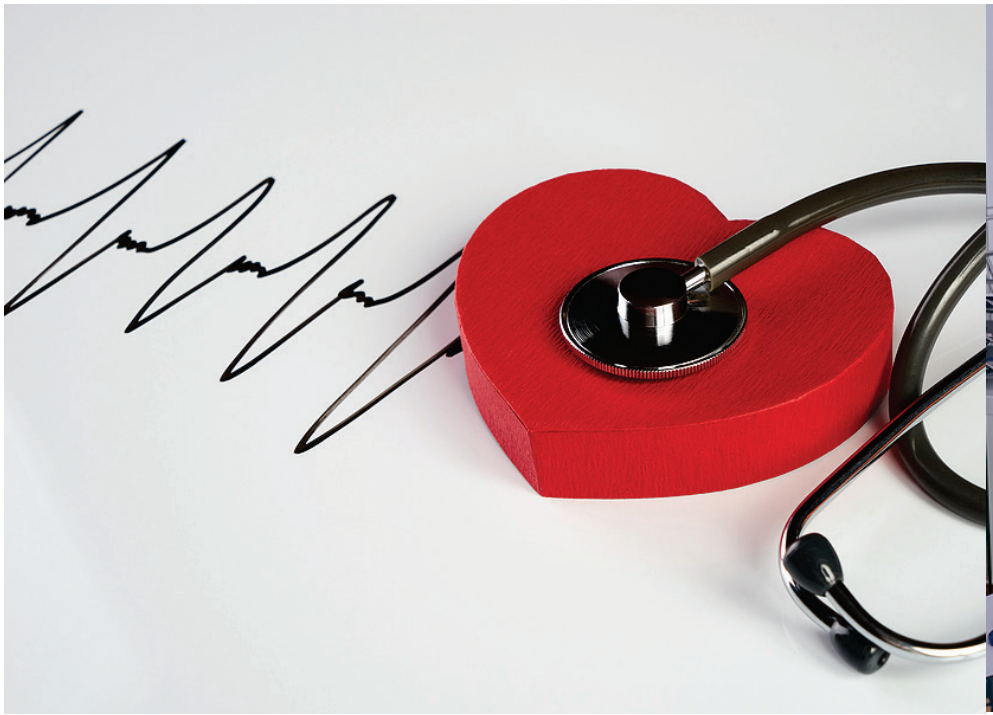
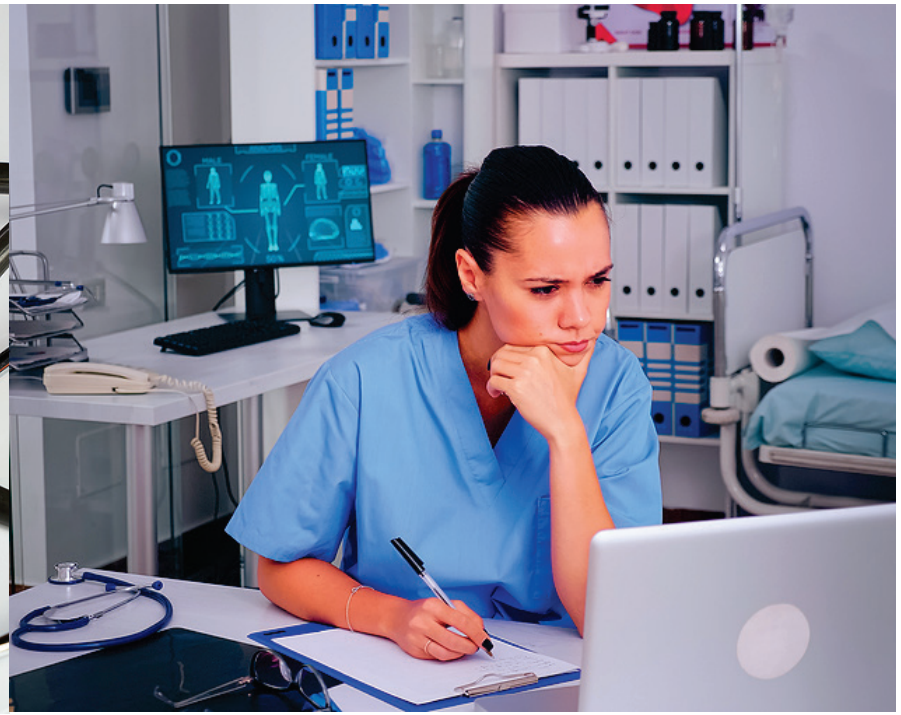
KCE REPORT 345

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

REMOTE MONITORING OF PATIENTS WITH CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES: A HEALTH TECHNOLOGY ASSESSMENT

(UPDATE OF THE KCE REPORT 136)





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SOPHIE GERKENS, DOMINIQUE ROBERFROID, LORENA SAN MIGUEL, NANCY THIRY, CHRIS DE LAET, CÉLINE POUPPEZ

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Disclaimer:

- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
- **Finally, this report has been approved by common assent by the Executive Board.**
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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AF	Atrial Fibrillation
AIMDD	Active Implantable Medical Devices Directive
ADS	Anxiety and Depression Scale
ARS	Regional Health Authorities (‘Autorité Régionale de Santé’– ARS)
AT	Atrial Tachycardia
ATP	Atrial tachycardia pacing
AV node	Atrioventricular node
BeHRA	Belgian Heart Rhythm Association
bpm	beats per minute
CCA	Cost consequences analysis
CDMA	Code-division multiple access
CEA	Cost-effectiveness analyses
CHF	Congestive Heart Failure
CIED	Cardiovascular Implantable Electronic Devices
CMA	Cost-minimisation analyses
CRM	Cardiac Rhythm Management
CRT	Cardiac resynchronisation therapy
CRT-D	Cardiac resynchronization therapy devices with a defibrillator function
CRT-P	Cardiac resynchronization therapy devices with only pacemaker function
CS	Coronary Sinus
CUA	Cost-Utility Analysis
CVA	Cerebrovascular Accident
DBC	Diagnosed-treatment combination (Diagnose Behandeling Combinatie)

DPA	Data Protection Act (Belgium)
DPD	Data Processing Directive (EU)
EBM	Catalogue for outpatient services (Einheitlicher Bewertungsmaßstab)
EPS	Sample of the IMA – AIM database (‘échantillon permanent – permanente steekproef’)
ESC	European Society of Cardiology
ETAPES	Expérimentations de Télémédecine pour l'Amélioration des Parcours en Santé
FAMHP	Federal Agency for Medicinal and Health Products (Belgium)
FDA	Food and Drugs administration (USA)
FFS	Fee-for-service
FPAS	Florida Patient Acceptance Survey
FSCA	Field Safety Corrective Action
FSN	Field Safety Notice
GS-PEQ	Generic Short Patient Experiences Questionnaire
GRPR	General Data Protection Regulation
HAS	Haute Autorité de Santé
HF	Heart failure
HRQoL	Health-Related Quality of Life
HRS	Heart Rhythm Society
HTA	Health Technology Assessment
ICD	Implantable cardioverter-defibrillator
ILR	Implantable Loop Recorder
IQWIG	German Institute for Quality and Efficiency in Health Care (‘Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen’),

IVDR	In vitro Diagnostic Medical Devices Regulation
KCCQ	Kansas City Cardiomyopathy Questionnaire
LPP	List of reimbursed products and services (‘Liste des produits et prestations remboursables’)
MDCG	Medical Devices Coordination Groupe
MDD	Medical Devices Directive
MDR	Medical Devices Regulation (in the context of this study Regulation 2017/745)
MI	Myocardial infarction
MLHFQ	Minnesota Living with Heart Failure Questionnaire
NIHDI	National Institute for Health and Disability Insurance
NIS Directive	European Directive on security of network and information systems
NYHA	New York Heart Association
Nza	Dutch Health Care Authority “Nederlandse Zorgautoriteit”
OPS	German procedure classification (‘Operationen- und Prozedurenschlüssel’)
PBA	Primary attending physician in Germany ('primär behandelnde Arzt/Ärztin')
PIT	Patient initiated transmissions
PM	Pacemaker
RCT	Randomized Clinical Trial
RM	Remote monitoring
SA	Sinoatrial node
SM	Standard monitoring
TMZ	RM Centre in Germany (‘Telemonitoringzentrum’)

SCIENTIFIC REPORT

1 INTRODUCTION

1.1 Rationale

A previous KCE report on the remote monitoring of patients with implanted defibrillators was published in 2010.[1] This report concluded that there was insufficient evidence on relevant clinical benefits for the patient and on the cost-effectiveness of such technology and therefore did not recommend its reimbursement.

Ten years later, many more studies are available and the technology is used in many cardiology centres (see chapter 3), without being reimbursed. The Belgian Federation of the Medical Technology industry (beMedTech) therefore asked for an update of the 2010 KCE report, with an extension to other cardiovascular implants and a reflection on appropriate funding mechanisms.

In addition to this, in 2019, the National Institute for Health and Disability Insurance (NIHDI) announced a reform project of the National Fee Schedule ("*nomenclatuur/nomenclature*"), including adaptations to include new models of care such as telemedicine. NIHDI was therefore also interested by this update. With the COVID-19 pandemic, the need for telemedicine increased and NIHDI asked for this report to be completed as soon as possible so that it could be considered in their work on telemedicine in general and on remote monitoring in particular. In order to be able to respond to this request in a context of limited resources (due to the high number of urgent requests relating to the COVID-19 pandemic), we could not investigate all aspects of a full Health Technology Assessment (HTA) (see section 1.2) and our analysis integrated as much as possible good quality evidence already gathered by other HTA institutions.

1.2 Scope

This HTA concerns the remote monitoring of patients with cardiovascular implantable electronic devices (CIEDs), i.e. implantable cardioverter-defibrillators (ICDs), pacemakers (PMs), and implantable loop recorders (ILRs). Cardiac resynchronization therapy with or without a defibrillator function (CRT-D / CRT-P) are also considered.

This report follows the standard methodology of HTA reports of the KCE (see Box 1). However, in contrast to full HTA reports, ethical issues and social aspects were not addressed, and patient's aspects were only considered in the legal section and in the analysis of foreign experiences. These aspects should therefore be explored more in details at a later stage. Additionally, information on the cost-effectiveness was only searched through a literature review. No economic evaluation in the Belgian setting was performed because of the unavailability of data. Patients with CIEDs that are remotely monitored (RM) cannot be identified from existing Belgian databases and only proxies, questionnaires and assumptions can be used (low level of quality).

It should also be noted that a review of good clinical practice guidelines is usually not part of HTA reports and is therefore out-of-scope.

Box 1 – Standard structure of full HTA reports performed at KCE

- **Health problems and technical characteristics**
- **Current use of the technology**
- **Clinical effectiveness and safety**
- **Cost-effectiveness**
- **(Ethical aspects)**
- **Organisational aspects**
- **(Patient and social aspects)**
- **Legal aspects**

Inspired by the EUnetHTA HTA Core model®

1.3 Study objectives

The aim of this report is to summarize the existing clinical and economic evidence on the remote monitoring of patients with CIEDs, i.e. ICDs, PMs, CRT-P, CRT-D, and ILRs and to investigate reimbursement practices in other countries in order to provide recommendations for a potential reimbursement of these technologies.

The main research questions are:

- What are the technical characteristics of RM systems for CIEDs and what health problems do they address? The aim of chapter 2 is to summarize the technology characteristics, mostly based on information provided by the RM systems providers.
- What is the current use of RM of CIEDs in Belgium? The aim of chapter 3 is also to investigate the adoption and perception of these RM systems by Belgian cardiology centres, mainly based on a short survey.
- What are the clinical benefits and risks of remote monitoring of CIEDs? The aim of chapter 4 is to provide a clear synthesis of the evidence on the clinical effectiveness and safety based on other existing HTA reports, systematic reviews and randomized clinical trials.
- What is the cost-effectiveness of remote monitoring of CIEDs? The aim of the chapter 5 is to provide a clear synthesis of the evidence on the cost-effectiveness based on other existing HTA reports, systematic reviews and economic evaluations.
- Which legal aspects need to be considered? The aim of chapter 6 is to identify the changes in the legal frameworks affecting cardiac remote monitoring since the 2010 report and to discuss the current most debated issues in this sector. Therefore, the focus of this chapter is the impact of the new medical devices' regulations and the new personal data protection rules as well as changes in the Belgian rules applicable to health care delivery.

- What forms of financing are available for health care professionals and for the equipment and services provided by RM systems providers in other countries? What are the quality criteria and other organizational aspects included in the reimbursement conditions? The aim of chapter 7 is to give examples of reimbursement conditions, financing mechanisms and quality criteria based on an international comparison in selected European countries.
- Which models could be considered in Belgium and what may be their budget impact? The aim of chapter 8 is to discuss the impact of the financing models identified in chapter 7 for the Belgian context.

