

OHTAC Recommendation: Internet-Based Device-Assisted Remote Monitoring of Cardiovascular Implantable Electronic Devices

Ontario Health Technology Advisory Committee

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Issue Background

The Ontario Health Technology Advisory Committee (OHTAC) met on January 28, 2011 to review the effectiveness, safety, and cost-effectiveness of Internet-based device-assisted remote monitoring systems (RMSs) for therapeutic cardiac implantable electronic devices (CIEDs) based on an evidence-based review by the Medical Advisory Secretariat (MAS).

Clinical Indication

Sudden cardiac death (SCD) is a major cause of fatalities in developed countries. In Canada each year more than 40,000 people die from a cardiovascular-related cause; approximately half of these deaths are attributable to SCD. Most cases of SCD occur in the general population, typically in those without a known history of heart disease. Most SCDs are caused by cardiac arrhythmia, an abnormal heart rhythm caused by malfunctions of the heart's electrical system. Up to half of patients with significant heart failure (HF) also have advanced conduction or electrical abnormalities.

Cardiac arrhythmias are managed by a variety of drugs, ablative procedures, and therapeutic CIEDs. The range of CIEDs includes pacemakers (PMs), implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT) devices. Bradycardia (slow heartbeat) is the main indication for PMs and increased risk for SCD is an indication for ICDs. Heart failure is also a significant health problem and is the most frequent cause of hospitalization in those over 65 years of age. Patients with moderate to severe HF may also have cardiac arrhythmias, although these may be more likely to be related to heart pump or hemodynamic failure. The presence of HF, however, increases the risk of SCD five-fold, regardless of aetiology. Patients with HF who remain highly symptomatic despite optimal drug therapy are sometimes also treated with CRT devices.

With an increasing prevalence of age-related conditions such as chronic HF and the expanding indications for ICD therapy, the rate of ICD placement has been dramatically increasing. The appropriate indications for ICD placement, as well as the rate of ICD placement, are increasingly an issue. In addition to the increased ICD placement and the up-front device costs, there is the need for life-long follow-up or surveillance, placing a significant burden on patients and device clinics. In 2007, over 1.6 million CIEDs were implanted in Europe and the United States; that translates to over 5.5 million patient encounters per year if the recommended follow-up practices are considered. A safe and effective RMS could potentially improve the efficiency of long-term follow-up of patients and their CIEDs.

The Technology

In addition to being therapeutic devices, CIEDs have extensive diagnostic abilities. All CIEDs can be interrogated and reprogrammed during an in-clinic visit using an inductive programming wand. Remote monitoring (RM) would allow patients to transmit information from their CIEDs from the comfort of their own homes. Currently most ICD devices also have the potential to be remotely monitored. Remote monitoring can be used to check system integrity, to alert on arrhythmic episodes, and to potentially replace in-clinic follow-ups and manage disease remotely. Cardiac implantable electronic devices do not currently have the capability of being reprogrammed remotely, although this feature is being tested in pilot settings.

Internet-based device-assisted RMSs for CIEDs are intended to function as surveillance systems rather than emergency systems. Currently there are 2 general types of RMSs: those that transmit device diagnostic information automatically and without patient assistance to secure Internet-based registry

systems, and those that require patient assistance to transmit information. Both systems employ the use of preprogrammed alerts transmitted either automatically or at regular scheduled intervals to patients and/or physicians.

All Internet-based device-assisted RMSs have common components. The implanted device is equipped with a microantenna that communicates with a small external device (at bedside or wearable) commonly known as the transmitter. Transmitters are able to interrogate programmed parameters and diagnostic data stored in the patients' implant devices. The information transfer to the communicator can occur at preset time intervals, with or without the participation of the patient. The encrypted data are then uploaded to a web-based database registry system on a secure central server. The data processing facilities at the central database, depending on the clinical urgency, can trigger an audible alert for patients or an alert for the physician(s) that can be sent via email, fax, text message, or phone. The details are also posted on the secure website for viewing by the physician (or their delegate) at their convenience.

