Population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian healthcare context	Applicable to Australian healthcare context with few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to Australian healthcare context

Source: NHMRC (2005). *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*. Pilot Program 2005–2006. National Health and Medical Research Council, Canberra. Available from: www.nhmrc.gov.au/consult/docfeedback.htm

Results of assessment

Summary

Analysis of results from a literature review of remote monitoring systems was bifurcated according to whether investigated devices had Therapeutic Goods Administration (TGA) listing. This split was required because of limited evidence concerning TGA approved devices.

Several reviews of literature evaluating remote monitoring system use performed by a French health technology assessment (HTA) group (Haute Autorité de Santé) in 2005 were identified. The key findings from the reviews indicated that the trialled pacemaker, Biotronik BA03 DR, provided sufficient evidence regarding transmission success and clinically relevant data for the Biotronik Home Monitoring® system for this evaluation. These studies were limited by lack of comparative data, inadequate patient management reporting, and reported impact of remote monitoring systems on patient outcomes.

Ellery et al (2006) and Varma et al (Study B 2005) conducted low quality (level IV), non-comparative studies of TGA listed devices. Ellery et al (2006) investigated remote monitoring of the Kronos® LV-T (a cardiac resynchronisation therapy [CRT] device) and Stratos® LV-T (an implantable cardioverter defibrillator [ICD]) applied to Biotronik's Home Monitoring® system to determine its ability to predict events requiring patients to be admitted to hospital. Retrospective data review detected an increase in mean heart rate (both at rest and over a 24 hour period) in 70 per cent of re-admitted patients. Decreased need for CRT was observed among 43 per cent of re-admitted patients. Unclear reporting of the limited follow-up period, and inadequate indication of outcomes meant that the validity of remote monitoring systems as a predictive test was not adequately demonstrated by this study.

Varma et al (Study B 2005) sought to determine if remote monitoring systems were useful for early detection of atrial fibrillation events. Biotronik's Home Monitoring® system was used to measure output from Biotronik's Philos® DR-T pacemaker. It was reported that remote monitoring identified silent atrial events in three patients, whose anticoagulation therapy was changed as a result. This study was limited by unclear patient follow-up and ill-defined outcomes. 'Atrial fibrillation days' were used as a surrogate measure, but inadequate data reporting meant that determination of how this measure corresponded to clinical outcomes could not be established.

Supporting evidence was elicited from studies by Elsner et al (2005), Brugada et al (2006), Clementy et al (2003), Lazarus et al (2007), Varma et al (2005) and Wallbruck et al (2002) and Joseph et al (2004). These studies had limited applicability to the Australian setting because they investigated implanted cardiac devices that are not listed by the TGA.

Elsner et al (2005) aimed to demonstrate the impact of remote monitoring systems on clinical management and patient follow-up in a randomised controlled trial. The study's key finding was that there was no difference in mortality or hospitalisation rates in either the 3 or 12 month arms. Inadequate data reporting and lack of comparison with clinical follow-up, meant that limited conclusions could be drawn from reported results.

Brugada et al 2006 compared clinician judgement of data from remote monitoring and information obtained during a regular clinical follow-up to measure remote monitoring system accuracy. Biotronik's Home Monitoring® of the Biotronik ICD Belos® VR-T were investigated. The authors estimated that 81 per cent of clinician visits could be avoided by using remote monitoring, but they also described a false negative rate of 14 per cent associated with the tested system. This study was limited by reporting inconsistencies, limited applicability, non-consecutive patient enrolment and potential that blinding may have been incomplete.

Biotronik's Home Monitoring® system was further trialled by Clementy et al (2003), Lazarus et al (2007), Varma et al (2005) and Wallbruck et al (2002). Medtronic's CareLink® system was trialled by Schoenfeld et al (2004). St Jude's Housecall® system was investigated in a study by Joseph et al (2004).

These studies provided limited evidence to support remote monitoring. Studies by Joseph et al (2004), Schoenfeld et al (2004) and Wallbruck et al (2002) were non-comparative, and clinical follow-up schedules were unclear. Lazarus et al (2007), Varma et al (Study A 2005) and Clementy et al (2003), applied unblinded comparisons with the reference standard and overall clinical follow-up was short.

Although no direct safety implications associated with remote monitoring were identified, successful and complete data transmission was regarded as a significant indirect safety outcome in this assessment. The potential for failure of data transmission presents a potential safety issue of which treating clinicians need to be aware. Consistent data transmission failures may indicate that remote monitoring is unsuitable for specific patients. The studies presenting transmission data indicated that between 88 and 100 per cent of patients maintained remote monitoring system coverage during the study periods. Inadequate data reporting meant that it was unclear whether patients who could not maintain remote monitoring were the same throughout the entire study periods, or if patients differed over the course of the study and follow-up. The studies also reported that 89 to 100 per cent of scheduled reports were successfully transmitted by remote monitoring. Reporting of transmissions outcomes was insufficient in all studies. Brugada et al (2006) and Schoenfeld et al (2004) did not report numbers of successfully transmitted scheduled reports, and Varma et al (Study A 2005) did not report the number of patients who were able to maintain remote monitoring. Unclear reporting meant that it was uncertain whether standard clinical practice was used in regular scheduled clinical follow-ups in most studies.

Safety

No direct safety issues associated with remote monitoring of implanted cardiac devices were identified.

Effectiveness

Health technology assessment reports

The literature search indicated that the Haute Autorité de Santé (HAS) conducted seven reviews relating to the assessment of remote monitoring of implanted cardiac devices (HAS 2005). These reviews were published in French and translated into English for inclusion in the current review (Table 14). The reports evaluated use of remote monitoring (Biotronik Home Monitoring®) with different defibrillators or pacemakers. The scope, included studies and conclusions were similar among the reports. It is unclear whether a systematic review of the remote monitoring literature was undertaken; the included studies appear to be a reasonable representation of the available evidence base for Biotronik Home Monitoring® when the reviews were conducted.

The seven HAS reviews indicated that transmission data presented in studies of the prototype BA 03 DR pacemaker provided sufficient evidence of transmission success and clinically relevant data relating to the Biotronik Home Monitoring® system. The reviews identified a study by Saubermann et al (2004)[1] that assessed the potential value of remote monitoring to inform medical decision-making. Because the study was non-comparative, and did not adequately address the potential impact on patient management resulting from remote monitoring, evidence was insufficient to inform further analysis. The health technology assessment (HTA) reports did not identify any studies that evaluated the impact of remote monitoring on patient outcomes.

The reports recommended that the evidence currently available was insufficient to support the use of remote monitoring of implanted cardiac devices. The reviews highlighted a need for comparative studies that directly evaluate the impact of remote monitoring on clinical and economic outcomes.

[1] This study was reported in an abstract but could not be retrieved. Information reported in the French HTA reports could therefore not be verified.

Table 14 Characteristics of identified HTA reports evaluating remote monitoring of implanted cardiac devices

HTA agency (year) Country	Scope of reviews	Conclusions
Haute Autorité de Santé [a] (2005) France	To assess the evidence relating to the safety and effectiveness of remote monitoring of defibrillators and pacemakers **Population**: Patients with ventricular rate/rhythm disorders recognised by the French Society of Cardiology **Index test**: Defibrillators [b]: Kronos LV-T, Lexos VR-T, Lumos VR-T, Lumos DR-T, and Lexos DR-T and Lexos VR-T Pacemakers [c]: Philos II DR-T and Stratos LV-T **Comparator**: Currently available defibrillators and pacemakers **Outcomes**: Safety, effectiveness and cost-effectiveness	The evidence of transmission success from older versions of the technology was regarded as satisfactory. The information transmitted was also determined to be relevant The evidence relating to change in patient management has yet to be established The clinical benefit to patients has yet to be established The current available evidence is insufficient to support the use of these defibrillators or pacemakers with remote monitoring

Abbreviations: HTA, health technology assessment; LV-T, left ventricular tachycardia

[a] These reports were published in French language. They were translated using Babel Fish (http://babelfish.altavista.com)

[b] The same seven studies were included in each report

[c] The same five studies were included in each report: two were unique to the pacemaker reports

Primary studies

The literature search identified nine papers relating to 10 studies that were eligible for review. Varma et al (2005) reported on outcomes from two related studies—a small feasibility study using a BA 03 DR pacemaker (Study A); and a larger study characterising atrial fibrillation (AF) episodes using Philos DR-T pacemakers (Study B).

TGA approved remote monitoring systems

Ellery et al (2006) and Varma et al (Study B 2005) reported investigation of the TGA-approved remote monitoring systems, Stratos LV-T and Kronos LV-T with Home Monitoring® and Philos DR-T with Home Monitoring®, respectively. The characteristics of these studies are presented in Table 15. The other studies either reported use of non-TGA approved remote monitoring systems or inadequately documented remote monitoring characteristics. The characteristics of these studies are presented in Table 17.

Ellery et al (2006) reported preliminary results from the HOME-CARE pilot study that retrospectively analysed remote monitoring data to evaluate its value in predicting events that lead to readmission. This study was classified as providing low quality (level IV) evidence because no comparisons were made to a valid reference standard. Ellery and colleagues also observed the numbers of deaths and adverse events that occurred during the follow-up period, but the ability of remote monitoring to predict outcomes was not reported. Applicability of this study to current clinical practice was reduced because of the short duration of the study and lack of clarity in participants' clinical follow-up.

Outcomes reported by Varma et al (Study B 2005) provided low quality (level IV) evidence (there was no reference standard). This study retrospectively analysed remote monitoring data to categorise atrial fibrillation episodes. The reported results focused on a small sub-group of patients who experienced atrial fibrillation episodes. This cohort did not represent the study population. Because the analysis was retrospective, clinical data were not available for all patients in the atrial fibrillation sub-group. This study was

classified as low quality because of inadequacies in reporting patient characteristics for the entire study population, and atrial fibrillation sub-group analysis outcomes. Because of these inadequacies, and lack of clarity concerning clinical follow-up of patients, applicability of this study to Australian clinical practice was limited.

Table 15 Characteristics of the included studies evaluating TGA approved remote monitoring systems for implanted cardiac devices

Author (year) Region	Study design	Patients	Test characteristics	Study quality [a]
Ellery (2006) Europe	Retrospective, non-consecutive patient enrolment No reference standard Recruitment period not reported 3 month mean follow-up duration	Patients with clinical indications for CRT (123 patients, 17% female) Mean age: 67 years NYHA Class 1 (3%), Class 2 (6%), Class 3 (77%), Class 4 (14%) Ischemic heart disease: 74 (60%) Primary prevention: 52 (42.3%)	**Index test**: Stratos LV-T (CRT) and Kronos LV-T (ICD) with Home Monitoring® system. Unclear clinical follow-up	Level IV CX, P2, Q2 *Quality:* Medium Inadequate data reporting (study outcomes) *Applicability*: Limited Unclear/short study duration Unclear clinical follow-up
Varma Study B [b] (2005) USA	Retrospective, consecutive patient enrolment No reference standard Mar 2002–Apr 2003 12 months follow-up	Patients implanted with PM for class I/II indications (276 patients)	**Index test**: Philos DR-T (PM) with Home Monitoring® system Unclear clinical follow-up	Level IV CX, P2, Q3 *Quality:* Low Inadequate data reporting (patient characteristics, study outcomes) *Applicability*: Limited Sub-group results only Unclear clinical follow-up

Abbreviations: CRT, cardiac resynchronisation therapy; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PM, pacemaker; TGA, Therapeutic Goods Administration

[a] According to criteria outlined in Table 11, Table 12 and Appendix F

[b] One of two related studies reported in the same paper by Varma et al (Study B 2005)

Results from the study by Ellery et al (2006) are summarised in Table 16. This review of remote monitoring data indicated that changes in mean heart rate, level of CRT therapy, and patients' daily activities preceded hospital readmissions. The authors suggested that it may be possible to predict events leading to hospital admission based on home monitoring data. It was unclear if similar patterns in remote monitoring parameters (that preceded readmissions) also occurred among patients who did not experience such events. This study demonstrates the potential use of remote monitoring as a predictive test.

Results reported by Varma et al (Study B 2005) are summarised in Table 16. This retrospective review of remote monitoring data identified 29 patients who experienced 645 atrial fibrillation (AF) days. The concept of AF day is a surrogate measure defined by the authors as a mode switch burden greater than 20 per cent per 24 hours. It is unclear how this surrogate measure corresponds with clinical outcomes. The study also reported the management of 20 patients who experienced AF days. The authors claim that remote monitoring detected new silent atrial fibrillation events in three patients.

Detection of these events led to initiation of anticoagulation therapy. This demonstrates the potential for remote monitoring to change patient management.