1.4 Terminology

The following terms were used in this report:

- **Patients with a remote monitoring (RM patients):** The monitoring is mainly carried out remotely using RM systems. This monitoring includes scheduled remote data interrogation, remote management of alerts and in-clinic visits. The latter include scheduled in-clinic visits and unscheduled in-clinic visits triggered by a (suspected) event or other needs (MRI, perioperative, etc.).
- **Patients with a standard monitoring (SM patients):** The monitoring is carried out face-to-face, exclusively by means of in-clinic visits. The latter include scheduled in-clinic visits (usually 2-4 per year) and unscheduled in-clinic visits generated by a (suspected) event or other needs (MRI, perioperative, etc.).
- **In-clinic visits:** This term is used to refer to face-to-face visits with the medical specialist in cardiology. These visits usually take place in the hospital but may also take place in another care setting (e.g. visits in an outpatient centre). Although the care setting may vary between countries, the term 'in-clinic visits' was chosen because it is a commonly used term in the literature and it corresponds to Belgian practice. In-clinic visits can either be scheduled or unscheduled (event-driven).
- **Scheduled remote data interrogations:** Implanted devices are 'interrogated' by the remote monitoring system at predefined intervals. The tests and data analysed are similar to those normally performed during in-clinic visits.
- **Alerts:** "Alerts" are sent by the remote monitoring system when a technical (system alert) or a medical (clinical alert) problem is detected.
- **Events :** Two types of events are detected by remote monitoring systems: "system" events related to the integrity and proper functioning of the implant and "clinical" events such atrial tachycardia/atrial fibrillation burden, fast ventricular rates during atrial fibrillation episodes, ventricular fibrillation, ventricular tachycardia, ICD shocks, or signs of heart failure decompensation.

2 HEALTH PROBLEM AND TECHNOLOGY

2.1 Introduction

This chapter describes the health problem and the available technologies for remote monitoring (RM) of cardiovascular implantable electronic devices *(CIED)* in Belgium. It includes implantable cardioverter-defibrillators (ICDs), pacemakers (PMs) including cardiac resynchronization therapy devices (CRTs) with or without a defibrillation function (CRT-Ds and CRT-Ps, respectively), and implantable loop recorders (ILRs) also called implantable cardiac monitors (ICMs). Throughout this report all of these will be referenced as cardiovascular implantable electronic devices (CIEDs).

Traditionally, individuals with those devices implanted have a regular in-clinic follow-up visit, during which the results are analysed and if needed the device is reprogrammed through an inductive programming wand, specific for each manufacturer of CIEDs.

Nowadays, remote monitoring of these devices allows for the transfer of the information stored in the device at regular moments through a network, so that it can be accessed and interpreted by the medical staff through secured websites. This (theoretically) would allow to replace scheduled in-clinic follow-up visits partially by scheduled remote data interrogation. It could also allow for unscheduled follow-up visit in case of remotely detected problems (alerts either cardiac condition or device related) and for patient-initiated transmissions (PITs) in case of health complaints experienced by the patient. Reprogramming at a distance, however, is not permitted as this would potentially endanger patients when the system would be abused (hacked), however for some manufacturers it is available for ILRs since these devices are only passive monitors.

This chapter describes the general context of remote monitoring systems for CIEDs. It also provides a more detailed description on the systems available from several manufacturers on the Belgian market.

Remote monitoring (RM) of ICDs has previously been the subject of a KCE rapport published in 2010.[1] This report is an update including the changes in technology and the changes in the use of this technology that occurred since. Moreover, and apart from ICDs, it now also includes PMs including both the simple (single- or double chamber) PMs but also PMs for cardiac resynchronisation therapy (CRT) with or without additional defibrillation function and ILRs. It should be emphasised that this technology is still evolving rapidly and that the current assessment was made in the spring of 2021.

2.2 Methods

Remote cardiac monitoring relies heavily on the use of information- and communication technology. In the next sections, the main aspects of the technological building blocks enabling remote cardiac monitoring are described. Specific features of the systems provided by different manufacturers are also described.

Conversations during 2020-2021 with physicians and staff of implanting and monitoring centres through face to face meetings[a], with members of the Belgian Heart Rhythm Association (BeHRA), information provided by the RM systems providers through BeMedTech (https://www.bemedtech.be/nl/), analysis of information on the manufacturers' websites, a recent 'Health Quality Ontario' report,[2] and a French report from HAS,[3] formed the basis for the contents of this chapter.

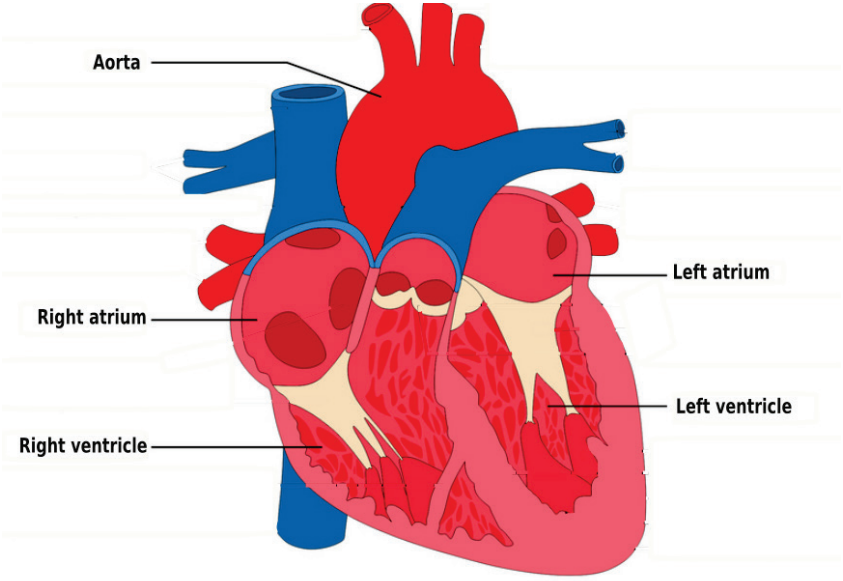
[a] All face to face meetings where in reality screen to screen meetings due to the COVID-19 pandemic in 2020-21.

2.3 Health problem and possible CIED solutions

2.3.1 Normal heart function

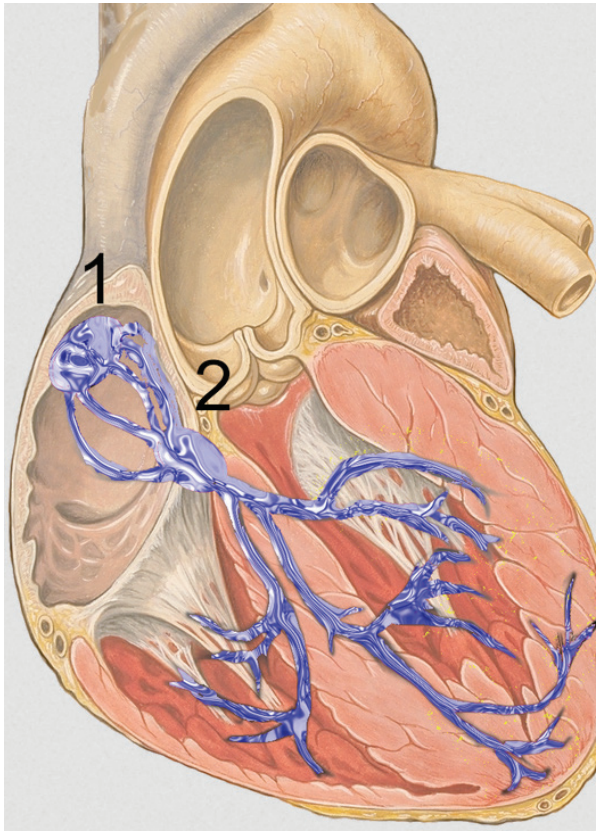
For reference to the normal condition of the heart, a basic diagram of several parts of the heart is provided in Figure 1, while a scheme of the normal electric pacing system of the heart is shown in Figure 2.

Figure 1 – Basic diagram of the heart



Source :Bigstock

Figure 2 – Scheme of the normal electrical conduction system of the heart



1: sinoatrial node (SA) 2: atrioventricular node (AV)
By J. Heuser – self-made, based upon Image: Heart anterior view coronal section.jpg by Patrick J. Lynch (Patrick J. Lynch; illustrator; C. Carl Jaffe; MD; cardiologist Yale University Centre for Advanced Instructional Media), CC BY 2.5, https://commons.wikimedia.org/w/index.php?curid=1686121

Normally, the heart rhythm is regulated by a natural pacemaker, a concentration of pace-making cells in a node located in the right atrium, the so-called sinoatrial node (SA, see Figure 2). The resultant normal rhythm is therefore called the sinus rhythm. The purpose of this natural pacemaker is to maintain an adequate heart rate. Heart rate is the speed of the heartbeat measured by the number of contractions of the heart expressed as beats per minute (bpm). The heart rate can vary according to the body's physical needs, including the need to absorb more oxygen and excrete more carbon dioxide during physical activity, but is also modulated by many other factors including genetics, physical condition, stress or psychological status, diet, drugs, hormonal status, environment, and illnesses as well as the interaction between these factors.

2.3.2 Potential health problems and solutions manageable by the use of CIEDs

2.3.2.1 Arrhythmias

If the SA node does not function properly and is unable to control the heart rate, a group of cells further down the heart electrical circuit can become the ectopic pacemaker of the heart. These cells form the atrioventricular node (AV, see Figure 2) in an area between the left atrium and the right ventricle within the atrial septum, and they can take over the pacemaker function. This rhythm is called an escape rhythm. Chronic occurrence can progress into heart rhythm complications such as tachycardia, bradycardia, or ventricular fibrillation. Another problem that can occur are blocks in the electrical conduction system that again may lead to heart rhythm problems. For some of these problems, medication can help to control it.

2.3.2.2 Heart failure (HF)

Heart failure (HF), also known as congestive heart failure (CHF), is a condition when the heart is unable to sustain adequate blood flow for the body tissues' needs. The symptoms of HF include shortness of breath, excessive tiredness, and leg swelling. Shortness of breath is usually worse with exercise or while lying down. As a result, there is a limited ability to exercise. Signs of angina, however, do not necessarily occur. Causes of heart failure include coronary artery disease, including a previous myocardial infarction (MI) causing scars in the cardiac muscle, hypertension, atrial fibrillation, cardiac valvular problems, but also infection and cardiomyopathy of known or unknown origin.

Treatment depends on the severity and cause of the disease. In people with chronic stable mild heart failure, treatment commonly consists of lifestyle modifications such as stopping smoking, physical exercise and dietary changes, as well as medication. In some cases, cardiac resynchronization therapy (CRT) may be indicated. Heart failure is a common and potentially fatal condition and is an important cause of hospitalization in older adults.

2.3.3 Implantable cardioverter defibrillators (ICDs) including cardiac resynchronisation therapy devices with defibrillation function (CRT-Ds)

An ICD is a battery-powered device placed under the skin of the chest that keeps track of the heart rate and rhythm. It combines a pacemaker with a defibrillation function. In most cases (not with subcutaneous ICD), thin wires with electrodes (leads) connect the ICD to the heart. With subcutaneous ICD, the lead remains outside the heart. If a threatening abnormal heart rhythm (arrhythmia) is detected the device will deliver an electric shock (high voltage) to restore a normal heartbeat if the heart is not pumping anymore (totally chaotic electrical activity called ventricular fibrillation) or is beating extremely fast (very rapid ventricular tachycardia).

ICDs are useful in preventing sudden death in patients with known sustained ventricular fibrillation or tachycardia. Studies have shown that they have a role in preventing death from cardiac arrest in high-risk patients who haven't had but are at risk for life-threatening ventricular arrhythmias.

There are different types of ICDs; single-chamber, double-chamber as well as triple-chamber ICDs, the latter also being referred to as biventricular ICDs or CRT-Ds devices, i.e. cardiac resynchronisation therapy (CRT) combined with a defibrillator function (CRT-D) as opposed to CRT with only pacemaker function (CRT-P, see below).

The main differentiator between all these defibrillator types are the sites in the heart where pacing (low voltage) therapy can be delivered. Single-chamber ICDs can deliver pacing therapy exclusively to the right ventricle (RV), whereas double-chamber ICDs can pace both in the right atrium (RA) and right ventricle (RV). Finally, triple-chamber ICDs, offer pacing therapy in the right atrium (RA), the right ventricle (RV) and the left ventricle (LV). LV-pacing is achieved by either placing a lead intravenously in a tributary of the coronary sinus (CS) vein, by surgically placing an epicardial lead on the outer wall of the left ventricle (LV) or by using a more recent technique consisting in screwing the pacing lead in the high/mid right ventricular septum to capture the conduction system of the heart.