Regulatory Status

There are currently 4 manufacturers of RMSs in Canada—Medtronic Inc., Biotronic, Boston Scientific Corp., and St Jude Medical Inc.—that have regulatory approval for remote transmitting ICD devices. Remote monitoring systems are proprietary to the manufacturer of the implant device. Remote monitoring systems for one manufacturer's device will not work with another manufacturer's device and RMSs may not be available for all versions of the manufacturers' devices. Further customization of Internet-based device-assisted RMSs also includes details such as the website and application, multiplatform sensors, software algorithms, programming information, and types and methods of alerting patients and/or physicians. The addition of peripherals for monitoring weight and pressure or to communicate with patients through the onsite communicators also varies by manufacturer.

Evidence

The MAS evidence review was performed to review available evidence on Internet-based device-assisted RMSs for CIEDs published until September 2010. The search identified 6 systematic reviews, 7 randomized controlled trials, and 19 reports for 16 cohort studies. The evidence is summarized in the 3 sections below.

1. Effectiveness of Remote Monitoring Systems for CIEDs for Cardiac Arrhythmia and Device Functioning

In total, 15 reports on 13 cohort studies involving investigations with 4 different RMSs for CIEDs in cardiology implant clinics were identified in the review. The 4 RMSs were: Care Link Network® (Medtronic Inc, Minneapolis, MN, USA); Home Monitoring® (Biotronic, Berlin, Germany); House Call 11® (St. Jude Medical Inc., St Pauls, MN, USA); and a manufacturer-independent RMS. Eight of the 15 reports were with the Home Monitoring® RMS (12,949 patients), 3 were with the Care Link Network® RMS (167 patients), 1 was with the House Call 11® RMS (124 patients), and 1 was with a manufacturer-independent RMS (44 patients). All of the studies, except for 2 in the United States (1 with Home Monitoring® and 1 with House Call 11®), were performed in European countries.

The RMSs in the studies were evaluated with different cardiac implant device populations and included ICDs only (6 studies), ICD and CRT devices (3 studies), PM and ICD and CRT devices (4 studies), and PMs only (2 studies). The patient populations were predominately male (range, 52%–87%) in all studies,

with mean ages ranging from 58 to 76 years. One study population was unique in that RMSs were evaluated for ICDs implanted solely for primary prevention in young patients (mean age, 44 years) with Brugada syndrome, which carries an inherited increased genetic risk for sudden heart attack in young adults.

Most of the cohort studies reported on the feasibility of RMSs in clinical settings with limited follow-up. In the short follow-up periods of the studies, the majority of the events reported in follow-up were related to the detection of medical events rather than system configuration or device abnormalities. The results of the studies are summarized below:

- Interrogation of devices on the web platform, both for continuous and scheduled transmissions, was significantly quicker with remote follow-up, both for nurses and physicians.
- Two studies examined the role of RMSs in following ICD leads under regulatory advisory in a European clinical setting and noted:
 - There were fewer inappropriate shocks in the RM group.
 - Urgent in-office interrogations and surgical revisions were performed within 12 days of remote alerts.
 - Lead fractures were not detected at in-office follow-up; all were detected at remote follow-up.
- Quality of life for patients was generally not reported.
- Patient satisfaction was evaluated in 5 cohort studies, all in short-term follow-up: 1 for the Home Monitoring® RMS, 3 for the Care Link® RMS, and 1 for the House Call 11® RMS.
 - Patients reported a sense of security from the transmitter, a good relationship with nurses and physicians, positive implications for their health, and satisfaction with RM and organization of services.
 - Although patients reported that the system was easy to implement, many patients reported the need for assistance of a caregiver for their transmission.
 - The majority of patients would recommend RM to other ICD patients.
 - Patients with hearing or other physical or mental conditions hindering the use of the system were generally excluded from studies, but the frequency of this was not reported.
- Physician satisfaction was evaluated in 3 studies, all with the Care Link® RMS:
 - Physicians reported an ease of use and high satisfaction with a generally short-term use of the RMS.
 - Both nurses and physicians reported a high level of satisfaction with the web registry system.
 - Physicians reported being able to address the problems in unscheduled patient transmissions or physician-initiated transmissions remotely and were able to handle the majority of the troubleshooting calls remotely.