Table 16 Results of the included studies evaluating TGA approved remote monitoring systems for implanted cardiac devices

Author (year)	Summary of results
Ellery et al (2006)	There were 11 unplanned readmissions, 9 deaths and 16 adverse events during follow-up. In 70% of the readmissions, a retrospective review of home monitoring data detected an increase in mean heart rate (both at rest and over a 24 hour period) preceding admission to hospital. A decrease in cardiac resynchronisation therapy (CRT) was observed in 43% of re-admitted patients, and a reduction in patients' daily activity was observed in 30% of re-admitted patients
Varma et al Study B [a] (2005)	A retrospective review of patient data indicated that there were a total of 645 AF days [b] experienced by 29 patients (10.5% of implants). Clinical data were available for 20 of these patients; home monitoring indicated new-onset silent AF in 3 patients which resulted in anticoagulation therapy being initiated; monitoring was increased for 2 patients for whom anticoagulation therapy was contraindicated; 12 patients adopted a rate control strategy, but no therapeutic changes were made; 3 patients adopted a rhythm control strategy, but no therapeutic changes were made

Abbreviations: AF, atrial fibrillation; CRT, cardiac resynchronisation therapy; TGA, Therapeutic Goods Administration

[a] One of two related studies reported in the same paper by Varma et al (Study B 2005)

[b] An atrial fibrillation day was defined as a mode switch burden >20% per 24 hours

Both studies that considered TGA-approved remote monitoring systems presented data concerning potential applications for remote monitoring to predict clinical events (Ellery et al 2006) or change patient management (Varma et al Study B 2005). These studies present evidence that has limited applicability to the current assessment; there were limitations in the study design and relevance to the Australian clinical setting.

Non-TGA approved remote monitoring systems

Studies by Brugada et al (2006), Clementy et al (2003), Elsner et al (2006), Wallbruck et al (2002), Joseph et al (2004), Schoenfeld et al (2004), Varma et al (2005) and Lazarus et al (2007) provided supportive evidence for use of remote monitoring for clinical management of patients with implanted cardiac devices. These studies either used non-TGA approved implanted cardiac devices as components of remote monitoring systems, or reported details of the implanted cardiac devices inadequately. The characteristics of these studies are summarised in Table 17.

Elsner et al (2006) assessed the impact of remote monitoring with different clinical follow-up schemes on patient management and resource use in a low quality (level II evidence) randomised control trial (RCT). Patients were randomised three months post-implantation to either remote monitoring with quarterly follow-up or remote monitoring with annual follow-up This study did not compare remote monitoring with standard clinical follow-up so the comparative evidence has limited relevance to the current assessment. The internal validity of this trial was also reduced by the unblinded comparison between patient groups, inadequate reporting of the implanted cardiac devices, insufficient detail about the randomisation process and the number of patients randomised to each patient group. The applicability of this trial may be limited by the short study duration (mean observation time of approximately four months).

Brugada et al (2006) evaluated the ability of remote monitoring systems to reduce the need for scheduled clinical follow-up. The study design required clinicians to determine need for patients' scheduled clinical follow-up based on remote monitoring data. All patients then attended scheduled clinical follow-up and the findings from this assessment were compared with clinicians' initial judgement based on remote monitoring data.

This enabled evaluation of remote monitoring, test accuracy, and impact on patient management. The study design allowed for blinding of the index test from the reference standard, but the reference standard could have been interpreted with knowledge of the index test (level III-2 evidence).

Low quality studies (level III-2 evidence) by Clementy et al (2003), Lazarus et al (2007) and Varma et al (Study A 2005) also compared the capabilities of remote monitoring with clinical follow-up. These studies were limited by unblinded comparisons with clinical follow-up and inadequate reporting of study details. Clementy et al (2003) and Varma et al (Study A 2005) followed-up patients until three months post-implantation only. It is unclear if the presented clinical follow-up schemes in these studies represent standard clinical practice.

The studies by Joseph et al (2004), Schoenfeld et al (2004) and Wallbruck et al (2002) were classified as providing level IV evidence. None of these studies involved making comparisons with valid reference standards. The studies evaluated the remote monitoring capabilities of the Biotronik Home Monitoring® system (Wallbruck et al 2002), the Medtronic CareLink® system (Schoenfeld et al 2004) and the St Jude Housecall II® system (Joseph et al 2004). All were regarded as providing high quality evidence, but the applicability of studies by both Schoenfeld et al (2004) and Wallbruck et al (2002) was limited by short study durations and unclear clinical follow-up schedules.

Table 17 Characteristics of the included supportive studies evaluating non-TGA approved remote monitoring systems for implanted cardiac devices

Author (year) Region	Study design	Patients	Test characteristics	Study quality [a]
Brugada et al (2006) Europe	Prospective, non-consecutive patient enrolment Index test blinded to reference standard May 2002–Apr 2004 339 ± 109 days mean follow-up duration	Patients with clinical indications for ICD (271 patients, 15% female) Mean age: 62 years Mean LVEF: 39 ± 15% IHD: 177 (65%) Primary prevention: 11 (4%)	**Index test**: Belos VR-T/ DR-T (ICD) with Home Monitoring® system Office device interrogation every 3 months for a year after discharge, and intermittent controls at the clinician's own discretion	Level III-2 CX, P2, Q2 *Quality:* Medium Reference standard blinded to index test *Applicability*: Limited Non-TGA approved device
Clementy et al (2003) [b] France	Prospective, non-consecutive patient enrolment Unblinded comparison with reference standard Recruitment period not reported Duration ranged between 28 days and 3 months	Patients with clinical indications for PM (10 patients, 40% female) Mean age: 70 years IHD: 1 (10%)	**Index test**: *Prototype* BA03 DR (PM) with Home Monitoring® system Office device interrogation after between 28 days–3 months follow-up	Level III-2 CX, P2, Q3 *Quality:* low Unblinded comparison Inadequate data reporting (study outcome *Applicability*: Limited Unclear/short study duration Small patient population Non-TGA approved device
Elsner et al (2006) Europe	Prospective, randomised patient enrolment Unblinded comparison between diagnostic arms Recruitment period not reported 117 days mean duration, duration ranged between 23 and 513 days	Patients with clinical indications for ICD (115 patients, 14% female) Mean age: 62 years Mean LVEF: 24 ± 6% NYHA Class I (3%), Class II (50%), Class III (47%) IHD: 115 (100%) Primary prevention: 115 (100%)	**Index test**: ICD with Home Monitoring® system. 3 months after implantation patients underwent office device interrogation every 12 months **Comparator**: ICD with Home Monitoring® system. 3 months after implantation patients underwent office device interrogation every 3 months	Level II C1, P2, Q3 *Quality:* Low Unclear randomisation Unblinded comparison Inadequate data reporting (test characteristics) *Applicability*: Limited Unclear/short study duration Non-TGA approved device Wrong comparator
Joseph et al (2004) USA	Prospective, non-consecutive patient enrolment No reference standard Sep 1999–Mar 2002 6 months follow-up	Patients with clinical indications for ICD (124 patients, 24% female) Mean age: 63 years	**Index test**: Profile MD, Angstrom II, Angstrom MD, Contour II, Contour MD, Contour and Cadet (ICD) with Housecall® II system Office device interrogation 6–12 weeks after implantation; annual office device interrogations	Level IV CX, P2, Q1 *Quality:* High *Applicability*: Limited Non-TGA approved device
Lazarus et al (2007) Global	Retrospective, non-consecutive patient enrolment Unblinded comparison with reference standard Jan 2002–Feb 2006 10.5 months mean duration, duration ranged between 1 and 49 months	Patients with clinical indications for PM, ICD or CRT (11624 patients)	**Index test**: PM, ICD and CRTs with Home Monitoring® system. Standard follow-up of bi-annual office device interrogations of PM and quarterly office device interrogations of ICD and CRTs was assumed	Level III-2 CX, P2, Q3 *Quality:* Low Unblinded comparison Inadequate data reporting (patient characteristics, test characteristics) *Applicability*: Limited Non-TGA approved device

Author (year) Region	Study design	Patients	Test characteristics	Study quality [a]
Schoenfeld et al (2004) USA	Prospective, non-consecutive patient enrolment No reference standard Recruitment period not reported Follow-up duration not reported	Patients with clinical indications for ICD (59 patients, 24% female) Mean age: 64 years NYHA class I (44%), class II (34%), class III (17%), unknown (5%)	**Index test**: Medtronic GEM II DR (ICD) with CareLink® system Unclear clinical follow-up	Level IV CX, P2, Q1 *Quality:* High *Applicability*: Limited Non-TGA approved device Unclear/short study duration Unclear clinical follow-up
Varma et al Study A [c] (2005) USA	Prospective, non-consecutive patient enrolment Unblinded comparison with reference standard Recruitment period not reported 3 months follow-up	Patients implanted with PM for class I/II indications (107 patients)	**Index test**: *Prototype* BA03 DR (PM) with Home Monitoring® system Office device interrogation at 2, 4, 8 and 12 weeks	Level III-2 CX, P2, Q3 *Quality:* Low Unblinded comparison Inadequate data reporting (patient characteristics) *Applicability*: Limited Non-TGA approved device Unclear/short study duration
Wallbruck et al (2002) Europe	Prospective, non-consecutive patient enrolment No reference standard Recruitment period not reported Follow-up duration not reported	Patients with clinical indications for PM (93 patients, 33% female) Mean age: 70 years	**Index test**: *Prototype* BA03 DR (PM) and RUC-1000 patient device with Home Monitoring® system. Unclear clinical follow-up	Level IV CX, P2, Q1 *Quality:* High *Applicability*: Limited Non-TGA approved device Unclear/short study duration Unclear clinical follow-up

Abbreviations: CRT, cardiac resynchronisation therapy; ICD, implantable cardiac defibrillator; IHD, ischaemic heart disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PM, pacemaker

[a] According to criteria outlined in Table 11, Table 12 and Appendix F

[b] This study also compared remote monitoring to Holter monitoring but did not compare between Holter monitoring and office device interrogation

[c] One of two related studies reported in the same paper by Varma et al (study A 2005)

Of the eight studies presenting supportive evidence for remote monitoring use in the management of patients with implanted cardiac devices, six presented transmission data relating to non-TGA approved remote monitoring systems (Brugada et al 2006, Clementy et al 2003, Joseph et al 2004, Schoenfeld et al 2004, Varma et al Study A 2005, Wallbruck et al 2002; see Table 18). Elsner et al (2006) did not report transmission outcomes, and Lazarus et al (2007) presented transmission data in graphical form only.

Although there were no direct safety issues associated with remote monitoring identified, inclusion of transmission data in this assessment was considered to be important to inform safety outcomes of remote monitoring systems use. Treating clinicians should be informed of the potential safety issue associated with data transmission failure. Consistent data transmission failures may indicate that remote monitoring is unsuitable for some patients. Transmission outcomes are presented in Table 18. Categorisation of transmission data varied among studies. Definitions of transmission outcomes and criteria are summarised in Table 29 (Appendix D).

The studies presenting transmission data indicated that between 88 and 100 per cent of patients were able to maintain remote monitoring coverage during the study periods. It is unclear if all studies used the same criteria to define maintenance of remote

monitoring coverage. Inadequate data reporting meant that it was not apparent whether the patients who could not maintain remote monitoring were the same throughout the entire study period. These studies also reported that 89 to 100 per cent of scheduled reports were successfully transmitted by remote monitoring systems.

Varma et al (Study A 2005) reported 22,356 transmissions for 107 patients over a three month follow-up period. The study reports use of the Biotronik Home Monitoring® system with a prototype remote monitoring-capable pacemaker. The reported number of messages sent per patient per day was considerably more than indicated by Biotronik's information about Home Monitoring® (one per day). This may indicate that the scheduled reporting by Home Monitoring® was broken down into its component variables. It is also possible that patients in the study were monitored more intensively than those indicated by the currently marketed Home Monitoring® system.

Varma et al (Study B 2005) reported 14 patient-initiated messages in the first two weeks, but the significance of this result is unclear. Wallbruck et al (2002) reported 1223 patient-initiated messages during the study period; this can be compared with the 5911 scheduled messages during the same period. The 1223 patient-initiated transmissions resulted in approximately 792 reports (64.8% success).

No study reported the number of event-initiated transmissions.

Table 18 Transmission outcomes of the included supportive studies evaluating non-TGA approved remote monitoring systems for implanted cardiac devices

Author (year) Region	Transmission outcomes			
	Number of patients able to maintain remote monitoring (%)	Number of successfully transmitted scheduled reports (%)	Patient initiated messages	Event initiated messages
Brugada et al (2006) Europe	239/271 (88.2%)	NR	NR	NR
Clementy et al (2003) France	10/10 (100%)	720/784 (91.8%)	NR	NR
Joseph et al (2004) USA	124/124 (100%)	569/570 (99.8%)	NR	NR
Schoenfeld et al (2004) USA	53/57 (93.0%)	NR	NR	NR
Varma et al Study A[a] (2005) USA	NR	19897/22356 (89%)	14[c]	NR
Wallbruck et al (2002) Europe	117/120 (97.5%)	5311/5911 (89.8%)	1223[c]	NR

Abbreviation: NR, not reported

[a] One of two related studies reported in the same paper by Varma et al (Study A 2005)

[b] Only during the first two weeks of the study

[c] Varma et al (Study A 2005) reported 14 patient initiated messages from 107 patients during the first 2 weeks of the study. Wallbruck et al (2002) reported 1223 patient initiated messages from 93 patients, but the duration of follow-up was not reported

Results reported by Elsner et al (2006) indicated no difference in the mortality or admission to hospital rates between the three and 12 month remote monitoring arms

(Table 19). This result should be interpreted with caution because the study's mean observation time was approximately four months. The study also examined differences between patient-induced and remote monitoring-induced additional visits. The 12 month follow-up remote monitoring arm had considerably more patient-induced and remote monitoring-induced additional visits than the three month remote monitoring arm. The interpretation of these results is unclear. Overall, clinicians reported that 80 per cent of remote monitoring-induced visits were classified as high need evaluations.