ICDs are externally programmable (after implantation) and allow a medical specialist in cardiology, particularly a cardiac electrophysiologist, to select the optimal settings for individual patients.

2.3.4 Implantable pacemakers (PMs) including cardiac resynchronisation therapy devices without defibrillation function (CRT-Ps)

When intrinsic stimulation fails or is unreliable, either because the heart's natural pacemaker is not functioning properly or because there is a block in the heart's electrical conduction system an artificial pacemaker (PM) can be implanted.

A PM is a battery-powered implantable medical device placed under the skin of the chest (also referred to as implantable pulse generator (IPG)). It keeps track of the heart rate and rhythm. It generates small electrical impulses (low voltage) delivered by a thin wire with an electrode (lead) to cause the heart muscle chambers (the upper, or atria and/or the lower, or ventricles, see Figure 1) to contract and therefore pump blood. By doing so this device replaces the natural pacemaker and regulates the function of the electrical conduction system of the heart (see Figure 2).

Cardiac Resynchronisation Therapy (CRT) is used to treat the symptoms and complications associated with certain types of heart failure. It helps the pumping chambers to beat in a coordinated manner so that the heart works properly. By improving blood flow, CRT may reduce heart failure symptoms, improving patients' quality of life and reducing mortality. CRT is available with pacing function only (CRT-P) or in combination with a defibrillation capability (CRT-D). Recently, a new approach has been developed to ensure synchronicity during ventricular pacing by screwing the pacing lead in the high/mid right ventricular septum to capture the natural conduction system of the heart.

PM are externally programmable (after implantation) and allow a medical specialist in cardiology, particularly a cardiac electrophysiologist, to select the optimal settings for individual patients.

2.3.5 Implantable loop recorders (ILR)

When infrequent heart rhythm problems are suspected, a standard electrocardiogram (ECG or EKG) might not provide a diagnosis. An alternative is a Holter monitor. A Holter monitor[a] is a small, battery-powered external medical device that measures the heart's activity, such as heart rate and rhythm. Holter monitoring is a continuous test to record the heart's rate and rhythm for a short period. It typically records between twelve to 48 hours (sometimes a full week) while the patients continue their normal daily routines (sometimes with exceptions such as not being allowed to swim or to shower because of the recording electrodes). It is a portable, external device with external leads or a directly recording device sticked to the skin in the vicinity of the heart. It records the heart rate, rhythm and potential arrhythmias. However, even this Holter monitor misses some heart rhythm abnormalities when they occur very infrequently.

An implantablebl loop recorder (ILR) is a battery-powered monitoring device like a Holter monitor. An ILR is a heart-monitoring device that records the heart rhythm continuously for up to three to four years (until battery expires). It records the electrical signals of the heart and allows for remote monitoring by way of a small device inserted just beneath the skin of the chest without any need for electrodes to be put in place. It records the heart rhythm continuously for a longer period up to diagnosis. It can capture information that a standard electrocardiogram (ECG or EKG) or Holter monitor misses because some heart rhythm abnormalities occur very infrequently. ILRs are also named Insertable Cardiac Monitor (ICM).

2.3.6 Battery longevity

In recent years an extension of device longevity for ICDs and CRT devices has been obtained through improved battery chemistry and device technology and thereby delivering important clinical benefits (reduced need for device replacements and associated complications), as well as economic benefits, in line with patient preferences and needs.[4] Up to a few years ago, estimated battery longevity was on average around seven years for ICDs and PMs, but more recent studies suggest it has gone up to twelve years for more recent devices. On the contrary, ILR devices, as they only need to be used for a more limited period, mainly have a longevity of around three to four years. Moreover, in Belgium, NIHDI requires a guaranteed battery longevity for ICDs, PMs and ILRs. This guaranteed longevity is depending on the implant and its settings (single, double or triple chambers), varying between 3 to 7 years for ICDs, 6 to 8 years for PMs and being of 2 years for ILRs.

2.4 In-clinic monitoring of CIEDs versus Remote Monitoring (RM)

Reasons to consider remote monitoring

Patients with CIEDs, but also the devices themselves require regular monitoring. Depending on the patient condition and the specific device this requires normally one or more in-clinic visits per year. For some cardiac centres this presents a capacity problem with increasing patient volumes and complexity.

[a] It was first introduced by the American biophysicist Norman J. Holter (1914–1983) in the 1940s. The first commercial Holter monitor was developed by Holter Research Laboratory in Montana (USA). The first Holter monitor became available in 1962. It allowed home ECG monitoring of patients with suspected cardiac arrhythmias. The original Holter monitor was a heavy backpack with a reel-to-reel FM tape recorder, analogue patient interface electronics, and large batteries. It could record a single ECG lead for several hours and provided the first opportunity to record and analyse ambulatory ECG data outside a standard hospital or outpatient care setting.

[b] Actually, not really implanted but a subcutaneous insertion.

Therefore, many of these centres embrace a RM approach for suitable patients. Using this approach, selected patients can be monitored from a distance replacing some of the scheduled in-clinic visits by scheduled remote data interrogation which is in principle less time-consuming.

Moreover, there might be benefits (and potential harms) for the patient (see chapter 4 on efficacy and safety).

Given the current financing of RM of CIEDs (quod non in Belgium), there are important hurdles because cardiac centres need to invest in organisation and personnel to deliver these remote monitoring services.

2.5 Technical characteristics of RM systems

2.5.1 Trans Telephonic Monitoring: an early precursor of current remote monitoring

The earliest emanation of remote monitoring was the concept of Trans Telephonic Monitoring (TTM), introduced in the USA in the early 1970s.[5-8] The system consisted basically of extending the cable of the inductive programming wand over an analogue telephone line. At first, this allowed the pacemaker battery of remote patients to be checked remotely. In subsequent decades this concept gradually evolved offering more advanced device and lead system checking, including real-time basic intracardiac electrogram and even reprogramming and pacing threshold testing. TTM was not or only scarcely adopted in Europe but it was widely employed across North America. The major drawbacks of TTM are the need for patient compliance and the absence of device-initiated transmission triggered by events. Remote monitoring overcomes these deficiencies by offering both scheduled monitoring and device-initiated communication. However, TTM allowed for device reprogramming, which is currently not permitted by remote monitoring, mainly for security reasons.

2.5.2 Common features of the available remote monitoring systems

2.5.2.1 Devices

First the patient needs to be implanted with a **CIED with RM capabilities** and those capabilities have to be switched-on. When within range, the implanted device communicates on predefined intervals and/or in case of an event (manufacturer-specific, see below), with the patient's bedside or portable **transmitter** (see overview scheme in Figure 3). Once the transmitter has successfully interrogated the implanted device, the data is transmitted over the cellular (or other) network to a **manufacturer-specific secured datacentre**. This datacentre works as a post-office, transmitting the data to the **cardiac monitoring centre** through a secured web application and/or through other means such as a text messaging in case of alerts. Only basic data interpretation occurs at the datacentre level, including the detection of alerts, and the full data set is reformatted for presentation through a web application.

This application may also help with the organisation of the workflow at the follow-up centre, for example, by prioritising alerts through a triage system. The technicians and physicians can also be alerted about specific urgent events by e-mail, text messaging or voicemail. The nature of events triggering alerts can be customised. The implementation of the systems differs slightly from one manufacturer to another and will be described in more detail below. The websites are also manufacturer specific and the programming of the CIED at the clinic still relies on **manufacturer specific programming devices**.

2.5.2.2 *Communication*

Information from the **CIED to the transmitter** occurs using radio frequency signals (RF), using the unique device identification number, in encrypted format, and over the Medical Implant Communication System (MICS)[a] frequency band.

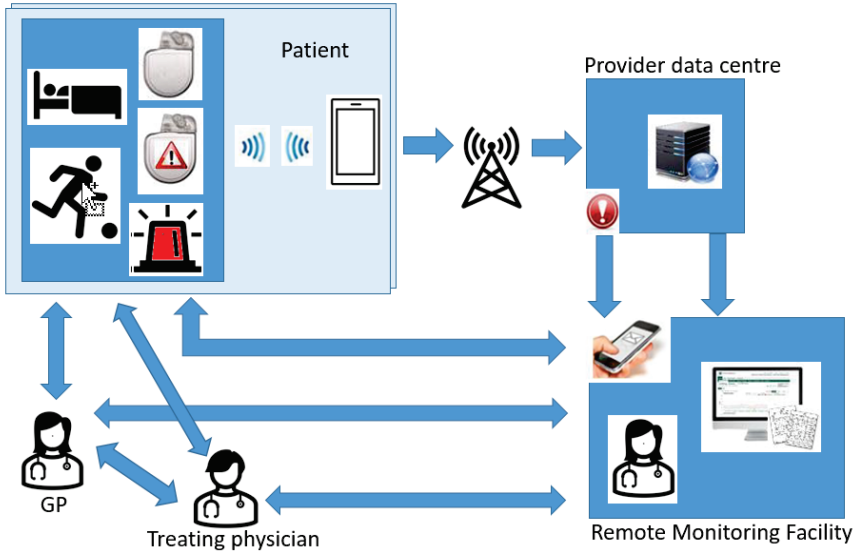
The **transmitter communicates with the datacentre** using the cellular (or other) network in an encrypted format, again using the unique device identification number.

Information from the **datacentre to the technicians and physicians** responsible for the follow-up of specific patients (identified through the unique device identification number) occurs through web-based applications with encryption (HTTPS)[b].

None of the systems (apart from some ILR devices) offer remote reprogramming of the device although during discussions with the RM systems providers, it was indicated that their current technology platform could technically allow for this. This feature is not introduced for both safety (cybersecurity) and liability reasons. Changing the settings of the implanted device can only occur during a patient in-clinic visit and using a **manufacturer specific programmer device**. Communication between the programmer and the implanted device takes place through telemetry through an inductive programming wand or using RF signals. However, some ILR devices do offer the capability of remote programming as these are only monitoring devices without an active impact on the patient.

All providers give extreme attention to data security (both for transmission and storage) and declare, in the European Union, to be General Data Protection Regulation (GDPR) compliant.

Figure 3 – General scheme of the components of a remote monitoring communication system



[a] The Medical Implant Communication System (MICS) is a low-power, short-range (2-3 m), high-data-rate, 401–406 MHz (the core band is 402–405 MHz) communication system that has been accepted worldwide for transmitting data to support the diagnostic or therapeutic functions associated with medical implanted devices.

[b] Hypertext Transfer Protocol Secure (HTTPS) is an extension of the Hypertext Transfer Protocol (HTTP). It is used for secure communication over a computer network and is widely used on the Internet. With HTTPS, the communication protocol is encrypted using Transport Layer Security (TLS) or, formerly, Secure Sockets Layer (SSL).

2.5.3 Functions of a RM system and concerned actors

2.5.3.1 System integrity alerts

One of the earliest applications of remote monitoring for CIEDs was to check device and lead system integrity. Although some CIEDs can give audible or vibration alerts to warn the patient, regular patient-initiated transmissions or scheduled remote monitoring could provide added value, especially in deciding whether an in-clinic visit is required. Device and lead system data is regularly automatically acquired by the device and send using the bedside transmitter to the datacentre where it is forwarded to the responsible physicians.

Most current devices automatically execute periodic system tests that are similar with those that are normally performed during an in-clinic follow-up visit. This includes tests for battery status, lead impedances, sensing and pacing capture thresholds. Additionally, operational mode of the CIED (monitor & therapy, monitor only, electrocautery safe or off) is also reported upon.

Most remote monitoring systems offer the ability to send system integrity alerts almost as soon as they occur, i.e. as soon as the patient is in the immediate vicinity of the bedside or portable transmitter. Thresholds for these alerts are, depending on the manufacturer, either pre-set at in-clinic follow-up or configurable from the web application. Differently coloured alerts allow for a triage of the alerts arriving at the physician's office. When combined with ad hoc system integrity alerts, remote monitoring may reduce in many instances the time to respond to system faults.

2.5.3.2 Arrhythmic episode alerts

In case of defibrillation devices, the remote reporting and alerting of arrhythmia alerts happens in a similar fashion as described for system integrity reports and alerts. The only difference is that intracardiac electrograms (IEGMs) recorded over the duration of the arrhythmic episodes are also transmitted to the datacentre and made available to the physician for interpretation.

Remote monitoring may pre-emptively warn about inappropriate episode detections that resulted in inappropriate shocks. Common causes for inappropriate ICD therapy are oversensing, T-wave sensing, far-field sensing, the sensing of myopotentials, and the wrong classification and detection of a supraventricular tachycardia (SVT). If this is the case, the device will be reprogrammed with the intent to reduce the risk of future inappropriate shocks.