2. Effectiveness of RMSs in Heart Failure Patients for Cardiac Arrhythmia and Heart Failure Episodes

Remote follow-up of HF patients implanted with ICD or CRT devices, generally managed in specialized HF clinics, was evaluated in 3 small cohort studies: 1 involved the Home Monitoring® RMS and 2 involved the Care Link® RMS. In these RMSs, in addition to the standard diagnostic features, the cardiac devices continuously assess other variables such as patient activity, mean heart rate, and heart rate variability. Intra-thoracic impedance, a proxy measure for lung fluid overload, was also measured in the

Care Link® studies. The overall diagnostic performance of these measures cannot be evaluated, as the information was not reported for patients who did not experience intra-thoracic impedance threshold crossings or did not undergo interventions. The trial results involve descriptive information on transmissions, alerts, and management of selected small patient groups experiencing high morbidity and hospitalization in the short study periods.

3. Comparative Effectiveness of Remote Monitoring Systems for CIEDs

Seven randomized controlled trials (RCTs) comparing RMSs with in-office follow-up for CIEDs were identified: 2 were for PMs and 5 were for ICD/CRT devices. Clinical studies performed in the United States involved both the Care Link® RMS and the Home Monitoring® RMS, whereas all studies performed in European countries involved only the Home Monitoring® RMS.

3A. Randomized Controlled Trials of Remote Monitoring Systems for Pacemakers

Two trials, both multicenter RCTs, were conducted in different countries with different pacemaker RMSs and study objectives. The first trial conducted in the United States was designed to examine the ability of Care Link®, an Internet-based remote PM interrogation system, to detect clinically actionable events sooner than the current in-office follow-up supplemented with transtelephonic monitoring transmission, a limited form of remote device interrogation. Event rate detection and median time to detection was significantly faster in the RMS group. The second trial, performed in France, was designed to evaluate the ability of the Home Monitoring® RMS to shorten post-operative hospitalization while preserving the safety of conventional management of longer hospital stays. The mean duration of hospitalization was shorter in the RM group and mean medical reaction time following discharge was faster in the RM group.

3B. Randomized Controlled Trials Evaluating Remote Monitoring Systems for ICD or CRT Devices

The 5 studies evaluating the impact of RMSs with ICD/CRT devices were conducted in the United States and in European countries and involved 2 RMSs, Care Link® and Home Monitoring®. Three of the trials were smaller pilot investigations and 2 trials were large multicenter studies.

Randomized Controlled Trial Pilot Studies

The first of the 3 pilot studies evaluated patient satisfaction, achievement of patient outcomes, and the cost-effectiveness of the Care Link® RMS compared to quarterly in-office device interrogations with 1-year follow-up. Outcomes between the 2 groups were similar at 12-month follow-up.

The second small pilot study examined the impact of RM follow-up with the House Call® RMS on work schedules and cost savings in patients randomized to 2 study arms varying in the degree of remote follow-up. The outcome improvements reported included decreases in device interrogation time, transmission time, time required for data analysis, physician time, and in-clinic wait time.

The third pilot study examined the impact of RM with the Home Monitoring® system, compared to scheduled trimonthly in-clinic visits, on the number of unplanned visits, total costs, health-related quality of life (SF-36), and overall mortality. A reduction in the number of in-office visits in the RM group was reported, with no differences in hospitalizations and overall mortality.

Large Multicenter Randomized Controlled Trials

The first of 2 large multicenter RCTs comparing RMSs with in-office follow-up involved a study conducted at 102 centers in the United States with the Home Monitoring® RMS for ICD devices. The primary objectives of the trial were to determine if remote follow-up could be safely substituted for in-office clinic follow-up, while still enabling earlier physician detection of clinically actionable events. The key outcomes from the trial were as follows:

- Adherence to the protocol follow-up schedule was significantly higher in the RM group ($P < 0.001$).
- The overall mean number of in-clinic and hospital visits was significantly lower in the RM group than in the in-office follow-up group (2.1 per patient-year vs. 3.8 per patient-year, $P < 0.001$), representing a 45% visit reduction at 12 months.
- The median time from onset of first arrhythmia to physician evaluation and the median time to detect *clinically asymptomatic arrhythmia events* were significantly shorter ($P < 0.001$) in the RM group for all arrhythmias.
- System-related problems occurred infrequently in both groups. The adverse event rate (individual and overall) and 12-month cumulative survival were not significantly different between the 2 groups.

The second major multicenter RCT evaluating RM involved the Care Link® RMS for ICD/CRT devices at 133 sites in the United States and followed patients for 15 months. The primary objective of the trial was to determine whether automatically transmitted physician alerts decreased the time from the occurrence of clinically relevant events to medical decisions.