Brugada et al (2006) reported that clinicians' decisions informed by remote monitoring data would have avoided 81 per cent of scheduled follow-up visits (Table 19). This study indicated a false negative rate of 14 per cent associated with remote monitoring data. The reasons provided by the authors for false negatives were: routine check and permanent programming of pacing amplitude (47.3%); detection of increase in ventricular or atrial pacing threshold (17.8%); no precise reason (7.8%); ventricular episodes disregarded in home monitoring data (5.4%); optimisation of ICD therapy (5.4%); and necessary change in medication (3.9%).

If Brugada et al (2006) had used remote monitoring data to determine patient management, approximately 17.5 per cent (129/737) of scheduled follow-up visits would have been avoided inappropriately. Brugada et al (2006) also reported a false positive rate of 3 per cent, but this relates to unnecessary scheduled follow-up visits in this study. In practice, a false positive result could also be an outcome of an unnecessary unscheduled follow-up visit. Brugada and colleagues (2006) proposed a management scheme that minimised false negative results and indicated that 509 of 1079 scheduled visits could have been avoided with only one safety concern.

Results reported by the low quality, level III-2 studies by Clementy et al (2003) and Lazurus et al (2007), and level IV studies by Joseph et al (2004) and Schoenfeld et al (2004) are summarised in Table 19.

Table 19 Results from the included supportive studies evaluating non-TGA approved remote monitoring systems for implanted cardiac devices

Author (year) Region	Summary of results
Brugada et al (2006) Europe	Of 908 pairs of home monitoring data and standard follow-up data, physicians indicated that based on initial judgement of remote monitoring data, 737 (81%) standard follow-up visits could have been avoided. When the remote monitoring forecasts were compared with findings from the clinical exam, 129 (14%) false negative results were detected
	A retrospective analysis using a management scheme to avoid false negative results indicated that 509 of 1079 scheduled visits could have been avoided with only one safety concern
Clementy et al (2003) France	Home monitoring provided parameters (mean heart rate, atrial sensed events, time at maximum sensor rate, maximum heart rate, maximum ventricular ectopic/hour) that had significant variations (> 25%) compared with pacemaker memory data and 24 hour Holter monitoring results
Elsner et al (2006) Europe	The study revealed no significant difference in hospitalisation rates and patient mortality between monitoring arms
	After 3 months follow-up 15.7% of overall visits in the 12 month group were home monitoring-induced, and 0.75% of visits in the 3 month group were home monitoring-induced
	After 3 months follow-up 31.6% of additional visits in the 12 month group were patient-induced, and 1.5% of additional visits in the 3 month group, were patient-induced
	Effectiveness of the visits was shifted from 36% high or medium necessity in the 3 month group to 47% high or medium necessity in the 12 month group
	Over 80% of the home monitoring-induced visits had high need evaluation and all were classified high or medium
Joseph et al (2004) USA	93–99% of patients indicated complete or high satisfaction with remote interrogation in terms of ease of learning the system, using the system to transmit, feeling that the system saved them time, convenience of routine follow-up, confidence in the system measures used to gauge satisfaction
Lazarus et al (2007) Global	The mean interval between last follow-up and occurrence of unconfirmed asymptomatic events notified by home monitoring was 26 days; this represents the detection of an event 154 or 64 days earlier in patients usually followed at 6 and 3 month intervals, respectively
	The mean number of events per patent per month reported to the carer for the overall population was 0.6. On average, 47.6% of patients were event-free
	Mean interval between clinical follow-up visits for patients with remote monitoring capable pacemakers, single chamber ICDs, dual chamber ICDs, and CRT-D systems was 5.9 ± 2.1, 3.6 ± 3.3, 3.3 ± 3.5, and 1.9 ± 2.9 months, respectively
Schoenfeld et al (2004) USA	98% of pooled patient feedback responses indicated that the remote monitoring system was very easy or somewhat easy to set up. 86% of pooled patient feedback responses indicated that it was very easy or somewhat easy to position the remote monitoring antenna. 98% of pooled patient feedback responses indicated that the remote monitoring system was very easy or somewhat easy to use
	96.5% of physicians were satisfied with reviewing data remotely
	Clinical observations such at detection of silent atrial fibrillation, assessment of anti-arrhythmic therapy, detection of previously unobserved atrial under-sensing and ventricular tachycardia were made using the remote monitoring data

Abbreviations: CRT-D, cardiac resynchronisation therapy and defibrillator; ICD, implantable cardioverter defibrillator; TGA, Therapeutic Goods Administration

Body of evidence for remote monitoring systems

Evidence is limited—there were two level IV studies available. The body of evidence concerning remote monitoring of enabled TGA listed devices was assessed according to the NHMRC body of evidence matrix (Table 13). Individual rankings for components of the body of evidence are shown in Table 20. Low studies quality and limited applicability to current Australian practice meant that the body of evidence was narrow.

Table 20 Body of evidence criteria for remote monitoring of TGA listed devices with remote monitoring capabilities

Component	Rank	Reason
Volume of evidence	D	Only two studies reported data for TGA listed devices. Both studies were level IV with high risk of bias as both were retrospective with no comparison to reference standard and unclear follow-up
Consistency	D	Overall evidence was inconsistent between both studies Study design was not consistent in both reports One study was non-consecutive while the other was consecutive Clinical outcomes not consistent between studies One study reports on CRT the other on pacemakers
Clinical impact	D	One study reported limited evidence regarding the clinical impact on two types of indications Relevance of evidence to the clinical questions was unclear Size of the effect if the results was unclear due to inadequate reporting of the results Clinical impact cannot be determined as evidence was not comparative Study duration in one study is very short (3 months)
Generalisability	B	Patients populations correspond to those defined in the research questions Patient characteristics were insufficiently described in both studies
Applicability	C	Both studies identified in this report generally inadequately reported test characteristics

Abbreviations: TGA Therapeutic Goods Administration, CRT cardiac resynchronisation therapy

Evidence for remote monitoring of non-TGA listed devices with remote monitoring capabilities was similarly limited—a small number of levels III and IV studies were available. The body of evidence related to non-TGA listed devices was assessed according to the NHMRC body of evidence matrix (Table 13), and individual rankings for components of the body of evidence are shown in Table 21. Like the TGA listed devices, evidence was limited because of study quality deficits and limited local applicability.

Table 21 Body of evidence criteria for remote monitoring of non-TGA listed devices with remote monitoring capabilities

Component	Rank	Reason
Volume of evidence	D	A small number of studies reported data for non-TGA listed devices. Most studies were level III or IV (only one was classified as level II) There was risk of study bias because most were non-consecutive, some were retrospective, and many were unblinded or non-comparative Most studies did not report follow-up clearly
Consistency	D	Overall, evidence was inconsistent among studies Study design was not consistent; some studies were prospective, others retrospective; some were non-consecutive, others consecutive Clinical outcomes, where reported, were inconsistent among studies There was inherent inconsistency because studies considered variations of devices (CRT, ICD, pacemaker or combinations). Results could therefore differ depending on the type of device being tested
Clinical impact	C	Overall relevance to the clinical questions was unclear Size of the effect of the results was unclear because of inadequate reporting The trial outcome was unclear in one study Follow-up was not reported by two studies Study duration reported by two studies was very short (28 days to 3 months, and 6 months)
Generalisability	B	Patient populations correspond to those defined in the research questions Patient characteristics were insufficiently described by two studies in particular
Applicability	C	Two studies did not describe test characteristics Most studies did not describe test characteristics adequately Applicability of studies to Australian health care settings was limited; devices were not listed by the TGA

Abbreviations: TGA, Therapeutic Goods Administration; CRT, cardiac resynchronisation therapy; ICD, implantable cardioverter defibrillator

Economic considerations

Summary

There is insufficient appropriate clinical evidence regarding patient outcomes and resource cost savings associated with remote monitoring systems to conduct an economic analysis. Chan and Chun (2002), Elsner et al (2006), and Fauchier et al (2005) reported economic evaluations of remote monitoring. These studies have major design limitations and their results are not generalisable to an Australian setting.

It is proposed that the Medicare Benefits Scheme (MBS) fee for data analysis by remote monitoring should account for the opportunity cost of cardiologists' time in analysing results of remote monitoring system data. The fee could also account for capital costs incurred by cardiologists, such as the amortised cost of equipment used to analyse data. An annual fee per patient is likely to be the most appropriate method and would avoid incentive to over-service patients.

As well as the proposed fee, a future cost-effectiveness study of data analysis by remote monitoring should, at a minimum, include the costs of clinical follow-up visits and admissions to hospital for cardiac events. Use of remote monitoring systems is expected to reduce the number of these events compared with regular clinical follow-up.

The analysis should also include all capital costs attributable to the home monitoring system (such as patient device, service centre, cardiologist equipment). An analysis from the societal perspective could include productivity costs (time away from work due to clinic visits and cardiac events) and transportation costs, which are expected to be lower with remote monitoring.

More data are required to determine whether the cost savings due to remote monitoring exceed the cost of data analysis, or whether the net cost of remote monitoring is value for money in terms of the benefits provided by the service, particularly cardiac events and deaths avoided.

Economic analysis

The lack of clinical evidence regarding patient outcomes (such as rates of stroke, sudden cardiac death, and cardiac episodes) and resource use data meant that an economic analysis of remote monitoring systems for patients with implanted cardiac devices could not be conducted for this evaluation.

In the review of clinical evidence (see *Results of assessment*) no high quality clinical studies were identified that enabled comparison of the effectiveness of remote monitoring systems with regular follow-up of cardiac devices.

Similarly, the literature review did not yield any reliable data to estimate cost offsets attributable to remote monitoring. Chan and Chun (2002), Elsner et al (2006), and Fauchier et al (2005) conducted economic evaluations of cardiac remote monitoring technology. These studies were undertaken in the USA, Germany and France and did not report data that can be reliably translated to an economic evaluation performed from the Australian perspective.

For these reasons, it was not possible to estimate the cost per additional unit of clinical benefit (cost-effectiveness) associated with remote monitoring systems. An analysis will be required as more data become available.

This section proposes considerations for inclusion in a future cost-effectiveness study of remote monitoring in Australia.

Cost of remote monitoring

The applicant has requested Medicare reimbursement for physician analysis of home monitoring of medical implant telecommunications (MIT) data.

The applicant has requested an MBS fee of $840 per patient per year, which is based on:

- 2.5 hours per patient annually on average for routine analysis of data received from the service centre, and a cost of $300 per hour for physician time

- 10 minutes per patient annually on average for additional data analysis and correspondence with the patient following any abnormal readings, at a cost equivalent to an average specialist consultation ($70; presumably an approximation of the average MBS fee for items 11721 and 11727)

- The value of a dedicated computer and colour printer ($2400) amortised over three years and serving 40 patients per year ($20 = 2400 ÷ [3 × 40]).

The appropriate MBS fee for data analysis by remote monitoring would be partly dependent on the scope used to define this service. At a minimum, the fee payable to a cardiologist performing data analysis by remote monitoring should cover the opportunity cost of their time spent analysing data and following up on any abnormal results. The times proposed by the applicant have been assumed and are not based on any published evidence. In particular, cardiologist time involved in the analysis and follow-up of abnormal readings is likely to vary substantially between stable low-risk and unstable high-risk patients, and the estimate of 10 minutes per year cannot be qualified without

further data. Furthermore, the applicant's estimated time for routine data analysis per year (2.5 hours) is likely to be substantially overestimated (expert opinion, advisory panel).

The MBS fee could also cover the cost of any cardiologist equipment used in data analysis by remote monitoring. The applicant's proposed cost of a computer and printer may be an appropriate inclusion in the MBS fee. However, an adjustment should be made for the proportion of time that equipment is used for the specific purpose of remote data analysis. No evidence has been identified from which to estimate this proportion at the current time.

Potentially, a cardiologist would incur other costs of remote data analysis, including the cost of receiving data from the remote monitoring service centre. It is unclear whether a cardiologist practice would pay directly for this service and, if so, what the service cost would be. The MBS fee could also incorporate the annual costs of maintaining a server connection with the service centre (accounting for the number of patients transmitting data to the service), and receiving and transmitting data from/to the service centre. Importantly, no costs should be incorporated in the MBS fee for infrastructure that would have been or would be incurred in the absence of remote monitoring service.

Remote monitoring service equipment also includes the patient device used to transmit data to the service centre. It might not be appropriate to account for the cost of the patient device in the MBS fee for data analysis by remote monitoring, because this cost is likely to be incurred by the patient or wider health care system, and not the cardiologist performing the remote data analysis.

In the absence of clear evidence on cardiologists' time, use of equipment in providing remote data analysis, and applicable economic evaluations, it is difficult to determine an appropriate MBS item fee for the service of remote monitoring of implanted cardiac devices (expert opinion, advisory panel).

Cost of current practice

Currently, testing of implanted pacemakers and ICDs are reimbursed under MBS items 11721 *Implanted pacemaker testing* ($62.95 per service) and 11727 *Implanted defibrillator testing* ($85.65 per service), respectively. As well as these services, MBS item 116 *Subsequent attendance* ($68.20) for follow-up with a consultant physician is also likely to be billed. In any cost-effectiveness analysis of remote monitoring, the total annual cost of current practice would incorporate these MBS fees and the annual number of scheduled visits for equipment testing and patient monitoring, in the absence of remote monitoring.