As with device integrity alerts and depending upon the manufacturer, arrhythmic episode alert triggers can be either pre-set at a previous in-clinic follow-up or can be configurable from the web application. Differently coloured alerts allow for the triage of alerts arriving at the physician's office. In many instances, ad hoc arrhythmic episode alerts may significantly reduce the time to respond to actionable events requiring reprogramming of the device or adaptation of medication. This could possibly lead to fewer hospital admissions for these patients.

2.5.3.3 Device interrogation and reprogramming

All CIEDs can be interrogated and reprogrammed by placing a manufacturer-specific inductive programming wand on the skin of the patient over the site where the device is implanted. This inductive programming wand connects to a proprietary designed computer called '*the programmer*' that allows visualisation, printing and storage of the interrogated data and programming parameters.

Later radiofrequency enabled CIED became available, incorporating a small RF antenna in their connector block, also known as the header. This RF transmission can also be used to interrogate and program the CIED (in-clinic). This circumvented the problem of keeping an inductive programming wand sterile during the implantation procedure. There are small differences in remote monitoring and programming capabilities between the systems offered by different manufacturers and these are discussed further in this chapter.

2.5.3.4 *Replacement of in-clinic follow-up visits by remote data interrogation*

Routine out of in-clinic follow-up evaluations for CIED patients (hereafter called 'in-clinic visits') are scheduled every 3 to 6 months. More frequent visits are also due shortly after implantation and towards the end of battery life. Also, when there are manufacturer warnings *('recalls')* it might be important to use RM for continuously checking device parameters, for example battery life. The frequency of this follow-up is obviously very dependent on the patient condition and the underlying pathology.

Provided the patient is in a stable clinical condition, there often is no need for the patient to be physically present, i.e. no physical examination, no hospitalisation or CIED reprogramming is required. It is therefore argued that some of these in-clinic visits could be replaced by remote monitoring at regular intervals (hereafter called scheduled remote data interrogations).

2.5.3.5 *Remote disease management*

Remote monitoring of CIED can also be used to monitor underlying diseases and comorbidities remotely, including risk of cerebrovascular incidents (CVA) caused by emboli, and congestive heart failure (CHF). These possibilities are largely dependent on the type of implanted device and the possibilities offered by the manufacturer and the remote monitoring services provider.

2.5.3.6 *Requirements for a well-performing RM system*

Apart from the devices, the software, and the transmissions many other elements are needed for a well performing and secure remote monitoring system. The *'Haute Authority de Santé'* listed them in 2017 as: [3]

- Automatic data transmissions to the transmitter at scheduled dates and intervals
- Automatic data transmissions to the transmitter in case of a clinical or system alerts
- Patient initiated transmissions to the transmitter in case of clinical symptoms
- Automatic data transmissions to the transmitter of the data in memory
- Automatic data transmission from the transmitter to the provider datacentre
- Taking care of the communication costs from the transmitter to the provider datacentre
- The transmitted data should be equal to those seen with the device specific programmer during an in-clinic visit
- Personal health data storage should be secured and compliant with the relevant legislations in all concerned countries
- Access to these data needs to be secured and should be possible at all moments (7/24)
- Provision and maintenance of the data consultation interface, related software and applications
- The provision of data export capabilities in an interoperable format towards other health information systems
- A direct alerting systems in case of clinical or system alerts within 24 hours of the event

- Provision to the patient of all needed devices and connections for the data transmission towards the provider data centre
- Provision of technical assistant to patients, and formal and informal caregivers on working days
- Recovery of the devices and connections afterwards
- Initial and continued practical and theoretical training of concerned health care professionals
- Provision of technical assistance to health care professionals
- Provision of written technical documentation on all aspects of functioning and maintenance of the system

2.5.4 *Manufacturers active in Belgium*

At this moment there are five CIED providers that provide options of RM.[a]

- Abbott® (formerly St Jude Medical) with the Merlin@home™ system (www.abbott.com and www.sjm.com/merlin).
- Biotronik® with the Home Monitoring® system (www.biotronik.com).
- Boston Scientific® with the Latitude® system (www.bostonscientific.com).
- Medtronic® with the CareLink® system (www.medtronic.com).
- Microport® (formerly LivaNova) with the Smartview™ system (www.livanova.com).

The first four providers were already active in Belgium at the moment of writing the previous KCE rapport published in 2010.[1]. Microport is a new player in this game but currently with a low market share in Belgium (see current use section).

The five providers provide several CIED's. There are subtle differences in their capabilities and the choice for a specific brand is mostly made by the implanting physician based on their knowledge of both their patient and the specific technology required.

Also concerning RM of these devices there are subtle differences in the capabilities, but they are out of scope for this Heath Technology Assessment of the performance of RM systems. The most important aspects of those different systems are summarized in Table 1.

[a] From here onwards we will omit the trademark™ and registered trademark® symbols for ease of reading.

Table 1 – Overview of the main characteristics for different providers of RM

Manufacturer	Biotronik®	Medtronic®	Abbott® (formerly St Jude Medical)	Boston Scientific®	Microport® (formerly LivaNova)
Brand Name of RM system	Home Monitoring®	CareLink®	Merlin@home™	Latitude®	Smartview™
Home transmitter (pictures only used for illustration purposes, not all CIEDs work with all types of transmitters)					
Transmitter	Fixed or mobile	Fixed (transportable)	Fixed (transportable)	Fixed (transportable)	Fixed (transportable)
Data transmission	Cellular or landline	Cellular or WIFI	Cellular	Cellular	Cellular
Communication range	2 meter	3 meter	unknown	3 meter	3 meter
Power	Mains or battery	Mains	Mains	Mains	Mains
Compatible CIEDs	ICD (including CRT-D), PM (including CRT-P), ILR	ICD, PM, ILR	ICD, PM, ILR (via a mobile phone)	ICD, PM, scale, BP metre	ICD
Legal status	Processor of stored data: data centre / Controller of stored data: responsible physician	Processor of stored data: data centre / Controller of stored data: responsible physician	Processor of stored data: data centre / Controller of stored data: responsible physician	Processor of stored data: data centre / Controller of stored data: responsible physician	Processor of stored data: data centre / Controller of stored data: responsible physician
CE marking	Yes	Yes	Yes	Yes	Yes
GDPR compliant	Yes, self declared	Yes, self declared	Yes, self declared	Yes, self declared	Yes, self declared
Wireless communication between CIED and transmitter	Radiofrequency	Radiofrequency (some of the devices have Bluetooth® capability)	Radiofrequency	Radiofrequency	Radiofrequency
Frequency of regular data transmission	Automatically sent from CIED to monitor / PIT / Data sent daily to provider data centre and available for physicians reponsable for follow-up.	Programmable initiated by transmitter	Programmable initiated by CIED	Programmable initiated by transmitter	Programmable initiated by transmitter
Frequency of alerts transmission	Immediately when red alert (if patient is near the tranmitter) Daily for other alerts	Daily interrogation			
Patient Initiated Transmission (PIT)					
Notification of alerts to physician	fax, phone, email and through secure website	fax, phone, email and through secure website	fax, phone, email and through secure website	fax, phone, email and through secure website	fax, phone, email and through secure website
Remote alert setting by physician	Yes				
Additional features	IEGM-Online HD® (High Definition)	HF triage through Optivol feature allowing to calculate a HF risk score			
Reprogramming of CIED through RM	No	No	No	No	No
Company website for additional information	www.biotronik.com	www.medtronic.com	www.abbott.com	www.bostonscientific.com	www.microport.com

Source: This table is based on the best available knowledge from the 'Health Quality Ontario' report,[2] and a French report from HAS,[3] with additional information from manufactures and data available on the companies' websites.

2.6 Discussion and limitations

In practice, it is the implanting physician who decides on the type of device that will be implanted depending on the patient's needs and his/her best judgement. It is also at that moment, or sometimes later, that it will be decided in mutual consent by patient and physician whether RM will be used. Therefore, many cardiac centres involved in RM allow for the monitoring of different brands since they can also be responsible for the follow-up of patients with CIED implanted in other centres. They do this mainly by using the manufacturer provided web application or rarely by an in-house developed monitoring application encompassing multiple platforms. This latter can also be provided by a third-party company such as Fysicon (DataLinQ®) or Lindacare (OnePulse®).

The different available systems are quite similar in their basic setup. However, a more detailed comparison reveals that each of the different systems, through the subtle interplay of differences in hardware and software, can be somewhat different. However, a comparison of the different systems is not the scope of this report.

3 CURRENT USE OF REMOTE MONITORING

This chapter aims to describe the current use of remote monitoring of patients with CIEDs in Belgium.

3.1 Introduction

Difficulties to estimate current use of RM for CIED implants

In Belgium, no reimbursement for RM is currently provided. Cardiac centres must finance themselves the personnel needed to provide for remote monitoring capability. Neither hospitals, physicians nor RM systems' providers receive any specific fee for the service of remotely monitoring data nor for performing remote follow-ups. The obvious consequence is that no official data are available on current use.

For more information on financing and reimbursement we refer the reader to section 8.2.

3.2 Methods

Since use of RM is currently not registered, we needed to use data from different data sources provided by NIHDI, the permanent sample (EPS), BeMedTech and data obtained through conversations with selected cardiac centres.

To complement this lack of information and to obtain additional data on numbers of follow-up, effect on workload, advantages experienced and barriers encountered, we additionally performed a survey among those centres who concluded a NIHDI agreement (convention) for ICD implantation, knowing that those centres do not perform the follow-up of all

patients with a CIED[a,b] Therefore, this sample is biased. We invited those 23 centres to contribute to the survey and we received responses from 19 of them. However, two of those questionnaires were incomplete and not usable for the quantitative analysis. Therefore, the quantitative analysis is based on only 17 answers. Although this is a reasonable participation rate for this kind of survey, we need to mention that the centres missing in the quantitative analysis also included some large centres.

Although the data are therefore incomplete and probably biased, they provide an indication of the current main tendencies of use, and of the barriers and facilitators for its use in Belgium. Please note that the numbers provided are often estimates. Limited number of observations, missing data and uncertainties prevent us to go beyond purely descriptive statistics.

The detailed questionnaires (Dutch and French) can be found in the appendix.

Below we give a brief description of the data while the full data can be found in the appendix.

3.3 Yearly number of CIED implantations

From the approximately 15 000 yearly implantations of CIEDs in Belgium, over 15% are ICDs, over 70% are PMs and over 10% are ILRs but data from NIHDI and BeMedTech differ slightly, see in appendix for comparison. The number of implanted ILRs is steadily increasing in recent years (see Table 4 and Table 5 in appendix).

3.4 Yearly number of patients followed-up and mean number of in-clinic follow-up visits per year

For the total number of patients with CIEDs followed-up, we relied on the data from NIHDI. We assessed them in two different ways: global numbers from NIHDI per year, and the extrapolated numbers of the so-called permanent sample (Echantillon Permanent – Permante Steekproef, EPS) which gives more granular information but requires extrapolation since it is only a sample. We shortly present in text the data for 2019 and the full data can be found in the appendix (see Table 6 to Table 8 in appendix).

3.4.1 Overall numbers from NIHDI

Reimbursed services in Belgium are listed in a national fee schedule, called the nomenclature[c], and are associated with a nomenclature code. For most services, there is two codes according to the setting, i.e. a code for hospitalized patients and a code for ambulatory patients.

There are 2x3 specific nomenclature codes for the control of patients with CIEDs. These codes were used to estimate the number of patients monitored and the mean number of in-clinic visits[d] per CIED type (see Table 2). More detailed information on these codes can be found in the appendix with their full description in Dutch and French. For ILR follow-up control, there is no specific nomenclature code, and this is mainly considered a normal cardiology consultation. Therefore, specific data for ILRs follow-up are not included in these numbers.

In 2019, 89 048 patients with CIEDs were monitored, i.e. they had at least one in-clinic visit for the control of their implant (see Table 2). This number includes only patients with PMs and ICDs, since there is no specific code for ILR follow-up (considered as a normal consultation with a medical specialist

a https://www.inami.fgov.be/SiteCollectionDocuments/liste_centre_defibrilateurs_cardiaques_implantables_lijst_centra_implanteerbare_hartdefibrillator.pdf

b https://www.riziv.fgov.be/nl/professionals/verzorgingsinstellingen/revalidatiecentra/Paginas/default.aspx

c Except services covered by other mechanisms such as NIHDI conventions

d As explained in chapter 1, the term “in-clinic visit” is used for both hospitalized and ambulatory patients

in cardiology). From NIHID data, it is also not possible to have the share of patients under remote monitoring.

It is also important to note that the total number of monitored patients does not correspond to the sum per type of CIEDs because some patients were controlled for different CIEDs (either due to a change of device or to a wrong code used[a]). The mean number of in-clinic visit per patient per type of device reported in Table 2 must therefore be used with caution.