- Of the 575 clinical alerts, 246 did not trigger an automatic physician alert. Transmission failures were related to technical issues such as the alert not being programmed or not being reset and/or a variety of patient-related factors. The overall mean time from the clinically relevant event to the clinical decision was significantly faster by 17.4 days in the RM group ($P < 0.001$).
- Similar low numbers of events involving low battery and of ventricular fibrillation detection/therapy being turned off were noted in both groups. More alerts however were noted for out-of-range lead impedance in the RM group, and the time to detect these critical events was significantly shorter in the RM group (same day vs. 17 days).
- The total number of in-office clinic visits was reduced by 38% in the RM group compared to the in-office group (6.27 visits per patient-year vs. 3.29 visits per patient-year).
- Health care utilization, including cardiovascular-related hospitalizations, emergency department visits, and unscheduled clinic visits, was not significantly higher in the RM group.
- The overall mean length of hospitalization was significantly ($P = 0.002$) shorter for those in the RM group, and was shorter both for patients with ICD and CRT implants.
- The mortality rate was not significantly different between the follow-up groups for ICD or CRT patients.

Conclusion





There is limited clinical trial information on the effectiveness of RMSs for PMs compared to ICD devices. However, for RMSs for ICD devices, multiple cohort studies and 2 large multicenter RCTs demonstrated feasibility and significant reductions for in-office clinic follow-ups in the first year post implantation. The detection rates of clinically significant arrhythmia events (and asymptomatic events) were higher and the time to a clinical decision for these events was significantly shorter in remote follow-up groups than in the in-office follow-up groups. The earlier detection of clinical events in remote follow-up groups, however, was not associated with lower morbidity or mortality rates. The substitution of almost all the first-year in-office clinic follow-ups with RM was also not associated with increased health care utilization such as emergency department visits or hospitalization.

Internet-based device-assisted RMSs involve a new approach to monitoring patients, their disease progression, and their CIEDs. Remote monitoring also has the potential to improve the current post-market surveillance systems of evolving CIEDs and their ongoing hardware and software modifications. However, the broader issues surrounding the infrastructure, impacts on existing clinical care systems, and regulatory issues need to be considered for implementation of Internet-based RMSs in jurisdictions involving different clinical practices. At this point therefore, there is insufficient information to evaluate the overall impact to the health care system, although the improved efficiency of long-term follow-up for physicians and the time saving and convenience to patients associated with a substitution of in-office follow-up by RM is more certain.

Decision Determinants

A decision-making framework has been developed by OHTAC that consists of seven guiding principles for decision making, and a decision-making tool, called the Decision Determinants (DD) tool. The evaluation of the four explicit main criteria (overall clinical benefit, value for money, feasibility of adoption into health system, and consistency with expected societal and ethical values) are reported in using 1 of 4 symbols.

Based on the evidence reported in the MAS review and the deliberations of OHTAC on January 28th, 2011 pertaining to this evidence, OHTAC made the following ratings with respect to the decision determinants criteria:

Internet-Based Device-Assisted Remote Monitoring for Cardiac Implantable Electronic Devices		
Overall clinical benefit		high
Consistency with expected societal and ethical values		moderate
Value for money		moderate/uncertainty
Feasibility of adoption into the health system		moderate/uncertainty

OHTAC Recommendations

In considering the above ratings, OHTAC took into account:

- the high burden of cardiac disease, the critical nature of arrhythmia events being monitored, and the high levels of effectiveness and safety of RMSs;
- the consistency with expected societal and ethical values;
- the moderate uncertainty of the cost-effectiveness due to limited cost information and the absence of economic studies;
- the moderate uncertainty of the feasibility of adoption into the health system.

Therefore, OHTAC made the following recommendations:

1. Based on high quality evidence that Internet-based device-assisted RMSs for ICDs can safely and effectively be substituted for in-office device clinic follow-up care, OHTAC recommends that these RMSs should be increasingly used in patients for whom access to clinic-mediated monitoring presents a problem for geographic or other reasons.
2. Due to the diversity of implementation, broader organizational issues, and lack of information on the real cost of RMSs, their overall impact to the health care system is uncertain. OHTAC therefore also recommends the establishment of an expert panel with a mandate for forward planning on the broader organizational issues that may influence the direction and potential outcomes of RMSs that are being implemented in clinical practices where efficiencies are being sought for long-term surveillance of a growing patient burden.