Cost savings from remote monitoring

Published evidence

There were three studies identified that described the potential cost savings from remote monitoring.

Chan and Chun (2002) compared the annual physician cost of care for data analysis by remote monitoring versus conventional pacemaker clinic follow-up according to US Medicare guidelines. This study has been reported only in conference abstracts which

could not be obtained for this evaluation. The quality of the study therefore could not be verified for inclusion in this assessment. Anecdotal reports about this study by the applicant indicated that Chan and Chun (2002) estimated data analysis by remote monitoring to reduce the frequency of annual clinical visits by one-third, eliminates elective replacement visits, and saved one electrocardiograph (ECG) examination, 0.5 Holter evaluations, and four telephonic ECG transmissions per year. Cardiologists' reimbursement for data analysis by remote monitoring was US$140 (A$148) per patient per year, and estimated savings to Medicare totalled US$267 (A$282) per patient annually, a 20 per cent reduction compared with conventional follow-up. The predicted annual healthcare cost reduction was US$552 (A$583) per patient, a 29 per cent reduction compared with conventional follow-up. Without access to the study details, the transferability of these results to the Australian setting cannot be assessed. However, it should be noted that health care cost structures differ substantially between the USA and Australia, and the study inputs and results are unlikely to be generalisable to the current evaluation.

Fauchier et al (2005) evaluated the cost savings attributable to remote monitoring of implantable cardioverter defibrillators in a study of 502 patients at six French teaching hospitals. In that study it was assumed that two clinic visits per patient on average would be prevented each year due to remote monitoring compared with conventional follow-up visits. Cost savings over five years (the expected life of the device) were US$2148; this included the reduction in the costs of physician fees, ECGs, ICD surveillance, and transportation costs. The cost savings exceeded the charge for the remote monitoring system (US$1200). Fauchier et al (2005) concluded that remote monitoring has the potential to reduce the overall costs of follow-up visits by saving on transportation costs, particularly when the patient resides more than 100 kilometres from the medical facility.

The economic study conducted by Fauchier et al (2005) has a number of major limitations:

- the study did not include a cost for the analysis of remote monitoring data
- the study population was highly selective: results only apply to ICD testing and not pacemaker testing, where follow-up visits are less frequent
- the study did not specify the elements of the remote monitoring system that are covered by the stated cost of US$1200
- transportation costs were based solely on medical vehicle use and not private transportation (such as patient's own car or public transport)
- the study did not include the costs of physician visits following the receipt of abnormal data using remote monitoring.

Elsner et al (2006) reported modelled economic outcomes in addition to clinical outcomes (see page 30). Resource use was based on 115 patients undergoing home monitoring with either annual or quarterly follow-up office visits, with patients being observed for an average of 117 days. Results were then interpolated for one year with 100 patients in each monitoring arm. Elsner et al (2006) concluded that remote monitoring systems with annual office visits reduced patient visits and transportation costs by 63.2 per cent, and reduced physician time in analysing results by 40.5 per cent, compared with remote monitoring systems and quarterly office monitoring.

This study also had a number of limitations, including:

- relatively high transportation costs: €20–60 (AUD$32–96) for a one-way journey
- lack of a comparison between the capital cost of remote monitoring and the potential cost savings achieved with remote monitoring
- interpolated data were used to model economic outcomes: this assumes that the trends based on observations of the 115 patients continue in a similar manner over time—no data were presented to support this
- absence of a comparison between remote monitoring and regular clinical follow-up without remote monitoring.

In light of these study limitations, it would be extremely unreliable to generalise the economic data or conclusions presented in any of these published studies to an Australian evaluation of remote monitoring.

Potential cost savings of remote monitoring

To comprehensively estimate the cost savings associated with remote monitoring (and hence, the cost-effectiveness of remote data analysis) from an Australian health care payer perspective, a range of direct health care costs should be included in the analysis, including the costs of scheduled and unscheduled physician visits, and hospitalisations.

Likely cost savings from remote monitoring would include a reduced number of annual scheduled physician visits for assessment of a patient's clinical condition and pacemaker/ICD functioning. With remote monitoring, less frequent physician visits are scheduled. Furthermore, scheduled visits may be cancelled if remote monitoring data suggest the patient to be in a stable clinical condition with a correctly functioning device.

The annual number of unscheduled visits may increase or decrease with remote monitoring. The net change in the frequency of unscheduled visits will depend on the true-positive and false-positive rates for abnormal clinical results transmitted from the device to the cardiologist. Functional failure of devices may also require an unscheduled patient visit for adjustment of the device.

Remote monitoring may reduce the hospitalisation rate for cardiac events, since abnormal cardiac events can be observed and followed-up between scheduled visits. The size of this reduction is dependent on the accuracy of the remote monitoring system in detecting clinical events and device events. These data have not been reported in the literature at the current time.

Savings in transportation costs would only be justified if the cost-effectiveness analysis were performed from a societal perspective. In any analysis performed from the health care payer perspective, only the costs of ambulance or other health care provider transportation would be included. Additional costs that could be required in any analysis from a societal perspective include productivity losses (lost work time due to cardiac events), and the costs of patient devices and the remote monitoring service centre, regardless of who incurs those costs.

Cost-effectiveness analysis

At the current time, a reliable cost-effectiveness analysis of remote monitoring cannot be undertaken. As described, there is a lack of comparative clinical evidence on the effectiveness of remote monitoring compared with physician monitoring during regular patient visits. Therefore, the potential clinical and economic benefits of remote monitoring cannot be adequately assessed.

Given the availability of appropriate data, the cost-effectiveness of remote monitoring in comparison with scheduled visits for device testing would be demonstrated by:

- the annual cost savings with remote monitoring exceeding the annual costs of the remote monitoring system (a zero or negative net cost of remote monitoring)

- the net cost of remote monitoring being considered acceptable in relation to the improved health outcomes provided by the service. The preferred measures of improved health outcomes should include cardiac events avoided, deaths avoided, increase in survival, and improvement in quality of life, with patient benefit in avoiding cardiac events demonstrated through physician visits and hospitalisations avoided.

In addition to the lack of clarity around the clinical benefits of remote monitoring, it is also unclear which costs of the remote monitoring system are incurred by the cardiologist performing remote data analysis; the wider health care service; and/or the patient. This has important implications for determining the appropriate costs to be included in any cost-effectiveness analysis of the service, and in setting an appropriate MBS fee should the service be funded.

Funding issues

There are a number of key issues with respect to the funding of remote monitoring on the MBS.

Fee per annum

The MBS fee could potentially be set either on a per service or per annum basis. A fee per annum could be preferable because, as suggested by the applicant, "(it will) compensate the physician for the average time spent, with no incentive to over-service any patient". An annual fee covering the time spent in following up abnormal results would also reduce the incentive to follow-up on results unnecessarily.

Incorporation of capital costs into the MBS fee

The costs of capital not owned or paid for by the cardiologist or their practice should probably not be included in the MBS fee for data analysis by remote monitoring, because these costs do not comprise an opportunity cost of the data analysis.

Funding of patient devices

Currently, patients are usually required to invest in home devices necessary for remote monitoring of their pacemaker or ICD. The issue of whether the government should fund these patient devices is considered to be outside the scope of this assessment. Essentially, if remote monitoring were cost-effective when the cost of the patient device is included as a cost in the economic evaluation, then potentially it would be

cost-effective for government to fund the patient device. However, the transmission of data from the patient device to the service centre is arguably a separate service to the data analysis performed by the cardiologist, and for which the applicant is requesting a MBS item.

The issues discussed here are also important considerations if remote monitoring devices were provided at local regional hospitals, with several patients effectively sharing a device at pacemaker/ICD clinics. If remote monitoring was implemented in this way there would be a potential cost saving to the patient from decreased transport costs (in the absence of remote monitoring, relative to clinic visits at a major centre). However, the service of remote data analysis by cardiologists would be the same as provided for patients who have their own devices. Implementation of remote monitoring using these means may have potential to be cost-saving.

Current reimbursement status

Data analysis by remote monitoring is not currently reimbursed by the MBS. However, testing of implanted pacemakers or ICDs at regular clinical follow-up visits (face-to-face patient-physician contacts) is currently funded under MBS item codes 11721 and 11727, at fees of $62.95 and $85.65 per service, respectively.

To estimate the likely size of the eligible patient population for remote monitoring, the number of patients with implanted ICDs and pacemakers must be determined. Medicare claims data for January to October 2007 report claims for 43,108 patients with an implanted pacemaker and 5156 patients with an ICD in Australia (Table 22). The true eligible patient population sizes are likely to differ significantly from these figures.

The data show that during the period January to October 2007 there was a mean of 1.6 services per patient with implanted pacemakers and a mean of 1.7 services per patient with ICD. There was a median of one service for both patient groups.

Table 22 Medicare claims data for implanted pacemaker and ICD testing, January to October 2007 inclusive

Number of services (A)	Total number of services (B)	Total number of patients (B ÷ A)
MBS item code 11721 (implanted pacemaker testing)		
1	24,987	24,987
2	26,678	13,339
3	10,092	3364
4	3940	985
5	1360	272
6	588	98
7	287	41
8	80	10
9	45	5
10	20	2
11	22	2
12	12	1
13	13	1
15	15	1
TOTAL	68,139	43,108
MBS item code 11727 (ICD testing)		
1	2698	2698
2	3,248	1624
3	1701	567
4	660	165
5	265	53
6	174	29
7	84	12
8	40	5
9	18	2
10	10	1
TOTAL	8898	5156

There are a number of factors suggesting that the true eligible patient population may be greater or smaller than these numbers:

- Not all patients have implanted pacemakers and ICDs that are compatible with remote monitoring systems

- Over time the number of patients implanted with devices capable of remote monitoring is likely to increase

- The presented data were not derived from a full year of claims information, and some patients with implanted pacemakers or ICDs may not have undergone testing or claimed for testing between January and October 2007

- Some patients with implanted pacemakers or ICDs would not be expected to adopt remote monitoring technologies, partly because remote monitoring requires purchase of

a device to receive data from the pacemaker or ICD for transmission to a service centre. The patient may choose to not invest in this equipment

- Patients followed in pacemaker clinics in public hospitals may not be billed under Medicare at present. However, these patients may be considered for Medicare funded remote monitoring if this service is shown to have clinical and economic benefits.

Other considerations

Matters relating to remote monitoring that may not have been addressed by the evidence identified to inform the analysis of the clinical safety; effectiveness and cost-effectiveness of the system are discussed in this section. Advice from the expert advisory panel and issues identified by the evaluators is presented. This information should be considered as additional to the evidence identified from the systematic literature review.

Legalities and responsibilities

Data protection must be continuously maintained and secured, especially when patient information is transmitted electronically.

Patients' informed consent must be obtained by providing comprehensive information about the advantages and disadvantages of remote monitoring, emphasising that this technology is not a replacement for emergency care (Deharo et al 2006).

Legislation must be clear about the responsibility of the treating clinician. Current European legislation requires that clinicians must acknowledge receipt of data from their offices; clinicians are not obliged to inform patients or the home monitoring service if they are absent from their office (Deharo et al 2006).

Parameters measured by remote monitoring

If remote monitoring is to be conducted to reduce or replace scheduled clinic visits, it is important that clinic and remote access data parameters are the same for both settings. Table 23 sets out the main categories of data parameters that are considered necessary for remote monitoring to reduce or replace clinic visits (expert opinion, advisory panel). Examples of parameters assessed in each category are presented to illustrate potential variations among different implanted cardiac devices.

Table 23 Data requirements for remote monitoring to reduce or replace clinic visits

Category	Examples of parameters
Battery parameters	Battery status +/– longevity estimations
	Battery voltage
	Cell impedance
	Capacitor charge time (ICD)
Lead function on 1, 2 or 3 leads in use (atrial, right ventricular and left ventricular)	Sensing values
	Pacing thresholds
	Lead impedance
	% pacing on each lead
Programmed parameters	Pacing mode
	Lower and upper rates
	Lead outputs
	Mode Switch ON
	Therapy ON (ICDs)
Arrhythmia logs	Atrial fibrillation episodes
	Atrial fibrillation burden (%)
	Atrial fibrillation maximum duration
	Episode electrograms
	Ventricular ectopy counters
	Ventricular tachycardia counters
	Ventricular tachycardia duration
	Episode electrograms
Arrhythmia treatments (ICDs)	Number of treated episodes of: • ventricular tachycardia • ventricular fibrillation
	Therapy success rates: • pace termination • low energy cardioversion • high energy defibrillation
	Episode electrograms

Abbreviations: ICD, implantable cardioverter defibrillator
Source: Expert opinion, advisory panel

Clinical trials

A number of clinical trials currently underway, many of which are randomised controlled trails, are likely to report findings in 2008. Evidence provided by these studies will contribute to evaluation of remote monitoring. A lower level RCT by Elsner et al (2006) from the current literature does not provide useful comparisons or report all study outcomes.