More data are shown in Table 6 in appendix.

Table 2 – Number of patients monitored and mean number of in-clinic follow-up visits per patient based on NIHDI data in 2019 (latest year available)

	Number of monitored patients	Number of in-clinic visits*	Mean number of in-clinic visits per patient*
Single chamber PM	14 634	22 492	1.54
Double chamber PM or CRT-P	63 291	110 928	1.75
ICD, including CRT-D	16 347	34 124	2.09
Total	89 048	167 544	1.88

*Source: Personal communication of NIHDI, Xavier Van Aubel (Number of patients monitored) and Doc N provided by NIHDI (Number of in-clinic visits). *As explained in chapter 1, the term "in-clinic visit" is used for both hospitalized and ambulatory patients.*

3.4.2 EPS data

IMA–AIM is a non-profit organisation that manages and analyses information on all reimbursements related to the compulsory health insurance, collected by the Belgian sickness funds on all insured citizens. These data cover all reimbursed services (consultations, pharmaceuticals, diagnostic and therapeutic procedures) and some patient socio-demographic characteristics as well as social security related data to the extent they influence reimbursement.

IMA–AIM composes and maintains a substantive sample called the Permanent Sample (EPS). The purpose of the EPS is to provide a permanent access to a representative sample of the IMA–AIM data to Belgian federal and federated institutions, conditional on their missions (see also art. 278 of the Program law (I) — 2002-12-24). The EPS is composed of randomly drawn members of the Sickness Funds, stratified by age and gender, approximately 1 in 40 for members younger than 65, and 1 in 20 for members aged 65 and older. The purpose of the larger sample of the 65 years and older is to increase the precision for this group, which has relatively more health expenditures, and in whom the older age groups would otherwise become too small. The sample is longitudinal and contains data since 2002. Every year, an additional sampling similar to the original sampling compensates for members lost to follow-up due to decease or other reasons.

EPS data are extrapolated in our analysis, so this is an estimate (see Table 7 in appendix). EPS data allowed us to analyse more in details patients with controls for multiple CIEDs during the year (see in appendix). The mean number of in-clinic visits in these patients was 2.7.

[a] According to an interviewed expert, errors in billing between single chamber PMs, double chamber PMs and CRT-Ps, or ICDs (including CRT-Ds) can be done by ticking the wrong box or because it is sometimes unclear what can be billed for a double chamber device that is programmed in VVI. Multiple codes can also be due to an upgrade from one system to another (single chamber PM to double chamber PM or CRT-P; or PM to ICD)

3.5 Number of patients followed-up through RM

There is no accurate data on the proportion of patients followed remotely. Based on the number of patients monitored in 2019 (NIHDI data) and an estimation of the number of patients that are remotely monitored (transmitted to BeMedTech by the RM systems providers), approximately 58% of the patients with ICDs (including CRT-Ds) would be followed remotely, against only 3.5% of patients with PMs (see Table 8 in appendix). Additional estimates based on a survey can also be found in section 3.6.1.

3.6 Results of the survey in a selection of Belgian ICD implanting and monitoring centres

In this survey a total of **36 231 patients** with a CIED were reported to be monitored in the 17 centres who answered this survey. Based on the 2019 number of patients monitored (89 048 – NIHDI data), this survey represents about 38% of patients with ICDs and PMs monitored in Belgium. One advantage of this survey is the inclusion of patients with ILRs (no other data available).

3.6.1 Proportion of patients with a remote monitoring

Overall, around **30%** of these patients are followed with RM. However, there are large differences between the different types of CIED as shown in Table 3. Excluding PMs, rarely followed through RM, the proportion of RM increases to 68% for the other types of CIED in those selected centres.

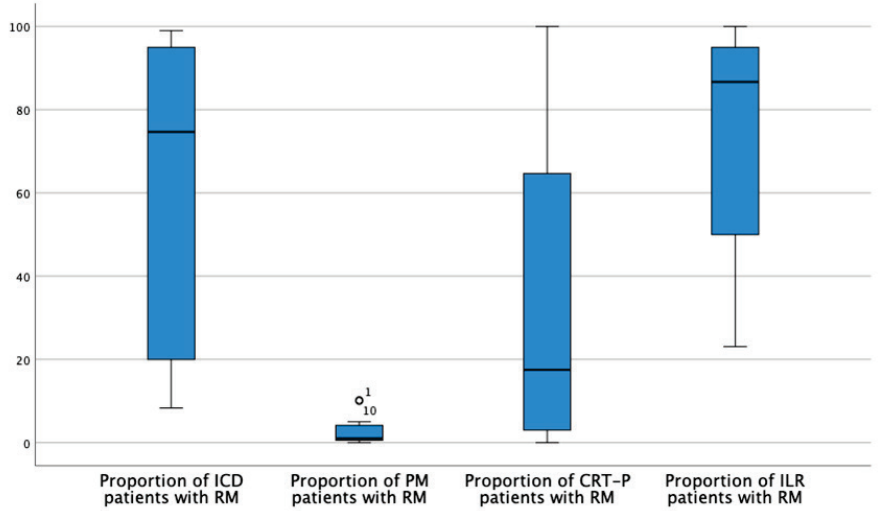
Table 3 – Total number of patients monitored, number monitored through RM and proportion by type of CIED

Type of CIED	Number monitored	Number monitored through RM	Proportion
ICD (including CRT-D)	10 501	7 639	**73%**
PM (single or double chambers)	21 169	708	**3%**
CRT-P	1 972	970	**49%**
ILR	2 589	1 610	**62%**
Total	36 231	10 927	**30%**
Total excluding PM	15 062	10 219	**68%**

The main types of devices followed through RM are ICD and ILR, followed by CRT-P. Simple PM (single or double chamber) are only occasionally followed through RM.

These numbers, however, hide large differences between hospitals although the main tendencies remain valid. The large variation between the 17 hospitals is shown in Figure 4.

Figure 4 – Proportion of patients with remote monitoring (variation between 17 cardiac centres)



The y-axis presents the proportion, the black bar in the middle of each box presents the median, while the blue box represents the distribution from first quartile till third. The whiskers present the minimum and maximum.

3.6.2 Effect of RM on the number of in-clinic visits

The reported number of in-clinic visits does not appear to be fundamentally different with or without RM as shown in Table 4. However, the total number of controls is higher in the RM group when remote interrogations are included.

Table 4 – Yearly number of controls (in-clinic visits and remote data interrogations) per patient with and without RM (RM patients and SM patients)

Type of CIED	In-clinic visits for SM patients	In-clinic visits for RM patients	Scheduled remote data interrogations for RM patients	Total number of controls for RM patients
ICD (including CRT-D)	2.3	1.9	4.9	**6.8**
PM (single or double chambers)	1.9	1.7	3.8	**5.4**
CRT-P	2.2	1.8	3.8	**5.6**
ILR	1.8	1.1	4.5	**5.5**

CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; ILR = Implantable Loop Recorder; PM= Pacemaker; RM = Remote Monitoring (in-clinic visits and remote data interrogations); SM = Standard Monitoring (exclusively based on in-clinic visits).

3.6.3 Number of alerts through RM leading to an in-clinic consultation

Not all RM alerts lead to an in-clinic consultation, but a few do. Yearly estimates for the weighted averages for RM alerts leading to in-clinic consultations per hospital are: 57 for ICD, 3.8 for PM, 16 for CRT and 17 for ILR.

3.6.4 Do you consider RM unsuited for some patients?

In general, there seems to be few objections to put a patient with CIED on RM. Six centres mention that there are no patients for whom RM is unsuited. The other centres mentioned the following reasons:

- Patient related issues: specific objections from the patient, psychic problems such as disorientation, or technical problems (cited 8 times). Arguments mainly mentioned were patient refusal (because they always want to see their own physician, privacy concerns, …), the condition of the patient needing a regular personal follow-up, computer illiteracy or technical problems such as bad cellular network. Also, anxiety induced by continuous confrontation with cardiac disease with transmitter at home or linguistic barriers was mentioned as a reason not to consider RM.
- Many mention that it is not helpful in patients with PM: little benefit and too much additional workload for the hospital. Patients with PM also tend to be older, with often problems of disorientation or dementia (cited twice)

3.6.5 Hurdles for the implementation of RM

The main hurdle is financing. Since there are no reimbursements, hospitals and especially the cardiology departments need to finance it directly. An excerpt of the comments:

> *There is no reimbursement for the additional work (all the participants mentioned this), therefore there is a lack of financing. If reimbursed, the organisation could be different, for example with nurses formed specifically for remote monitoring to do follow-up in a more systematic way. More patients would then be followed;*
>
> *Good organisation is needed to make RM performant; therefore, it requires optimal cooperation between those responsible for follow-up;*
>
> *Occasional technical problems and especially the lack of integration between the different providers and into the electronic health record;*

Legal framework GDPR about the storage of patient data on RM server requiring much paperwork;

Important workload for the daily follow-up of alerts, and somewhat for the initiation of RM after implant;

Cost for hardware and sometimes software for local integration into the electronic patient record;

Lack of sufficiently trained nurses within the hospital, linked to the hospital financing;

Less patient contact;

False alerts due to under- or oversensing;

Big problem is the different platforms and when transmission occurs;

More uniformity would enhance workflow;

Helpdesk from companies are not always working optimally;

Many false alerts, especially with ILRs. Personnel need to filter those out and discuss with the medical specialist;

Different provider platforms so need to invest in software for integration with EPR (middleware solution (Lindacare OnePulse®) at or own expense.

3.6.6 Advantages of RM in practice

Most advantages mentioned are the more rapid response to technical or medical problems, possibly leading to fewer hospital admissions if detect early. An excerpt of the comments:

More rapid response when problems (technical or medical) occur;

Stricter follow up of CIED related problems (batteries, leads);

Patient feels more secure;

Less emergency visits;

Closer follow up of patients with arrhythmia risks without overloading the cardiology consultations;

Early detection of arrhythmias, device problems and signs of decompensation;

Better patient care through faster recognition and treatment of pathology;

Sometimes this leads to fewer visits;

Very interesting, especially in times of a pandemic;

Detection and reduction (after reprogramming) of inappropriate shocks from ICD, for example shock because for atrial fibrillation rather than for ventricular fibrillation or because of technical reasons (lead failures);

To avoid early shock when the duration of fibrillation is limited (less than 10 seconds). Again, can be detected by RM and the device reprogrammed;

To avoid in-clinic visits when there are no problems;

Mainly for ICD and ILR, but, interesting for everyone;

Immediate alerts when problems;

RM of patients in a bad condition allows preventive follow-up and treatment;

Fewer inappropriate shocks for ICD (lead problems or early detection of atrial fibrillation or to avoid inappropriate shocks due to ATP (atrial tachycardia pacing);

Unforeseen battery depletions;

Follow-up with unforeseen problems such as recalls by companies (batteries, leads);

Optimized work flow;

Less mortality & morbidity, associated with less hospital admissions;

Prevention of inappropriate shocks;

Follow-up when device alerts, timely follow-up of atrial fibrillation (antico), monitoring of HF, adaptation of medication;

Win for patient: comfort, safety, trust, early detection and prevention of complications, longer battery time (no need for replacement when nearing end of life because of monitoring);

Win for hospital: optimising time taking care for only patients with problems, prospective planning;

Potential win for payer (see Heidbuchel et al. [9]);

Early detection of worrisome HF;

Early detection of worrisome arrhythmias;

Avoid consultations for ILR when no events occurred.

3.6.7 Providers of RM included

Only a few centres perform RM with all five providers. Most centres perform RM with two or three of the providers, some for four. The main raison is that their systems are incompatible so different platforms are needed.

Most commonly the centres perform RM for at least Biotronik and Medtronic, some for Abbott and/or Boston Scientific. Microport is sometimes mentioned.

3.6.8 Supplementary human resources needed

All respondents agree that supplementary human resources are needed. Some excerpt from the comments:

Yes, for sure, we spend about 3h/day for the management of RM;

Yes: 2 FTE specialised nurses;

Yes, one or two nurses to verify the alerts and take the measures needed. This requires 2 or 3 persons for a continuous service;

Yes: ideally, we would need the additional assistance of specialised nurses;

We do not have additional human resources, but we would need a dedicated person 1 day a week (0,2 FTE);

Yes, during weekdays all alerts and planned interrogations;

No really but personnel cannot perform other tasks in the meanwhile;

Yes of course, minimal 1 FTE but overloaded;

daily 270 to 370 transmissions are scanned daily (planned + alerts). With in-clinic visits the average is 25 patients a day, so with RM we can check many more patients;

Extra personnel needed if we use RM, but currently no reimbursement. When reimbursed time would become available for the in-clinic consultations for the most urgent patients;

Well organised team is needed to maximize the efficiency of RM;

Transition of MD time to paramedics' time;

Ideally, we would need 1 person (nurse or specialised technician) for daily review of transmissions.

They mentioned that the following types of health professionals were implied in the process: specialised nurses, medical specialists in cardiology, ICT staff, and other ('*attaché de recherche*'). In most hospitals RM was performed with the few people that can be freed specifically, and part-time.

3.6.9 Additional cost per patient in RM (for the hospital)

They mentioned an additional cost for the hospital since RM is not reimbursed. Most often, these costs were budgeted on the cardiology department. Some excerpts from the survey:

Estimate of additional cost of around 150€ per patient;

It is a financial loss: we have to solve the dilemma of providing good care and economically prudent approach;

Done in spare time (kind of voluntary work to care for patients);

Extra expenses payed from the cardiologist's honoraria;

56€ per patient/year (personnel), costs currently covered by honoraria of cardiologists;

Cost need to be covered by honoraria of cardiologists and therefore it is only performed when there is clear added value;

Cost covered by hospital, time et al.

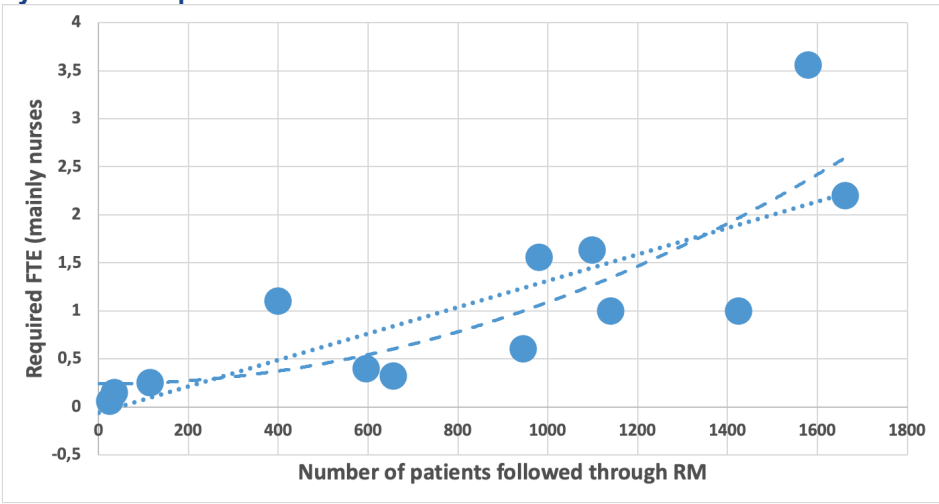
126€ / patient. At this moment the cost is paid by the cardiology department. That is also the reason to keep the in-clinic consultations;

On our own expenses;

It is currently from the cardiology department budget. This is untenable since RM is now standard practice.

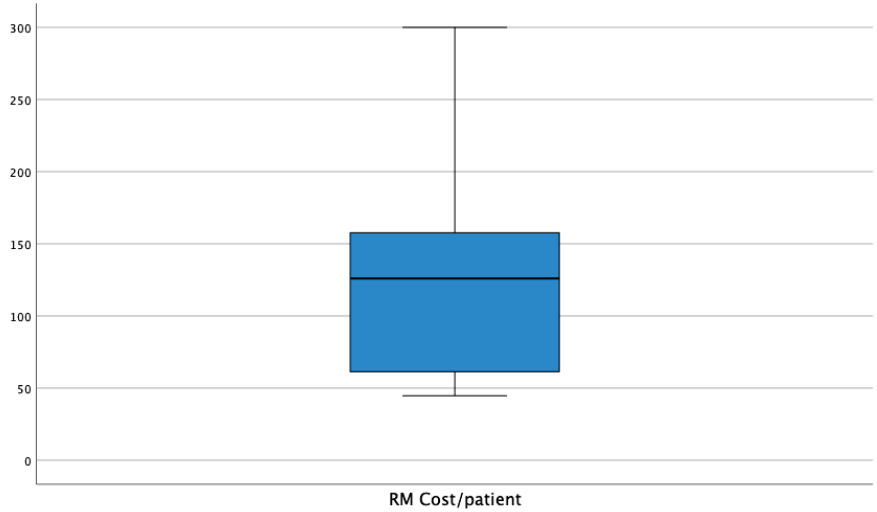
Estimating the additional cost of RM for a hospital, based on the self-reported responses of numbers of FTE needed was difficult. Based on their self-reported numbers of FTE required (see Figure 5) and an average yearly salary of €70 000 for 1 FTE (based on expert opinion), the median additional cost of RM was estimated at around €130. We are totally aware that this is a very rough estimate, but the results are shown in Figure 6.

Figure 5 – Estimates given in the survey for the required FTE for RM by number of patients followed



The straight line is a linear regression, the curve is a polynomial trend line (2nd order)

Figure 6 – Estimates of the yearly price per patient for RM for current FTE involved in the 17 cardiac centres that responded (several missing values and mainly rough estimates)



The y-axis presents the yearly cost (€) for RM, the black bar in the middle of each box presents the median, while the blue box represents the distribution from first quartile till third. The whiskers present the minimum and maximum.

3.6.10 Payments to manufacturers for providing the RM for hospitals and patients

Most centres agree that there is no specific price to be paid to the providers, since it is part of the package. However, this always seems to be part of the negotiations between the hospital and the provider. Some auxiliary costs are sometimes mentioned (e.g. the purchase of a smart phone by the patients or the purchase of software by the centres to allow for the monitoring of multiple brands in a same platform). Some excerpts of the remarks:

> *Included in price of the implant, but sometimes patient need to buy a smartphone for the transmission;*
>
> *Other supplements are possible (surveillance by third party for example, necessity to buy additional soft and hardware for compatibility;*
>
> *None so far but if there would be a public tender it would probably need to be negotiated separately;*
>
> *No, it is part of the tender we organise for acquiring the implants;*
>
> *Not to the vendors, included in price of the implant. The business model of providers can be used to incorporate RM in the price of the implants;*
>
> *We need to invest in software (middleware, Lindacare OnePulse) and our own software integration with EPR;*
>
> *No, included in the price of the implant.*

3.6.11 Hospitals not using RM

All cardiac centres replying to this survey use RM but at different degrees (some only managing red alerts), mainly for financial and organisational reasons. They agree that they would do RM for many more patients if a reimbursement for RM activities would be available. Some hospitals offer the option systematically to all patients (except for classic PM, unless problems are foreseen). Other hospitals are more prudent due to the lack of reimbursement and the considerable extra cost for the cardiology department.

3.7 Discussion and limitations

Around 90 000 patients with CIEDs are followed in Belgium but the bulk of them is for regular pacemakers. This chapters showed that while in theory remote monitoring could avoid in-clinic follow-up visits, the effect is currently rather low in Belgium. Moreover, hospitals in Belgium embrace remote monitoring in different ways. Some only following alerts while other trying to do more complete remote follow-up. Additionally, uptake of remote monitoring appears to be more frequent in the large centres. We noticed a big difference between the estimates of the proportion of patients with and without RM between the centres. In the survey of the centres with an ICD agreement, the proportion of patients on RM was substantially higher than overall, which is probably explained by the lack of human resources in the smaller centres.

Despite a high response rate, our survey to Belgian hospitals is nevertheless not exempt of limitations and its results should be carefully considered and interpreted. This is mainly due to the fact that they represent self-reported estimates which could in some cases differ from reality. In addition to this, the survey was drafted for those hospitals that concluded a convention with the NIHDI, while some patients may be followed-up in other hospitals (i.e. responders represent around 38% of all patients with ICDs and PM monitored in Belgium). The response rate amongst these of almost 74% missed some large centres who did not contribute to the survey.

Additionally, although the survey serves its purpose in offering an approximation to the current situation in our country, and highlighting any trends, it is important to note that the level of RM, the frequency of controls, and staff involvement are all factors likely to change if reimbursement becomes available for this type of monitoring.

It is therefore important to read and consider the results from the survey more as a general overview as opposed to taking any figures there presented as real facts.

4 EFFICACY AND SAFETY OF REMOTE MONITORING

4.1 Introduction

In this chapter, we aimed at assessing the clinical efficacy and safety of the remote monitoring of cardiovascular implantable electronic devices (CIED) combined with in-clinic visits, compared with standard monitoring alone. We carried out a systematic review of the literature on Implantable Cardioverter Defibrillator (ICDs), including Cardiac Resynchronization Therapy devices with Defibrillator function (CRT-Ds); Pacemakers (PMs), including Cardiac Resynchronization Therapy devices without defibrillation (CRT-Ps); and Implanted Loop Recorders (ILRs) were the devices considered in our study.

4.2 Methods

4.2.1 Search strategy

Following standard practice at KCE, we followed a two-step process. First, we assessed the availability of good-quality systematic reviews, with the aim of using the most recent one as the possible basis of our own literature review. In September 2020, a preliminary search for Health Technology Assessments (HTA) on the EUnetHTA and the INAHTA websites (see section 5.2.4.1 in review of economic studies) identified two potentially relevant recent systematic reviews. The first one was published in 2018 (search date up to June 2017) by the Health Quality Ontario and focused on ICD, CRT-D, CRT-P, and PM.[2] The second one focused on ILRs and was published in 2021 (bibliography surveillance up to January 2021) by the '*Haute Autorité de Santé*' (HAS).[10] Both reviews were considered good quality based on the AMSTAR 2 criteria[11] (see AMSTAR-2 grids in Appendix 3) and eligible for inclusion in our review. We refer hereafter to Ontario-HTA for the review by the Health Quality Ontario[2] and to HAS-HTA for the review by the HAS.[10]

Second, in early September 2020 we searched for systematic reviews and RCTs on ICDs, CRT-Ds, CRT-Ps, and PMs published since January 2017. Medline (through OVID), EMBASE, CINAHL and the Cochrane Library (Cochrane Reviews and Trials) were screened in September 2020. Search strings can be found in Appendix 4. There were no language restrictions. Reference lists of included articles were also checked for indications of other relevant publications. There was no attempt to update the literature review on ILRs given the very recent publication of the HAS-HTA on the topic (bibliography surveillance up to January 2021).

There was no attempt to extend the search to other study types for retrieving evidence on safety issues. As remote monitoring of CIEDs is principally about data transmission (i.e. no distance-based device setting), early detection of medical and/or technical problems, and replacement of part of in-clinic visits by scheduled remote data interrogations of the device, no significant safety issues were expected. Moreover, there was no obvious reason to assume the possible appearance in the long term of adverse events that would not have been observed during the shorter duration of clinical trials where the main outcomes, besides the number of in-clinic visits, concerned indeed plausible adverse events (e.g. hospitalisation for heart failure).

4.2.2 Selection procedure

Inclusion and exclusion criteria were defined (see Table 5). The references were imported into EndNote®. The screening of references on titles/abstracts to exclude publications obviously not fitting our inclusion criteria was done in Rayyan QCRI®. All articles potentially relevant were read in full, and papers excluded at this stage were listed with reason for exclusion. Study selection was done by one researcher, and any doubtful exclusion was discussed and agreed with a second reviewer.

Table 5 – Inclusion and exclusion criteria for systematic reviews or clinical studies

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Adult patients implanted with ICD, CRT-D, CRT-P, PM or ILR	Any other patient.
Intervention	Remote monitoring (combined with in-clinic visits) of health status and device functioning	Any standard monitoring system only; comparison of different modes of telemonitoring
Comparator	Standard monitoring	
Outcomes	• Hospitalisations (all-cause, heart failure/cardiovascular) • Emergency department visits • Number of in-clinic visits (total, scheduled, and unscheduled) • ICD shocks (total, appropriate, and inappropriate) • Arrhythmias (in pacemaker recipients) • Time from event onset to data review and clinical decision • Worsening of heart failure NYHA functional class • Stroke • Mortality (all-cause and cardiovascular) • Quality of life • Adverse events	Physical activity
Type of publication	Systematic reviews; RCTs	Observational studies, letters, editorials, notes, abstracts

4.2.3 Data extraction

Data extraction was performed by one researcher, and any doubtful information was discussed and clarified with a second reviewer. Quality appraisal was done by using the AMSTAR-2 grid for systematic reviews[11] and the Cochrane Risk of Bias Tool for primary RCTs.[a]

4.2.4 Data analysis

Meta-analyses by the Mantel-Haenszel method were performed when appropriate using Review Manager v. 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). To decide if an update of the meta-analyses presented in the Ontario-HTA[2] was necessary, we applied the Ottawa method[12] as also described in the KCE Process Note on rapid reviews.[b] In brief, qualitative and quantitative signals which may trigger an update of the reference systematic review are screened. Qualitative signals may include finding of a newly published pivotal trial with results opposite to that of the original SR with respect to an efficacy outcome. A trial whose sample size is at least triple that of the largest trial in the original SR may be considered pivotal. A quantitative signal is considered relevant if the incorporation of its evidence into the original meta-analysis changes a statistically non-significant pooled estimate into a statistically one or vice versa.