Table 24 Characteristics of potentially relevant ongoing trials using remote monitoring

Trial register details	Study characteristics
NCT00336284 Niraj Varma TRUST	**Study design**: Open-label parallel group RCT **Population**: Patients indicated for an ICD (n = 1000) **Index test**: Lumos-T (Biotronik) **Comparator**: Conventional follow-up **Outcomes**: *Primary*—ICD follow-ups, safety event rate; *Secondary*—silent events, patient initiated inquiries **Source**: http://clinicaltrials.gov/ct2/show/NCT00336284?term=lumos&rank=1 **Start date**: October 2005 **Completion date**: NR **Publications**: NR
NCT00325221 Robert Krahner QUANTUM	**Study design**: Open-label parallel group RCT **Population**: Patients indicated for an ICD (n = 150) **Index test**: Lumos-T (Biotronik) **Comparator**: Home Monitoring is introduced 9 months after ICD implantation **Outcomes**: *Primary*—HADS anxiety score; *Secondary*—HADS depression score, quality of life (SF-12), prevalence of Type D personality, frequency of contact, patient perceptions, patient mobility **Source**: http://clinicaltrials.gov/ct2/show/NCT00325221?term=lumos&rank=2 **Start date**: August 2006 **Completion date**: December 2009 **Publications**: NR
NCT00401466 Gerd Hindricks REFORM	**Study design**: Open-label parallel group RCT **Population**: Patients indicated for an ICD meeting MADIT II criteria (n = NR) **Index test**: Home Monitoring (Biotronik) **Comparator**: Conventional follow-up **Outcomes**: *Primary*—ICD follow-ups; *Secondary*—total costs, all-cause mortality, quality of life (SF-36), hospitalisations **Source:** http://clinicaltrials.gov/show/NCT00401466 **Start date**: January 2004 **Completion date**: May 2008 **Publications**: Elsner (2006)
NCT00475124 David Fluck VIRTUE	**Study design**: Open-label parallel group RCT **Population**: Patients indicated for an ICD (n = 120) **Index test**: Virtual clinic (Biotronik) **Comparator**: Conventional follow-up **Outcomes**: *Primary*—total work load; *Secondary*—hospitalisations, serious adverse events, quality of life, total costs **Source**: http://clinicaltrials.gov/show/NCT00475124 **Start date**: May 2007 **Completion date**: May 2014 **Publications**: NR

Trial register details	Study characteristics
NCT00294645	**Study design**: Open-label parallel group RCT
Medtronic	**Population**: Patients indicated for an ICD (n = 900)
	Index test: Remote Monitoring (Medtronic)
PREFER	**Comparator**: Conventional follow-up
	Outcomes: *Primary*—rate of diagnosis of first clinical actionable event; *Secondary*—frequency of response to clinical actionable event, rate of diagnosis for each clinical actionable event
	Source: http://clinicaltrials.gov/show/NCT00294645
	Start date: April 2004
	Completion date: April 2008
	Publications: NR
NCT00538356	**Study design**: Open-label parallel group RCT
Gerd Hindricks	**Population**: Patients indicated for an ICD with heart failure and impaired left ventricular function (n= 620)
IN-TIME	**Index test**: Home Monitoring (Biotronik)
	Comparator: Conventional follow-up
	Outcomes: *Primary*—Composite outcome (death, heart failure hospitalisation, NHYA class and global assessment); *Secondary*—heart failure rehospitalisation, correlation of HM to clinical status, incidence and reason for HM clinical intervention, HM workflow analysis
	Source: http://clinicaltrials.gov/show/NCT00538356
	Start date: July 2007
	Completion date: July 2010
	Publications: NR
NCT00559988	**Study design**: Open-label parallel group RCT
Jonathan Halperin, John Ip	**Population**: Patients indicated for an ICD (n = 2718)
	Index test: anticoagulation therapy directed by Home Monitoring (Biotronik)
	Comparator: anticoagulation therapy directed by conventional follow-up
IMPACT	**Outcomes**: *Primary*—Composite outcome (stroke, systemic embolism and major bleeding); *Secondary*—all-cause mortality, major bleeding, atrial fibrillation burden, quality of life, mean heart rate reduction
	Source: http://clinicaltrials.gov/show/NCT00559988
	Start date: January 2008
	Completion date: January 2014
	Publications: NR
NCT00395642	**Study design**: Observational study
Joseph Akar	**Population**: Patients indicated for an ICD (n = 200)
	Index test: Kronos LV-T (Biotronik) and Carematrix
TRIAGE-CRT	**Outcomes**: *Primary*—Changes in treatment regimen, correlation to clinical status; *Secondary*—patient compliance, NYHA class, heart failure and anti-arrhythmic medications, adverse events
	Source: http://clinicaltrials.gov/show/NCT00395642
	Start date: November 2006
	Completion date: NR
	Publications: NR

Trial register details	Study characteristics
ACTRN12607000517471 Medtronic ACQUIRE	**Study design**: Observational study **Population**: Patients indicated for an ICD (n = 225) **Index test**: CareLink (Medtronic) **Outcomes**: *Primary*—patient and clinician time burden, patient and clinician financial burden; *Secondary*—patient and clinician ease of use and acceptance **Source**: http://www.anzctr.org.au/trial_view.aspx?ID=82316 **Start date**: November 2007 **Completion date**: NR **Publications**: NR
NCT00334451 Leslie Saxon, John Boehmer RAPID-RF	**Study design**: Observational study **Population**: Patients indicated for an CRT-D with heart failure (n = 1000) **Index test**: Latitude (Boston Scientific) **Outcomes**: Type and frequency of alerts and resulting medical interventions, quality of life, NYHA class, mortality, hospitalisations, heart failure related events **Source:** http://www.clinicaltrials.gov/ct2/show/NCT00334451?term=RAPID-RF&rank=1 **Start date**: May 2006 **Completion date**: NR **Publications**: Saxon (2007)
NCT00376116 Stefan Sack & Vincent Paul HOME CARE	**Study design**: Observational study (randomised sub-study) **Population**: Patients indicated for an ICD with heart failure (n = 513) **Index test**: Home Monitoring (Biotronik) **Comparator**: Conventional follow-up (randomised sub-study) **Outcomes**: Quality of life, NHYA class, blood pressure, body weight, ECG parameters, change in management, cardiovascular events, heart failure symptoms **Source**: http://www.clinicaltrials.gov/ct2/show/NCT00376116?term=00376116&rank=1 **Start date**: March 2005 **Completion date**: November 2008 **Publications**: Ellery (2006)
NCT00402246 Medtronic CONNECT	**Study design**: Open-label parallel group RCT **Population**: Patients indicated for an ICD (n = 2000) **Index test**: Remote Monitoring (Medtronic) **Comparator**: Conventional follow-up **Outcomes**: *Primary*—time to clinical decision, cardiovascular disease progression, system issues; *Secondary*—healthcare utilisations **Source:** http://clinicaltrials.gov/ct2/show/NCT00402246?term=connect&rank=1 **Start date**: November 2006 **Completion date**: NR **Publications**: NR

Abbreviations: CRT-D, cardiac resynchronisation therapy-defibrillator; HADS, Hospital Anxiety and Depression Scale; HM, home monitoring; ICD, implantable cardioverter-defibrillator; LV-T, left ventricular tachycardia; MADIT, Multicenter Automatic Defibrillator Implantation Trial; NR, not reported; NYHA, New York Heart Association; RCT, randomised controlled trial; SF, short form

Research recommendations

The evaluators formulated specific research recommendations using a modified EPICOT (evidence, population, intervention, comparison, outcome, time stamp) format (Brown et al 2006) following review of the body of evidence relating to each research question. The research recommendations outlined in Table 25 were formulated to address the identified gaps in the body of evidence indicating remote monitoring use for patients with pacemakers that have remote monitoring capabilities. The research recommendations are inclusive of studies identified for Therapeutic Goods Administration (TGA) and non-TGA approved devices.

A systematic review of the literature did not identify any comparative evidence of the effectiveness of remote monitoring of TGA listed pacemakers versus clinical follow-up, the major comparator identified by the advisory panel. There was limited comparative evidence for non-TGA listed pacemakers (Lazarus et al 2007, Varma et al 2005); however, reporting was inadequate. Clinical outcomes, follow-up and diagnostic accuracy were also reported inadequately.

Table 25 Research recommendations for the use of remote monitoring systems in patients with pacemakers with remote monitoring capabilities

Element	Description
Evidence	No studies were identified that reported diagnostic accuracy of remote monitoring systems of pacemakers with remote monitoring capabilities
	No studies were identified which compared clinical follow-up to remote monitoring of TGA listed pacemakers with remote monitoring capabilities
	Limited evidence was available which compared clinical follow-up to remote monitoring of non-TGA listed pacemakers with remote monitoring capabilities
	Limited evidence was available in the studies identified, comparing non-TGA listed pacemakers to clinical follow-up
	No clinical outcomes were reported in the studies of remote monitoring of pacemakers with remote monitoring capabilities
Population	Patients who have pacemakers with remote monitoring capability
Prior tests	Not applicable
Intervention/test	Remote monitoring of pacemakers with remote monitoring capabilities plus regular scheduled clinic follow-up
Comparator	Current clinical practice ie, regular clinic follow-up of patients with implanted pacemaker
Outcome	Change in clinical management [a] Change in clinical outcomes [b] Diagnostic accuracy [c] Safety outcomes [d]
	Adverse events
Time stamp	November 2007 [e]
Study type [f]	Randomised control trials (see Table 24 for RCTs currently underway)

[a] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, reprogramming of the device for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, device reprogramming to reduce right ventricular pacing and possible left ventricular dysfunction)

[b] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient comfort and convenience), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, unnecessary pacing, ventricular arrhythmia); adverse event reports; adverse events known to be associated with pacemakers (abnormal lead impedance, displaced leads; sudden death, inappropriate pacing)

[c] Sensitivity, specificity

[d] Safety outcomes: incomplete or inaccurate download of device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review

[e] Date of literature search

[f] Study type recommended for the evaluation of this technology

The research recommendations outlined in Table 26 were formulated to address the identified gap in the body of evidence for remote monitoring system use for patients who have implantable cardioverter defibrillators (ICDs) with remote monitoring capabilities.

A systematic review of the evidence did not identify any comparative evidence for the use of TGA listed remote monitoring systems for patients with ICDs with remote monitoring capabilities. Ellery et al (2006) reported some clinical outcomes for TGA listed ICDs. Clinical follow-up and diagnostic accuracy were inadequately reported. Non-TGA listed ICDs with remote monitoring capabilities had limited comparative data and insufficient reporting of clinical outcomes.

Table 26 Research recommendations for the use of remote monitoring systems in patients with implantable cardioverter defibrillators with remote monitoring capabilities

Element	Description
Evidence	No studies were identified that reported diagnostic accuracy of remote monitoring systems of TGA listed implantable cardioverter defibrillators with remote monitoring capabilities
	One study was identified that reported limited evidence for the diagnostic accuracy of non-TGA listed implantable cardioverter defibrillators with remote monitoring capabilities
	No studies were identified which compared clinical follow-up to remote monitoring of implantable cardioverter defibrillators with remote monitoring capabilities
	Two studies inadequately reported comparative data for non-TGA listed implantable cardioverter defibrillators with remote monitoring capabilities (with reference standard)
	Limited clinical outcomes were reported in the studies of remote monitoring of TGA-listed implantable cardioverter defibrillators with remote monitoring capabilities
	Limited clinical outcomes were reported in the studies of remote monitoring of non-TGA-listed implantable cardioverter defibrillators with remote monitoring capabilities
Population	Patients who have implantable cardioverter defibrillators with remote monitoring capabilities
Prior tests	Not applicable
Intervention/test	Remote monitoring of implantable cardioverter defibrillator with remote monitoring capabilities plus regular scheduled clinic follow-up
Comparator	Current clinical practice ie, regular clinic follow-up of patients with implantable cardioverter defibrillators
Outcome	Change in clinical management [a] Change in clinical outcomes [b] Diagnostic accuracy [c] Safety outcomes [d]
	Adverse events
Time stamp	November 2007 [e]
Study type [f]	Randomised control trials (see Table 24 for RCTs currently underway)

[a] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device programming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, reprogramming device to reduce right ventricular pacing and possible left ventricular dysfunction)

[b] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience, admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, ventricular arrhythmia); unnecessary shock from device, adverse event reports; adverse events known to be associated with ICD (abnormal lead impedance, displaced leads; sudden death)

[c] Sensitivity, specificity

[d] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review

[e] Date of literature search

[f] Study type recommended for the evaluation of this technology

The research recommendations outlined in Table 27 were formulated to address the gap identified in the body of evidence for use of remote monitoring systems for patients who have cardiac resynchronisation therapy (CRT) devices with remote monitoring capabilities.

A systematic review of the evidence did not identify any comparative evidence indicating the use of remote monitoring systems for patients with TGA approved CRT devices with remote monitoring capabilities. The study by Ellery et al (2006) reported limited clinical outcomes. Clinical follow-up and diagnostic accuracy were reported inadequately.