4.3 Results

4.3.1 Literature search

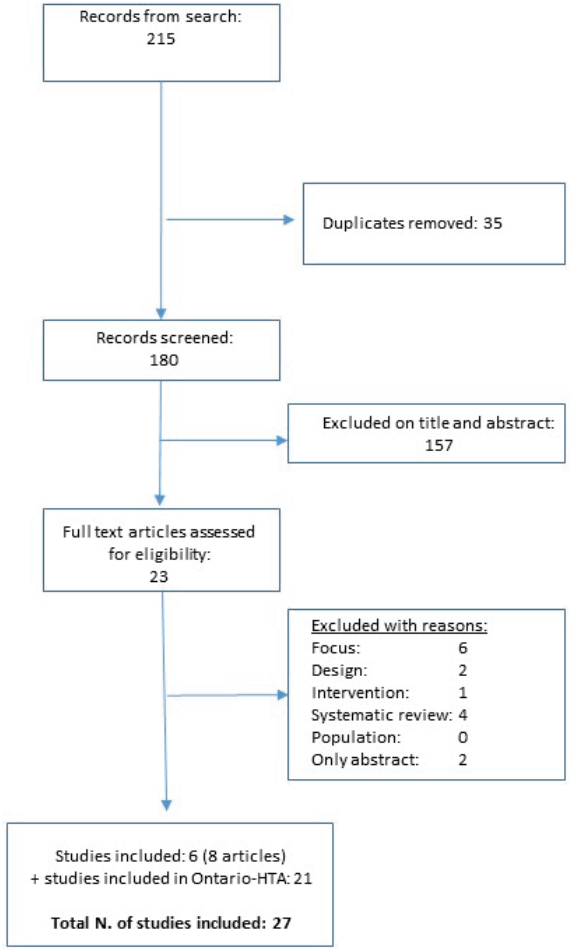
As the chapter on ILRs relies entirely on the very recent HAS-HTA[10] and no additional literature search was done, this section reports uniquely on the results of the literature search on ICDs, CRT-Ds, CRT-Ps and PMs. The search strategy yielded 214 references. An additional systematic review published in October 2020 (i.e. after the date of our search strategy) was retrieved and included.[13] After removal of duplicates (n=35), we screened the title and abstract of 180 publications, out of which 23 references potentially fulfilling our inclusion criteria were assessed on full text.

Five systematic reviews were retrieved[2, 13-16]. Main characteristics of these systematic reviews, as well as RCTs included, are compared in Appendix 5 by order of publication date. The most recent review was published by Jang et al. with a search date up to February 2020.[13] This review mixed implantable cardiac devices and wearable devices, and was limited to measuring atrial arrhythmia detection or incidence of stroke. It was thus discarded. The review by Alotaibi et al. had a search date up to June 2019 and mixed ICDs or CRTs and implanted hemodynamic systems.[14] However, it was not retained because the population was limited to adults with a diagnosis of heart failure and outcomes were limited to all-cause mortality and heart failure-related hospitalization.[14] The search date of the systematic review by Sequeira et al. was close to the one of the Ontario-HTA (February 2018) but did not review RCTs on PMs.[15] The next most recent review was the Ontario-HTA (search date up to November 2017) which was the only one to review ICDs, CRT-Ds, CRT-Ps and PMs.[2] The review from the German Institute for Quality and Efficiency in Health Care (‘*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen’*, -IQWIG) had a search date in August 2017, included only studies with patients suffering advanced cardiac failure, and was only available in German.[16] For these reasons, it was excluded.

a https://handbook-5-1.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm

b https://processbook.kce.fgov.be/sites/default/files/Rapid_Review_2.pdf)

Figure 7 – Flow Diagram of literature search on ICDs, CRT-Ds, CRT-Ps, and PMs



The Ontario-HTA was thus retained as the reference systematic review. For validation purpose, we cross-checked studies included in the Ontario-HTA with those included in the reviews by Jang et al.[13], Sequeira et al.[15] and Alotaibi and al.[14] (see Appendix 5). Only the study by Hansen et al.[17] was a relevant publication listed in the review by Alotaibi and al.[14] and not present in the Ontario-HTA because it was published in 2018. This study was identified during our update of the literature review and included. This analysis confirmed that the Ontario-HTA was a valid systematic literature review.

Among primary RCTs, eleven additional references were removed after assessment of the full text. Specific reasons for exclusion are explained for each study in Appendix 6. Eight publications were finally included in our review.[17-24] Three of them referred to the NORDLAND trial.[18-20], i.e. we included 6 new studies. For clarity reason, when citing the NORDLAND trial we will refer to the study by Lopez-Liria which reported trial outcomes at month 12.[19] Four studies concerned ICDs or CRT-Ds.[17, 22-24] Two studies (4 papers) concerned PMs[18-21]. Characteristics of studies and their quality appraisal are presented in Appendix 7.

Twenty-one studies were included in the Ontario-HTA. With the 6 additional studies of our update the total number amounted to 27 studies (Figure 7).

The literature review on the remote monitoring of loop recorder was based on the very recent systematic review published by the HAS.[10]

4.3.2 *Clinical outcomes of remote vs. standard monitoring of patients with ICDs and CRT-Ds*

The Ontario-HTA included 15 RCTs,[9, 25-39] and our update of the literature brought in 4 more studies.[a 17, 22-24] The studies consisted of open-labelled trials and mostly included patients with indications for either a new implantation or a replacement of an ICD or CRT-D, for either primary or secondary prevention of sudden cardiac death. The duration of follow-up varied between 12 and 42 months. In the remote monitoring group, the frequency of data transmission and review by the clinic staff varied widely, from once a day to once every 6 months.[2] The frequency of scheduled in-clinic visits varied between groups and between studies, and it was generally less frequent in the remote monitoring group than in the standard monitoring group. In most studies, the response to alerts was left to physician's discretion. All studies were at low risk of bias, except the study by Leppert et al. 2020 where an attrition bias was plausible (see Appendix 7 for more details).[23] However, all studies were open-labelled trials and performance and detection bias could occur. Detection bias were unlikely for hard outcomes (e.g. hospitalisation) but plausible for self-assessed outcomes such as quality of life. Main outcomes from studies included in the Ontario-HTA and in our update, and overall are presented in Table 6.

Table 6 – Overview of outcomes of remote vs. standard monitoring of patients with ICDs and CRT-Ds

Outcome		Ontario-HTA 2018			KCE update 2021			All studies	Meta-analysis update
		N° studies	n	**Results**	N° studies	n	**Results**		
1. ICD shocks	**RR (95%CI)**	3[28, 30, 34]	807	**0.84 (0.65;1.10)**	1[17]	210	**1.06 (0.44; 2.56)***	4[17, 28, 30, 34]	**No**
1.a. Appropriate shocks	**RR (95%CI)**	2[28, 34]	631	**0.98 (0.69;1.40)**	0		NA	2[28, 34]	**NA**
1.b. Inappropriate shocks	**RR (95%CI)**	4[28, 30, 34, 39]	958	**0.53 (0.32;0.89)**	0		NA	4[28, 30, 34, 39]	**NA**
2. Stroke	**RR (95%CI)**	2[25, 26]	997	**0.47 (0.17;1.27)**	1[22]	600	**2.01(0.37;10.91)**	3[17, 25, 26]	**0.71 (0.32;1.61)**
3. Hospitalisation for heart failure	**RR (95%CI)**	5[29, 30, 32, 38, 40]	4357	**1.00 (0.91;1.11)**	2[17, 22]	810	**0.78 (0.62;0.96)**	7[17, 22, 29, 30, 32, 38, 40]	**0.94 (0.83; 1.07)**
4. In-clinic visits per patient-year	**HR (95%CI)**	6[b25, 27, 31, 34, 35, 40]		**0.62 (0.57;0.66)**	2[17, 22]	810	No rate ratio provided[c]	8[17, 22, 25, 27, 31, 34, 35, 40]	**No**

a The study by Hansen et al. 2018 (InContact trial) had a specific design where the intervention consisted of remote monitoring with quarterly automated follow-up (n=102) and the comparison group was further randomised in 2 subgroups: remote monitoring with quarterly personal telephone calls and quarterly in-clinic visits only[17]

b There were 10 studies,[9, 25, 27, 28, 31, 32, 34-36, 40] but the rate ratio could be computed for only 6. All studies but one[32] reported a lower number of in-clinic visits in the remote monitoring group.

c In the study by Tajstra 2020[22], the mean number of in-clinic visits per patient-year was 2.5 in the RM group and 4.9 in the clinic visit group (p<0.001). However, the number of out-patient visits (unscheduled) per patient-year was higher in the RM group (2.1 vs. 1.5; p=0.003). In the study by Hansen 2018, there was no significant difference in total or unscheduled in-clinic visits.[17]

Outcome		Ontario-HTA 2018			KCE update 2021			All studies	Meta-analysis update
5.a Time from event onset to data review (days)	**Median (IQR) or Mean (SD)**	4[25, 31, 37, 41]		**3 (1;10) vs 37 (14;71) (p<0.001)[37]** **4.4 (11.9) vs 8.7 (16.9) (p=0.03)[41]** **1.4 (0.8;7.3) vs 24.8 (9.5; 48.8) (p<0.001)[31]** **1.0 vs 35.5 (p<0.001)[25]**	0		**NA**	4[25, 31, 35, 37, 41]	**NA**
5.b. Time from event onset to clinical decision (days)	**Median (IQR)**	2[35, 37]		**2 (1;4) vs 29 (3;51) (p=0.04)[37]** **4.6 vs 22.0 (p<0.001)[35]**	0		**NA**	2[35, 37]	**NA**
6.a. All-cause mortality	**RR (95%CI)**	12[9, 25, 26, 28-32, 34, 38-40]	7164	**0.89 (0.78;1.02) (p=0.11)**	2[17, 22]	810	**0.98 (0.56,1.70)**	14[9, 17, 22, 25, 26, 28-32, 34, 38-40]	**0.89 (0.76,1.03) (p=0.11)**
6.b. Cardiovascular mortality	**RR (95%CI)**	8[25, 26, 29, 30, 32, 34, 38, 40]	6312	**0.89 (0.75;1.05) (p=0.17)**	0		**NA**	8[25, 26, 29, 30, 32, 34, 38, 40]	**NA**
7. Adverse events (various definitions)	**%**	4[25, 27, 33, 40]		**39% vs 42% (p=0.53)** [a33] **10% vs 10% (p>0.05)**[b25] **No difference**[c27] **16% vs. 15%**[d] (p=0.92)[40]	2[17, 22]		**No difference**	6[25, 27, 33, 40]	**NA**
8. Quality of life (various definitions; see Table 7)		4[9, 31, 39, 40]		**No difference**[9, 40] **Some differences**[31, 39] (see Table 7 for details)	3[17, 22, 23]		**No difference**	7[9, 17, 22, 23, 31, 39, 40]	**NA**

**: our own computation; CI: confidence interval; CRT-D: Cardiac resynchronization therapy with a defibrillator function; HR: Hazard Ratio; ICD: implantable cardioverter-defibrillators; IQR: Interquartile range; RR: risk ratio; SD: Standard deviation*

[a] Major adverse events, including all-cause mortality and cardiovascular-, procedural-, and device-related events (≥1 inappropriate shock, ≥2 symptomatic, inappropriate anti-tachycardia pacing)

[b] Serious adverse events, including death, stroke, and surgical intervention

[c] Serious adverse events, including lead defect, stroke, hospitalisations

[d] Adverse events related to unspecified device problems

4.3.2.1 Composite end points

Ontario-HTA. Eight studies were included.[25, 29, 31-33, 37-39] The definition of the composite end point varied across studies but it commonly consisted of a combination of death and all-cause or cardiovascular/device-related hospitalisation or emergency room visits, hence a meta-analysis was considered inappropriate.[2] Based on a mean follow-up of 12 to 34 months, there was a statistically significant difference between the remote monitoring and the control group in only one study.[32] In that study, patients in the remote monitoring group had a lower risk (odds ratio=0.63; (95%CI: 0.43; 0.90); p=0.012) of having a worsened clinical score (death, heart failure hospitalisation, NYHA functional class, or global self-assessment) compared to patients without remote monitoring.[32]

KCE update. Two studies reported on composite endpoints.[17, 22] In the study by Tajstra et al. 2020, the primary outcome was also a composite of all-cause death and hospitalisation due to cardiovascular reasons within 12 months after randomisation. Hospitalisations for cardiovascular reasons included: progression of heart failure; persistent arrhythmia; embolic episode; acute coronary syndrome.[22] The risk of primary endpoint was significantly lower in the remote monitoring group (39.5% vs. 48.5%; RR=0.81; (95%CI: 0.68; 0.98)[a]; p=0.048). This was not related to a difference in all-cause mortality (6% vs. 6%; p=0.9), but in hospitalisation due to cardiovascular reason (37.1% vs. 45.5%; RR=0.82; (95%CI: 0.67; 0.99)[b]; p=0.045), and particularly in hospitalisation due to heart failure (29.8% vs. 38.5%; p=0.029).[22] In the study by Hansen et al. 2020, the Packer score included HF-related death, hospitalisation, and deterioration of New York Heart Association (NYHA) class or self-assessed health.[17] No difference in the change of the Packer score between month 1 and month 13 was retrieved between study groups (p=0.855).[17]

Overall. Over 10 studies, only two reported a marginally significant statistical difference between the remote monitoring and the control group.[22, 32] The definition of composite endpoints was highly study-dependent.