Table 27 Research recommendations for the use of remote monitoring systems in patients with cardiac resynchronisation therapy devices with remote monitoring capabilities

Element	Description
Evidence	No studies were identified that reported diagnostic accuracy of remote monitoring systems of devices for cardiac resynchronisation therapy with remote monitoring capabilities
	No studies were identified that compared clinical follow-up to remote monitoring of devices for cardiac resynchronisation therapy with remote monitoring capabilities
	Limited clinical outcomes were reported in the studies of remote monitoring of TGA-listed devices for cardiac resynchronisation therapy with remote monitoring capabilities
	No clinical outcomes were reported in the studies of remote monitoring of non-TGA-listed devices for cardiac resynchronisation therapy with remote monitoring capabilities
Population	Patients who have cardiac resynchronisation therapy with remote monitoring capabilities
Prior tests	Not applicable
Intervention/test	Remote monitoring of cardiac resynchronisation therapy with remote monitoring capabilities plus regular scheduled clinic follow-up
Comparator	Current clinical practice i.e. regular clinic follow-up of patients with cardiac resynchronisation therapy
Outcome	Change in clinical management [a] Change in clinical outcomes [b] Diagnostic accuracy [c] Safety outcomes [d]
	Adverse events
Time stamp	November 2007 [e]
Study type [f]	Randomised control trials (see Table 24 for RCTs currently underway)

[a] Alterations in treatment plan (eg, change in anti-arrhythmia drugs, increased or decreased follow-up visits, device programming for better arrhythmia treatment, warfarin therapy for documented atrial fibrillation, device programming to ensure biventricular pacing)
[b] Survival (complication-free survival, overall survival); morbidity (disease progression), stroke rate, sudden cardiac death; quality of life (patient convenience and comfort), admission/readmission (and length of stay), cardiac episode (increased heart rate, atrial fibrillation, ventricular arrhythmia); adverse event reports; adverse events known to be associated with cardiac resynchronisation therapy
[c] Sensitivity, specificity
[d] Safety outcomes: incomplete or inaccurate download of the device data and subsequent transmissions or failure of the data repository centre notifying the clinician in a timely and guaranteed method to allow for data review
[e] Date of literature search
[f] Study type recommended for the evaluation of this technology

Conclusions

The systematic review indicated that there was limited evidence available regarding Therapeutic Goods Administration (TGA) approved devices. This finding lead to conducting a bifurcated analysis based on devices' TGA listing status.

A suite of literature reviews conducted by the Haute Autorité de Santé (2005) evaluated the use of remote monitoring. The key findings of included studies indicated that the trialled pacemaker, Biotronik BA03 DR, provided sufficient transmission success evidence and clinically relevant data for the Biotronik Home Monitoring® system. The studies were found to be limited by a lack of comparative data, inadequate patient management reporting, and insufficient information to indicate the impact of remote monitoring on patient outcomes.

Among the 10 identified studies, Ellery et al (2006) and Varma et al (Study B 2005) examined TGA listed devices. The other eight studies provided supporting evidence for the use of remote monitoring of implantable cardiac devices (Elsner et al 2005, Brugada et al 2006, Clementy et al 2003, Lazarus et al 2007, Varma et al 2005, Wallbruck et al 2002, Schoenfeld et al 2004, Joseph et al 2004). Because non-TGA listed implanted cardiac devices were investigated by these eight studies, their applicability was limited in the context of Australian clinical settings.

Effectiveness

The studies by Ellery et al (2006) and Varma et al (Study B 2005) were non-comparative and classified as providing low quality (level IV) evidence.

Ellery et al (2006) investigated remote monitoring of the Kronos® LV-T (a cardiac resynchronisation therapy [CRT] device) and Stratos® LV-T (an implantable cardioverter defibrillator [ICD]) using the Biotronik Home Monitoring® system to determine if this system could be applied to predict cardiac events that require patients' admission to hospital. Retrospective review of home monitoring data detected an increase in mean heart rate (both at rest and over a 24 hour period) among 70 per cent of patients who were admitted to hospital. A decrease in need for CRT was observed in 43 per cent of patients admitted to hospital in this study. The limited follow-up period and inadequate reporting of outcomes meant that the validity of remote monitoring as a predictive test was not adequately demonstrated by this study.

Varma et al (Study B 2005) aimed to determine the usefulness of remote monitoring as a tool for early detection of atrial fibrillation events. Biotronik's Home Monitoring® system was used to measure output from the Biotronik Philos® DR-T pacemaker. The authors reported three patients in whom silent atrial events were detected by remote monitoring which lead to changes in administration rates of anticoagulation therapy. Unclear patient follow-up and ill-defined outcomes meant that evidence quality of this study was limited. 'Atrial fibrillation days' were used as a surrogate measure, but inadequate data reporting meant that it could not be determined how the measure corresponded to clinical outcomes.

In the group of eight studies that investigated non-TGA listed devices, the randomised controlled trial (RCT) conducted by Elsner et al (2005) aimed to demonstrate the impact

of remote monitoring on clinical management and patient follow-up. The study's key finding indicated that there was no difference in mortality or hospitalisation rates in either the 3 or 12 month remote monitoring arms. Inadequate data reporting and lack of comparison to clinical follow-up hampered drawing meaningful conclusions from this low quality study.

Brugada et al (2006) compared clinician judgement of remote monitoring data with information obtained during regular clinical follow-up to measure the accuracy of remote monitoring using the Biotronik Home Monitoring® component of the Biotronik ICD Belos® VR-T. The authors estimated that 81 per cent of clinician visits could be avoided by using remote monitoring, but they also described an associated false negative rate of 14 per cent. This study was limited by inconsistency in reporting, low relevance to the Australian setting, non-consecutive patient enrolment, and indications that blinding may have been incomplete.

The Biotronik Home Monitoring® system was trialled by Clementy et al (2003), Lazarus et al (2007), Varma et al (2005) and Wallbruck et al (2002). The Medtronic CareLink® system was trialled by Schoenfeld et al (2004). The St Jude Housecall® system was reviewed by Joseph et al (2004). These studies provided limited evidence to support remote monitoring.

The studies by Joseph et al (2004), Schoenfeld et al (2004) and Wallbruck et al (2002) were non-comparative and lacked clarity in their reporting of clinical follow-up schedules. Lazarus et al (2007), Varma et al (Study A 2005) and Clementy et al (2003) used unblinded comparisons to the reference standard, and overall, clinical follow-up was short (three months in Study A by Varma et al 2005).

Although there were no direct safety issues associated with remote monitoring identified, successful and complete transmission of data by remote monitoring was regarded as a significant indirect safety outcome in this assessment. The potential for failure of data transmission presents a safety issue that treating clinicians need to be aware of—consistent failure of data transmission may indicate that remote monitoring is unsuitable for a particular patient. The studies presenting transmission data indicated that between 88 and 100 per cent of patients maintained remote monitoring coverage during the study periods. Inadequate data reporting meant that it was not clear whether patients who maintained remote monitoring during the study were the same throughout, or this status applied to different patients at different times during follow-up. These studies also reported that 89 to 100 per cent of scheduled reports were successfully transmitted by remote monitoring systems. Transmissions outcomes were insufficiently reported. Brugada et al (2006) and Schoenfeld et al (2004) did not report the number of successfully transmitted scheduled reports; Varma et al (Study A 2005) did not indicate the number of patients who were able to maintain remote monitoring. Furthermore, unclear reporting meant that it was uncertain whether standard clinical practice was applied at regular scheduled clinical follow-ups.

Cost-effectiveness

An economic analysis of remote monitoring systems for patients with implanted cardiac devices is not presented in this assessment because there is lack of clinical evidence regarding patient outcomes and resource cost savings associated with remote monitoring systems.

Economic evaluations of remote monitoring by Chan and Chun (2002), Elsner et al (2006), and Fauchier et al 92005) were identified in the literature. These studies have significant limitations and their results are not generalisable to an Australian setting.

This assessment proposes that the MBS fee for data analysis by remote monitoring should account for the opportunity cost of cardiologists' time in analysing results of remote monitoring devices. It is further proposed that the fee could also account for capital costs incurred by cardiologists, such as amortised costs of equipment used to analyse data. It is recommended that consideration be made to assign an annual fee per patient as an appropriate solution that would diminish incentive to over-service patients.

In addition to the proposed fee, a future cost-effectiveness study of data analysis by remote monitoring should, at a minimum, include the costs of clinical follow-up visits and hospitalisations for cardiac events. The rate of these events is expected to be reduced by use of remote monitoring compared with regular clinical follow-up. The analysis should also include all capital costs attributable to the remote monitoring system (such as patient device, service centre, cardiologist equipment). An analysis from the societal perspective should also include productivity costs, such as time away from work due to clinic visits and cardiac events; and transportation costs, which are expected to be lower with remote monitoring systems.

More data are required to determine whether cost savings derived from use of remote monitoring systems exceed the cost of data analysis, or whether the net cost of remote monitoring is value for money in terms of the benefits provided by the service (such as cardiac events and deaths avoided).

Recommendation

MSAC has considered the safety, effectiveness and cost-effectiveness for the use of remote monitoring systems for patients with implanted cardiac devices including standard pacemakers, implanted cardioverter defibrillators and cardiac resynchronisation therapy compared with standard clinic-based follow-up alone.

MSAC finds that the procedure is safe.

MSAC finds that clinical effectiveness is not demonstrated.

A formal economic assessment was therefore not performed.

MSAC does not support public funding for the use of remote monitoring systems for patients with implanted cardiac devices.

–The Minister for Health and Ageing accepted this recommendation on 28 August 2008–

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures, and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, radiology, nuclear medicine, oncology, surgery, internal medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers and health administration and planning:

Member	Expertise or affiliation
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Associate Professor Michael Cleary	emergency medicine
Associate Professor Paul Craft	clinical epidemiology and oncology
Professor Geoff Farrell	gastroenterology
Dr Kwun Fong	thoracic medicine
Professor Richard Fox	medical oncology
Dr Bill Glasson	ophthalmology
Professor Jane Hall	health economics
Associate Professor Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Frederick Khafagi	nuclear medicine
Dr Ray Kirk	health research
Dr Ewa Piejko	general practice
Dr Ian Prosser	haematology
Ms Sheila Rimmer	consumer health issues

Dr Judy Soper	radiology
Professor Ken Thomson	radiology
Dr David Wood	orthopaedics

Appendix B Advisory panel

Advisory panel for MSAC application 1111

Associate Professor John Atherton (Chair) Cardiologist	Member of MSAC
Dr Ewa Piejko (Second Chair) General Practitioner	Member of MSAC
Professor Jane Hall Health Economist	Member of MSAC
Dr John Hayes Cardiologist/Cardiac Electrophysiologist	Nominated by the Cardiac Society of Australia and New Zealand
Dr Cameron Singleton Cardiologist/Cardiac Electrophysiologist	Nominated by the Cardiac Society of Australia and New Zealand
Mr Niall Gossland Consumer Health	Nominated by the Consumers' Health Forum

Appendix C Included studies

Table 28 Characteristics and results of studies evaluating remote monitoring of implanted cardiac devices

Author (year) Region Study design	Population characteristics	Test characteristics	Study outcomes	Study quality [a]
Brugada et al (2006) Europe Prospective, non-consecutive patient enrolment 339 ± 109 days mean follow-up duration May 2002–Apr 2004	Patients with clinical indications for ICD (271 patients, 15% female) Mean age: 62 years Mean LVEF: 39 ± 15% Ischemic heart disease: 177 (65%) Primary prevention: 11 (4%)	**Index test**: Belos VR-T/ DR-T (ICD) with Home Monitoring® system Office device interrogation every 3 months for a year after discharge, and intermittent controls at the clinician's discretion	Pts able to maintain remote monitoring: 239/271 (88.2%) Of 908 pairs of HM data and standard follow-up data, physicians indicated that based on initial judgement of remote monitoring data they could have avoided 737 (81%) of standard follow-up visits. When the remote monitoring forecasts were compared with the findings from the clinical examination 129 (14%) FN results were detected. A retrospective analysis using a management scheme to avoid FN results indicated that 509 of 1079 scheduled visits could have been avoided with only one safety concern	Level III-2 CX, P2, Q2 *Quality*: Medium Reference standard blinded to index test *Applicability*: Limited Non-TGA approved device
Clementy et al (2003)[d] France Prospective, non-consecutive patient enrolment Unblinded comparison with reference standard Duration ranged between 28 days and 3 months Recruitment period not reported	Patients with clinical indications for PM (10 patients, 40% female) Mean age: 70 years Ischaemic heart disease: 1 (10%)	**Index test**: *Prototype* BA03 DR (PM) with Home Monitoring® system. Office device interrogation after between 28 days – 3 months follow-up	Patients able to maintain remote monitoring: 10/10 (100%) Number of successful scheduled reports: 720/784 (91.8%) Home monitoring provided parameters (mean HR, atrial sensed events, time at max sensor rate, maximum HR, maximum ventricular ectopic/hour) which had significant variations (>25%) compared with pacemaker memory data and 24 hour Holter monitoring results	Level III-2 CX, P2, Q3 *Quality*: low Unblinded comparison Inadequate data reporting (study outcome *Applicability*: Limited Unclear/short study duration Small patient population Non-TGA approved device

Author (year) Region Study design	Population characteristics	Test characteristics	Study outcomes	Study quality [a]
Ellery et al (2006) Europe Retrospective, non-consecutive patient enrolment No reference standard 3 month mean follow-up duration Recruitment period not reported	Patients with clinical indications for CRT (123 patients, 17% female) Mean age: 67 years NYHA Class 1 (3%), Class 2 (6%), Class 3 (77%), Class 4 (14%) Ischaemic heart disease: 74 (60%) Primary prevention: 52 (42.3%)	**Index test**: Stratos LV-T (CRT) and Kronos LV-T (ICD) with Home Monitoring® system. Unclear clinical follow-up	During follow-up there were 11 unplanned re-hospitalisations, 9 deaths and 16 adverse events during follow-up. In 70% of the re-hospitalisation events, a retrospective review of home monitoring data detected an increase in mean heart rate (both at rest and over a 24 hour period) preceding hospitalisation. A decrease in CRT was observed in 43% of re-hospitalised patients and while a reduction in patients'' daily activity was observed in 30% of re-hospitalised patients	Level IV CX, P2, Q2 *Quality*: Medium Inadequate data reporting (study outcomes) *Applicability*: Limited Unclear/short study duration Unclear clinical follow-up
Elsner et al (2006) Europe Prospective, randomised patient enrolment Unblinded comparison between diagnostic arms 117 days mean duration, duration ranged between 23 and 513 days Recruitment period not reported	Patients with clinical indications for ICD (115 patients, 14% female) Mean age: 62 years Mean LVEF: 24 ± 6% NYHA Class I (3%), Class II (50%), Class III (47%) Ischaemic heart disease: 115 (100%) Primary prevention: 115 (100%)	**Index test**: ICD with Home Monitoring® system. 3 months after implantation patients underwent office device interrogation every 12 months. **Comparator**: ICD with Home Monitoring® system. 3 months after implantation patients underwent office device interrogation every 3 months	The study revealed no significant differences in the hospitalisation and mortality rates for the patients in either monitoring arm. After 3 months follow-up 15.7% of the overall visits in the 12 month group were HM-induced, and 0.75% of visits in the 3 month group were HM-induced. After 3 months follow-up 31.6% of additional visits in the 12 month group were patient-induced, and 1.5% of additional visits in the 3 month group were patient-induced. Effectiveness of the visits was shifted from 36% high or medium necessity in the 3 month group to 47% high or medium necessity in the 12 month group. Over 80% of the HM-induced visits had a "high" necessity evaluations and all were classified high or medium	Level II C1, P2, Q3 *Quality*: Low Unclear randomisation Unblinded comparison Inadequate data reporting (test characteristics) *Applicability*: Limited Unclear/short study duration Non-TGA approved device Wrong comparator
Joseph et al (2004) USA Prospective, non-consecutive patient enrolment No reference standard 6 months follow-up Sep 1999–Mar 2002	Patients with clinical indications for ICD (124 patients, 24% female) Mean age: 63 years	**Index test**: Profile MD, Angstrom II, Angstrom MD, Contour II, Contour MD, Contour and Cadet (ICD) with Housecall® II system Office device interrogation 6–12 weeks after implantation; annual office device interrogations	Pts able to maintain remote monitoring: 124/124 (100%) No of successful scheduled reports: 569/570 (99.8%) 93–99% of patients indicated complete or high satisfaction with remote interrogation in the five measures (ease of learning the system, using the system to transmit, feeling that the system saved them time, convenience of routine follow-up, confidence in the system) used to gauge satisfaction	Level IV CX, P2, Q1 *Quality*: High *Applicability*: Limited Non-TGA approved device

Author (year) Region Study design	Population characteristics	Test characteristics	Study outcomes	Study quality [a]
Lazarus et al (2007) Global Retrospective, non-consecutive patient enrolment Unblinded comparison with reference standard 10.5 months mean duration, duration ranged between 1 and 49 months Jan 2002–Feb 2006	Patients with clinical indications for PM, ICD or CRT (11624 patients)	**Index test**: PM, ICD and CRTs with Home Monitoring® system. Standard follow-up of bi-annual office device interrogations of PM and quarterly office device interrogations of ICD and CRTs was assumed	The mean interval between last follow-up and occurrence of unconfirmed asymptomatic events notified by HM was 26 days; this represents the detection of an event 154 or 64 days earlier in patients usually followed at 6- and 3- months' intervals, respectively. The mean number of events per patent per month reported to the caregiver for the overall population was 0.6. On average, 47.6% of the patients were event-free Mean interval between clinical follow-up visits for patients with remote monitoring capable pacemakers, single chamber ICDs, dual chamber ICDs, and CRT-D systems was 5.9 ± 2.1, 3.6 ± 3.3, 3.3 ± 3.5, and 1.9 ± 2.9 months, respectively	Level III-2 CX, P2, Q3 *Quality*: Low Unblinded comparison Inadequate data reporting (patient characteristics, test characteristics) *Applicability*: Limited Non-TGA approved device
Schoenfeld et al (2004) USA Prospective, non-consecutive patient enrolment No reference standard Follow-up duration not reported Recruitment period not reported	Patients with clinical indications for ICD (59 patients, 24% female) Mean age: 64 years NYHA Class I (44%), Class II (34%), Class III (17%), Unknown (5%)	**Index test**: Medtronic GEM II DR (ICD) with CareLink® system Unclear clinical follow-up	Patients able to maintain remote monitoring: 53/57 (93.0%) 98% of pooled patient feedback responses indicated that the remote monitoring system was very easy or somewhat easy to setup. 86% of pooled patient feedback responses indicated that it was very easy or somewhat easy to position the remote monitoring antenna. 98% of pooled patient feedback responses indicated that the remote monitoring system was very easy or somewhat easy to use 96.5% of physicians were satisfied with reviewing data remotely Clinical observations such at detection of silent AF, assessment of anti-arrhythmic therapy, detection of previously unobserved atrial under sensing and ventricular tachycardia were made using the remote monitoring data	Level IV CX, P2, Q1 Quality: High Applicability: Limited Non-TGA approved device Unclear/short study duration Unclear clinical follow-up

Author (year) Region Study design	Population characteristics	Test characteristics	Study outcomes	Study quality [a]
Varma et al Study A (2005)[b] USA Prospective, non-consecutive patient enrolment Unblinded comparison with reference standard 3 months follow-up Recruitment period not reported	Patients implanted with PM for class I/II indications (107 patients)	**Index test**: *Prototype* BA03 DR (PM) with Home Monitoring® system. Office device interrogation at 2, 4, 8 and 12 weeks	No. of successful scheduled reports: 19897/22356 (89%) No. of patient-initiated messages: 14[e]	Level III-2 CX, P2, Q3 *Quality*: Low Unblinded comparison Inadequate data reporting (patient characteristics) *Applicability*: Limited Non-TGA approved device Unclear/short study duration
Varma et al Study B (2005)[b] USA Retrospective, consecutive patient enrolment No reference standard 12 months follow-up Mar 2002–Apr 2003	Patients implanted with PM for class I/II indications (276 patients)	**Index test**: Philos DR-T (PM) with Home Monitoring® system. Unclear clinical follow-up	A retrospective review of patient data indicated that 29 patients (10.5% of implants) experienced a total of 645 AF days [c] experienced by 29 patients (10.5% of implants). Clinical data were available for 20 of these patients; home monitoring indicated a new-onset silent AF in 3 patients who required administration of anti-coagulation therapy; 2 patients for whom anti-coagulation therapy was were contraindicated from anticoagulation therapy underwent increased monitoring; 12 patients adopted a rate control strategy, but no therapeutic changes were made; 3 patients adopted a rhythm control strategy, but no therapeutic changes were made	Level IV CX, P2, Q3 *Quality*: Low Inadequate data reporting (patient characteristics, study outcomes) *Applicability*: Limited Sub-group results only Unclear clinical follow-up
Wallbruck et al (2002) Europe Prospective, non-consecutive patient enrolment No reference standard Follow-up duration not reported Recruitment period not reported	Patients with clinical indications for PM (93 patients, 33% female) Mean age: 70 years	**Index test**: *Prototype* BA03 DR (PM) and RUC-1000 patient device with Home Monitoring® system. Unclear clinical follow-up	Pts able to maintain remote monitoring: 117/120 (97.5%) Number of successful scheduled reports: 5311/5911 (89.8%) Number of patient-initiated messages: 1223	Level IV CX, P2, Q1 *Quality*: High *Applicability*: Limited Non-TGA approved device Unclear/short study duration Unclear clinical follow-up

Abbreviations: AF, atrial fibrillation; CRT, cardiac resynchronisation therapy; FN, false negative; HM, home monitoring; HR, heart rate; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PM, pacemaker

[a] According to criteria outlined in Table 11, Table 12 and Appendix F

[b] One of two related studies reported in the same paper by Varma et al (2005)

[c] An atrial fibrillation day was defined as a mode switch burden >20% per 24 hours

[d] This study also compared remote monitoring with Holter monitoring but did not compare Holter monitoring and office device interrogation

[e] Only during the first two weeks of the study

Appendix D Transmission criteria

Table 29 Transmission outcomes/ criteria definition summary

Author (year) Region	Transmission outcomes/ criteria
Brugada et al (2006) Europe	number of detections in the tachyarrhythmia zones
	therapy and event classifications
	pacing and shock impedances
	battery voltage
	system status
Clementy et al [a] (2003) France	heart rate
	atrial sensing pacing
	ventricular sensing or pacing
	relative time at maximum sensor rate
	maximum heart rate and maximum VEB/ hour (most hypothetic results provided by HM)
	AV synchronisation
	other data ie, AV junction ablation failure, AV synchronisation variations
Joseph et al (2004) USA	summary diagnostic information (ie, high-voltage charge/ therapy information, capacitor maintenance information, diagnoses inhibited by SVT discriminators, percentage bradycardia paced, etc)
	episode diagnostic information for each of up to 60 time-and date-stamped events (ie, SVT discrimination diagnostics, cycle length, episode duration and diagnosis time, etc)
	status information annotated on both stored and real-time EGMs (ie, sensed and paced events with interval classification, anti-tachycardia pacing, EGM trigger, inhibited diagnosis, etc)
	lifetime diagnostic data (ie, percent bradycardia pacing, patient and lead system information)
	real-time measurements (ie, pacing lead impedance, R-wave amplitude, variability on real time EGM, unloaded battery voltage, etc)
Schoenfeld et al [b] (2004) USA	stored episodes
	device parameters
	diagnostics
Varma et al—Study A [c] (2005) USA	warning signals or arrhythmias
	ventricular rates
	atrial fibrillation
Wallbruck et al (2002) Europe	intrinsic and pacemaker induced beats
	heart rate variations
	incidence of arrhythmia

Abbreviations: AV, atrioventricular; EGM, electrogram; HM, home monitoring; VEB, ventricular ectopic

[a] Atrial and ventricular sensing have to be precisely programmed before HM activation to improve reliability of VEB counting. Finally the reliability of HM provided data is close related to reliability of the information contained in the pacemaker theory

[b] A 10-second presenting rhythm EGM is also captured at the time of the interrogation. In addition, clinicians are able to identify potential programming irregularities and lead issues, diagnose previously unknown arrhythmias, and optimise device parameters

[c] Transmission may be periodic, patient-activated, or may be automatic alerts

Appendix E Excluded studies

Excluded: review, letter, etc

Braunschweig F 2007 'Therapeutic and diagnostic role of electrical devices in acute heart failure' *Heart Fail Rev* 12: 157–166.

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Germany R, Murray C 2007 'Use of Device Diagnostics in the Outpatient Management of Heart Failure' *Am J Cardiol* 99(10 SUPPL.): S11–S16.

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Spencker S, Mueller D, Marek A, Zabel M 2007 'Severe pacemaker lead perforation detected by an automatic home-monitoring system' *Eur Heart J* 28: 1432.

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Appendix F Literature search

Search strategies were used to identify relevant studies of remote monitoring in the clinical management of patients with implanted cardiac devices. The Medline and EMBASE databases were searched using the EMBASE.com interface. The PreMedline database was searched using the PubMed interface. The CDSR, DARE, CENTRAL, CMR, HTA, NHSEED databases were searched using the Cochrane Library interface. The search results for EMBASE.com are presented in Table 30, the results from PubMed are presented in Table 31 and the results of the Cochrane Library are presented in Table 32.

Table 30 EMBASE.com search results for studies of remote monitoring in the clinical management of patients with implanted cardiac devices (16 November 2007)

	Keywords / search history	Results
1.	'artificial heart'/exp	1965
2.	'heart assist device'/exp	3519
3.	'artificial heart pacemaker'/exp	21928
4.	'assisted circulation'/exp	5553
5.	'cardiac resynchronization therapy'/exp	1621
6.	'defibrillator'/de	10008
7.	'implant'/de	15807
8.	#6 AND #7	399
9.	'heart pacing'/de	10565
10.	'device'/de	48540
11.	#9 AND #10	249
12.	'pacemaker'/de	4563
13.	#1 OR #2 OR #3 OR #4 OR #5 OR #8 OR #11 OR #12	37490
14.	'artificial heart':ab,ti OR 'heart ventricle prosthesis':ab,ti	2542
15.	'mechanical heart':ab,ti OR 'heart assist device':ab,ti	1022
16.	'heart pump':ab,ti OR 'heart ventricle assist':ab,ti	103
17.	pacemaker*:ab,ti OR 'heart assist devices':ab,ti OR 'heart auxillary':ab,ti	25002
18.	'assisted circulation':ab,ti OR 'ventricular assistance':ab,ti	888
19.	'circulation assistance':ab,ti OR 'circulation support':ab,ti	45
20.	'circulatory support':ab,ti OR 'heart ventricle assistance':ab,ti	1709
21.	'biventricular pacing':ab,ti OR icd:ab,ti OR icds:ab,ti OR crt:ab,ti	16782
22.	'cardiac resynchronization':ab,ti OR 'cardiac resynchronisation':ab,ti	1478
23.	'ventricular resynchronisation':ab,ti OR 'ventricular resynchronization':ab,ti	78
24.	'implantable *1 defibrillator':ab,ti OR 'implantable *1 defibrillators':ab,ti	5368
25.	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	50129
26.	#13 OR #25	67105
27.	'patient monitoring'/exp	75574
28.	monitoring'/de	38714
29.	'monitor'/de	2606
30.	'personal monitor'/de	315
31.	'personal monitoring'/de	684
32.	'telemetry'/exp	7267
33.	'remote sensing'/exp	1075

	Keywords / search history	Results
34.	'telecardiology'/exp	34
35.	'telemonitoring'/exp	47
36.	'telemedicine'/exp	2029
37.	'teleconsultation'/exp	576
38.	#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37	125566
39.	'patient monitoring':ab,ti OR 'ambulatory monitoring':ab,ti	3176
40.	telemetry:ab,ti OR biotelemetry:ab,ti OR telemedicine:ab,ti	7499
41.	radiotelemetry:ab,ti OR teleradiometry:ab,ti OR telemonitoring:ab,ti	944
42.	radioelectrocardiography:ab,ti OR telecardiography:ab,ti	44
43.	'remote *3 monitoring':ab,ti OR 'long distance monitoring':ab,ti	375
44.	'remote sensing':ab,ti OR telesensing:ab,ti OR 'home monitoring':ab,ti	1995
45.	'tele cardiology':ab,ti OR telecardiology:ab,ti	92
46.	teleconsultation:ab,ti OR 'remote consultation':ab,ti OR 'tele consultation':ab,ti	424
47.	#39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46	13943
48.	#38 OR #47	132373
49.	#26 AND #48	2215
50.	carelink:ab,ti,dn	17
51.	cardiomessenger:ab,ti,dn OR (biotronik:ab,ti,dn AND 'home monitoring':ab,ti,dn)	6
52.	#49 OR #50 OR #51	2226

Table 31 PubMed search results for studies of remote monitoring in the clinical management of patients with implanted cardiac devices (16 November 2007)

	Keywords / search history	Results
1.	"artificial heart"[tiab] OR "heart ventricle prosthesis"[tiab]	2208
2.	"mechanical heart"[tiab] OR "heart assist device"[tiab]	953
3.	"heart pump"[tiab] OR "heart ventricle assist"[tiab]	101
4.	pacemaker*[tiab] OR "heart assist devices"[tiab] OR "heart auxillary"[tiab]	21998
5.	"assisted circulation"[tiab] OR "ventricular assistance"[tiab]	724
6.	"circulation assistance"[tiab] OR "circulation support"[tiab]	36
7.	"circulatory support"[tiab] OR "heart ventricle assistance"[tiab]	1475
8.	"biventricular pacing"[tiab] OR ICD[tiab] OR ICDs[tiab] OR CRT[tiab]	14088
9.	"cardiac resynchronization"[tiab] OR "cardiac resynchronisation"[tiab]	1300
10.	"ventricular resynchronisation"[tiab] OR "ventricular resynchronization"[tiab]	62
11.	implantable[tiab] AND defibrillator*[tiab]	4856
12.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	43404
13.	"patient monitoring"[tiab] OR "ambulatory monitoring"[tiab]	2730
14.	telemetry[tiab] OR biotelemetry[tiab] OR telemedicine[tiab]	6789
15.	radiotelemetry[tiab] OR teleradiometry[tiab] OR telemonitoring[tiab]	930
16.	radioelectrocardiography[tiab] OR telecardiography[tiab]	47
17.	remote[tiab] AND monitoring[tiab]	1134
18.	"long distance monitoring"[tiab] OR "home monitoring"[tiab]	677
19.	"remote sensing"[tiab] OR telesensing [tiab]	999
20.	"tele cardiology"[tiab] OR telecardiology[tiab]	88
21.	teleconsultation[tiab] OR "remote consultation"[tiab] OR "tele consultation"[tiab]	399
22.	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	13000
23.	#12 AND #22	364
24.	"carelink" [tiab]	11
25.	"cardiomessenger" [tiab] OR ("Biotronik" [tiab] AND "home monitoring" [tiab])	3
26.	#23 OR #24 OR #25	374
27.	#23 OR #24 OR #25 Limits: MEDLINE	363
28.	#26 NOT #27	11

Table 32 Cochrane Library search results for studies of remote monitoring in the clinical management of patients with implanted cardiac devices (16 November 2007)

	Keywords / search history	Results
1.	MeSH descriptor Pacemaker, Artificial explode all trees	433
2.	MeSH descriptor Defibrillators, Implantable explode all trees	534
3.	MeSH descriptor Heart, Artificial explode all trees	123
4.	MeSH descriptor Heart-Assist Devices explode all trees	120
5.	MeSH descriptor Cardiac Pacing, Artificial explode all trees	692
6.	MeSH descriptor Assisted Circulation explode all trees	232
7.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	1609
8.	"artificial heart" or "heart ventricle prosthesis"	84
9.	"mechanical heart" or "heart assist device"	59
10.	"heart pump" or "heart ventricle assist"	1
11.	(pacemaker* or "heart assist devices" or "heart auxillary")	1056
12.	"assisted circulation" or "ventricular assistance"	30
13.	"circulation assistance" or "circulation support"	2
14.	"circulatory support" or "heart ventricle assistance"	45
15.	"biventricular pacing" or ICD or ICDs or CRT	1491
16.	"cardiac resynchronization" or "cardiac resynchronisation"	112
17.	"ventricular resynchronisation" or "ventricular resynchronization"	6
18.	"implantable defibrillator" or "implantable defibrillators"	158
19.	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18)	2677
20.	(#7 OR #19)	3175
21.	MeSH descriptor Telemedicine explode all trees	600
22.	MeSH descriptor Electrocardiography, Ambulatory explode all trees	873
23.	MeSH descriptor Telemetry explode all trees	114
24.	MeSH descriptor Monitoring, Ambulatory explode all trees	1711
25.	MeSH descriptor Remote Consultation explode all trees	232
26.	(#21 OR #22 OR #23 OR #24 OR #25)	2369
27.	"patient monitoring" or "ambulatory monitoring"	686
28.	(telemetry or biotelemetry or telemedicine)	804
29.	(radiotelemetry or teleradiometry or telemonitoring)	79
30.	(radioelectrocardiography or telecardiography)	1
31.	"remote monitoring" or "long distance monitoring"	15
32.	"remote sensing" or telesensing or "home monitoring"	127
33.	"tele cardiology" or telecardiology	9
34.	(teleconsultation or "remote consultation" or "tele consultation")	253
35.	(#27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34)	1712
36.	(#26 OR #35)	3285
37.	(#20 AND #36)	120
38.	(carelink)	4
39.	(cardiomessenger or (biotronik and "home monitoring"))	0
40.	(#37 OR #38 OR #39)	124

Table 33 HTA websites searched in this review

Australia	Australian Safety and Efficacy Register of New Interventional Procedures—Surgical (ASERNIP-S) http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/default.htm
	Centre for Clinical Effectiveness, Monash University http://www.med.monash.edu.au/healthservices/cce/evidence
	Health Economics Unit, Monash University http://chpe.buseco.monash.edu.au
Austria	Institute of Technology Assessment / HTA unit http://www.oeaw.ac.at/ita/e1-3.htm
Canada	Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/site/index.php?home
	Institute of Health Economics (IHE) http://www.ihe.ca/index.html
	Canadian Coordinating Office for Health Technology Assessment (CCHOTA) http://www.ccohta.ca/entry_e.html
	Canadian Health Economics Research Association (CHERA/ACRES)—Cabot database http://www.mycabot.ca
	Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org
	Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca
	Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm
	Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca
Denmark	Danish Institute for Health Technology Assessment (DIHTA) http://www.dihta.dk/publikationer/index_uk.asp
	Danish Institute for Health Services Research (DSI) http://www.dsi.dk/engelsk.html
Finland	FINOHTA http://finohta.stakes.fi/EN/index.htm
France	L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES) http://www.anaes.fr/
Germany	German Institute for Medical Documentation and Information (DIMDI) / HTA http://www.dimdi.de/dynamic/en/index.html
The Netherlands	Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/adviezen.php
New Zealand	New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/
Norway	Norwegian Knowledge Centre for the Health Services http://www.kunnskapssenteret.no/index.php?show=38&expand=14,38
Spain	Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III"I/Health Technology Assessment Agency (AETS) http://www.isciii.es/htdocs/en/index.jsp
	Catalan Agency for Health Technology Assessment (CAHTA) http://www.aatrm.net/html/en/Du8/index.html
Sweden	Swedish Council on Technology Assessment in Health Care (SBU) http://www.sbu.se/www/index.asp
	Center for Medical Health Technology Assessment (CMT) http://www.cmt.liu.se/english?l=en
Switzerland	Swiss Network on Health Technology Assessment (SNHTA) http://www.snhta.ch/home/portal.php
United Kingdom	National Health Service Quality Improvement: Scotland (NHS QIS) http://www.nhshealthquality.org/nhsqis/43.0.140.html
	National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.hta.nhsweb.nhs.uk/
	University of York NHS Centre for Reviews and Dissemination (NHS CRD) http://www.york.ac.uk/inst/crd/
	National Institute for Clinical Excellence (NICE) http://www.nice.org.uk/
United States	Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/clinic/techix.htm
	Harvard School of Public Health—Cost-Utility Analysis Registry http://www.tufts-nemc.org/cearegistry/
	US Blue Cross/ Blue Shield Association Technology Evaluation Center http://www.bcbs.com/consumertec/index.html

Appendix G Quality criteria

Study design	Quality checklist
Systematic review	Was the research question specified?
	Was the search strategy documented and adequate?
	Were the inclusion and exclusion criteria specified, appropriate and applied in an unbiased way?
	Was a quality assessment of included studies undertaken?
	Were the methods of the study appraisal reproducible?
	Were the characteristics and results of the individual studies summarised?
	Were the methods for pooling the data appropriate?
	Were sources of heterogeneity explored?
	Was a summary of the main results and precision estimates reported?
Studies evaluating effectiveness of an intervention on health outcomes	
Randomised controlled trial	Were the inclusion and exclusion criteria specified?
	Was the assignment to the treatment groups really random?
	Was the treatment allocation concealed from those responsible for recruiting subjects?
	Was there sufficient description about the distribution of prognostic factors for the treatment and control groups?
	Were the groups comparable at baseline for these factors?
	Were outcome assessors blinded to the treatment allocation?
	Were the care providers blinded?
	Were the subjects blinded?
	Were all randomised participants included in the analysis?
	Was a point estimates and measure of variability reported for the primary outcome?
Cohort study	Were subjects selected prospectively or retrospectively?
	Was the intervention reliably ascertained?
	Was there sufficient description about how the subjects were selected for the new intervention and comparison groups?
	Was there sufficient description about the distribution of prognostic factors for the new intervention and comparison groups? Were the groups comparable for these factors?
	Did the study adequately control for potential confounding factors in the design or analysis?
	Was the measurement of outcomes unbiased (ie blinded to
	treatment group and comparable across groups)?
	Was follow-up long enough for outcomes to occur?
	What proportion of the cohort was followed-up and were there exclusions from the analysis?
	Were drop-out rates and reasons for drop-out similar across intervention and unexposed groups?

Study design	Quality checklist
Case-control study	Was there sufficient description about how subjects were defined and selected for the case and control groups?
	Was the disease state of the cases reliably assessed and validated?
	Were the controls randomly selected from the source of population of the cases?
	Was there sufficient description about the distribution of prognostic factors for the case and control groups? Were the groups comparable for these factors?
	Did the study adequately control for potential confounding factors in the design or analysis?
	Was the new intervention and other exposures assessed in the same way for cases and controls and kept blinded to case/control status?
	How was the response rate defined?
	Were the non-response rates and reasons for non-response the same in both groups?
	Was an appropriate statistical analysis used?
	If matching was used, is it possible that cases and controls were matched on factors related to the intervention that would compromise the analysis due to over-matching?
Case series	Was the study based on a representative sample selected from a relevant population?
	Were the criteria for inclusion and exclusion explicit?
	Did all subjects enter the survey at a similar point in their disease progression?
	Was follow-up long enough for important events to occur?
	Were the techniques used adequately described?
	Were outcomes assessed using objective criteria or was blinding used?
	If comparisons of sub-series were made, was there sufficient description of the series and the distribution of prognostic factors?
Study of diagnostic accuracy	Was the spectrum of patients representative of the patients who will receive the test in practice?
	Were selection criteria clearly described?
	Is the reference standard likely to correctly classify the target condition?
	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?
	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?
	Did patients receive the same reference standard regardless of the index test result?
	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?
	Was the execution of the index test described in sufficient detail to permit replication of the test?
	Was the execution of the reference standard described in sufficient detail to permit its replication?
	Were the index test results interpreted without knowledge of the results of the reference standard?
	Were the reference standard results interpreted without knowledge of the results of the index test?
	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?
	Were uninterpretable/ intermediate test results reported?
	Were withdrawals from the study explained?

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