4.3.2.2 ICD shocks

Ontario-HTA. Five[c] studies were included.[26, 28, 30, 34, 39] An ICD shock was considered appropriate if delivered as a result of a ventricular tachyarrhythmia[d]. There was no difference between the two groups in the number of patients with an ICD shock (either appropriate or inappropriate[e]) or an appropriate ICD shock only. However, in four studies there were fewer patients with inappropriate ICD shocks in the remote monitoring group compared to the standard monitoring group.[28, 30, 34, 39] The risk ratio was 0.53 (95% CI: 0.32;0.89; p=0.02) and the absolute risk difference was −0.04 (95%CI: −0.07; −0.01; p=0.01). The number of inappropriate shocks was generally higher in the standard versus remote monitoring group, although it is not clear if the difference in number of shocks was statistically significant.

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[a] RR and 95%CI are our own computation. P-value may differ slightly from the one reported in the original publication.

[b] RR and 95%CI are our own computation. P-value may differ slightly from the one reported in the original publication.

[c] A sixth study planned to evaluate the incidence of ICD shocks, but its results were not available in the literature (Heidbuchel H. et al.[9])

[d] An ICD shock was considered appropriate if delivered as a result of a ventricular tachyarrhythmia. Inappropriate shocks can occur due to supraventricular tachyarrhythmias, atrial fibrillation, ventricular oversensing, T wave oversensing, lead dysfunction, and surgical interventions/electrocauterization.[34]

[e] The reduction in inappropriate ICD shocks in the remote monitoring group may be due to an early warning of events that can trigger multiple inappropriate shocks provided by the remote monitoring system. Once the health care provider receives the warnings (alerts) from the system, they can act to prevent recurrence of inappropriate shocks.

KCE update. The study by Hansen et al. reported no difference in ICD shocks between groups (no differentiation between appropriate and inappropriate shocks was reported).[17]

Overall. Based on four studies with a follow-up duration between 12 and 37 months, there was no difference in the proportion of patients receiving ICD shocks between groups, but a decrease in those receiving inappropriate shocks (RR=0.53; (95% CI: 0.32;0.89); p=0.02).[28, 30, 34, 39] and the absolute risk difference was −0.04 (95%CI: −0.07; −0.01; p=0.01) The quality of evidence was considered moderate because of a likely publication bias.[2]

4.3.2.3 Stroke

Ontario-HTA. Two studies were included, with no statistically significant difference in the number of patients with a stroke between the remote and standard monitoring groups within a 12-month follow-up.[25, 26] However, the small number of events reported made it difficult to interpret the results.

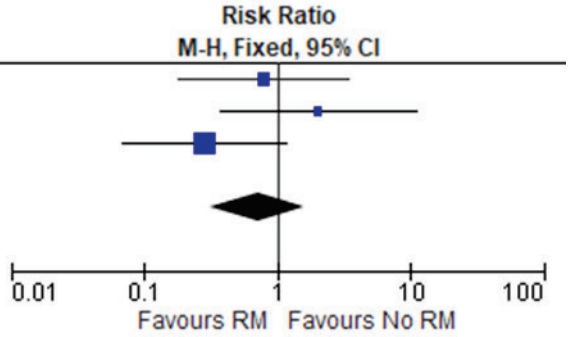
KCE update. One additional study was retrieved[22]. Consistently with previous studies,[25, 26] no significant difference in occurrence of ischaemic stroke was detected (see Table 6).[22]

Overall. The updated meta-analysis of the 3 available studies showed no difference in stroke incidence between groups (see Figure 8).[22, 25, 26]

Figure 8 – Meta-analysis of the effect of remote vs standard monitoring of ICDs on stroke incidence

	Remote Monitoring		No Remote Monitoring			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Sardu et al. 2016	3	89	4	94	30.7%	0.79 [0.18, 3.44]
Tajstra et al. 2020	4	299	2	301	15.7%	2.01 [0.37, 10.91]
Varma et al. 2010	3	908	5	431	53.5%	0.28 [0.07, 1.19]
Total (95% CI)		**1296**		**826**	**100.0%**	**0.71 [0.32, 1.61]**
Total events	10		11			

Heterogeneity: Chi² = 3.06, df = 2 (P = 0.22); I² = 35%
Test for overall effect: Z = 0.82 (P = 0.41)



Sardu et al. 2016[26], Tajstra et al. 2020[22], Varma et al. 2010[25]

4.3.2.4 *Time from event onset to data review or clinical decision*

Ontario-HTA. Four studies (five publications) were included.[25, 31, 35, 37, 41] Events included fluid accumulation, atrial tachycardia/atrial fibrillation burden, fast ventricular rates during atrial fibrillation episodes, ventricular fibrillation, ventricular tachycardia, ICD shocks, and device malfunction. Based on the results of three studies (four publications), the time from event onset or remote monitoring system alert to data review at the clinic was statistically significantly shorter in the remote versus the standard monitoring group.[2] The median times varied between 1 and 4 days versus 9 and 42 days, respectively.[25, 31, 37, 41] Two studies reported a statistically significant shorter time from event onset to clinical decision in the remote versus standard monitoring group, median times varied from 2 to 5 days compared with 22 to 29 days, respectively.[35, 37]

KCE update. We included one additional study. In the study by Tajstra et al. 2020 there was no difference in the time to first in-clinic visit (median days: 48 vs. 54; p=0.7).[22]

Overall. In 3 over 5 studies, remote monitoring decreased the time elapsed between event onset and data review or clinical decision. The quality of the evidence was considered moderate because of a likely publication bias.[2]

4.3.2.5 *Worsening of NYHA functional class or clinical status*

Ontario HTA. Based on 2 studies no statistical difference between groups could be demonstrated.[31, 32]

KCE update. Two additional studies reported on the heart failure-specific health status.[17, 24] In the study by Hansen et al. 2018,[17] there was no significant difference in NYHA class between groups (p=0.888). Versteeg et al. 2019 found no significant difference between groups in the heart failure-specific health status measured by the Kansas City Cardiomyopathy Questionnaire (at 3, 6, 12 & 24 months).[24]

Overall. Remote monitoring was not associated with a worsening of NYHA Functional class or clinical status in the four studies reviewed.[17, 24, 31, 32]

4.3.2.6 *Number of in-clinic visits*

Ontario-HTA. Ten studies were included.[9, 25, 27, 28, 31, 32, 34-36, 40] In 6 of them, the total number of in-clinic visits was statistically significantly lower in the remote monitoring group compared with the standard monitoring group.[25, 27, 31, 34, 35, 40] The pooled rate ratio was 0.62 (95%CI: 0.57; 0.66; p<0.00001), with a great heterogeneity between studies (I^2 = 96%). The mean total number of in-clinic visits per patient-year varied from 0.9 to 3.9 in the remote monitoring group and from 1.7 to 6.3 in the standard monitoring group within 12 to 37 months of follow-up.[2] The total number of in-clinic visits was also higher in 3 additional studies but it was not reported whether the difference was statistically significant.[31, 35, 36] There were 7 studies disaggregating scheduled and unscheduled visits. In 3 of them the number of unscheduled visits was significantly higher in the remote monitoring group.[9, 25, 40]

KCE update. Two additional studies reported on this outcome.[17, 22] The results in the study by Tajstra et al. 2020 (n=600) are fairly similar to those reported in the Ontario-HTA.[22] Although the mean number of unscheduled in-clinic visits per patient-year was higher in the remote monitoring group (2.1 vs. 1.5; p=0.003), the total number of in-clinic visits (scheduled/unscheduled) per patient-year was lower in this group as compared to the standard monitoring group (2.5 vs. 4.9; p<0.001). Rate ratios could not be calculated because numbers of person-years of observation were not provided. In the second study by Hansen et al. 2018 no significant difference was found between groups in the number of overall or unscheduled in-clinic visits (mean±SD=1.2 ± 2.6 vs. 0.9 ± 1.8; p=0.550).[17]

Overall. Even if unscheduled in-clinic visits were more frequent in the remote monitoring group (4 studies over 8[9, 22, 25, 40]), the total number of in-clinic visits was statistically significantly less frequent in the remote monitoring group in 7 studies over 12.[22, 25, 27, 31, 34, 35, 40] However, the number of in-clinic visits was highly study-dependent, as defined per varying clinical protocols. The quality of evidence was judged moderate because of a likely publication bias.[2]

4.3.2.7 Heart failure hospitalisations

Ontario-HTA. Seven studies were included.[29, 30, 31 , 32, 35, 38, 40] A meta-analysis was carried out on the 5 studies reporting the number of patients with at least one heart failure hospitalisation.[a29, 30, 32, 38, 40] No statistically significant difference between the two groups was observed (RR=1.00; (95%CI: 0.91;1.11); p=0.30). The results of the two remaining studies, which could not be included in the meta-analysis because not reporting patient numbers, also showed no difference in hospitalisation rate between the 2 groups.[31, 35]

KCE update. Two additional studies reported on this outcome.[17, 22] In study by Tajstra et al. 2020[22], hospitalisation due to cardiovascular reason (37.1% vs. 45.5%; p=0.045) and hospitalisation due to heart failure (29.8% vs. 38.5%; RR=0.77; (95%CI: 0.62;0.97); p=0.024)[b] were statistically lower in the remote monitoring group.[c] Not such difference was observed in the second study (9.8% vs. 12.0%; p=0.605).[17] Pooled together these two studies reported no significant difference between groups (RR=0.78; (95%CI: 0.62;0.96); p=0.36).

Overall. Seven studies with a follow-up duration between 11 and 33 months were included in our updated meta-analysis (see Figure 9).[17, 22, 29, 30, 32, 38, 40] The overall result was not significant (RR=0.94; (95%CI: 0.83; 1.07); p=0.36). Therefore, no significant reduction in HF hospitalisation was demonstrated for patients remotely monitored. Similarly, there was no difference in the proportion of patients with at least one all-cause hospitalisation.

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[a] In one study in which the information was not available, information on cardiovascular hospitalisations was used.[29]

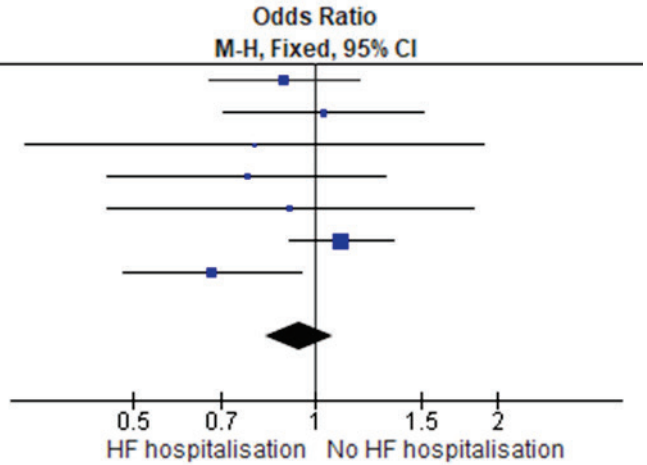
[b] RR and 95%CI are our own computation. P-value may differ slightly from the one reported in the original publication.

[c] The authors argued that this difference might be due to a more intensive daily follow-up of alerts by a well-trained staff.

Figure 9 – Meta-analysis of the effect of remote vs standard monitoring of ICDs on hospitalisation for heart failure

	HF hospitalisation		No HF hospitalisation			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Bohm 2016	119	505	128	497	20.8%	0.89 [0.67, 1.18]
Boriani 2017	63	437	60	428	10.9%	1.03 [0.71, 1.51]
Hansen 2018	10	102	13	108	2.4%	0.79 [0.33, 1.90]
Hindricks 2014	27	333	34	331	6.6%	0.77 [0.45, 1.31]
Luthje 2015	20	87	22	89	3.5%	0.91 [0.45, 1.82]
Morgan 2017	315	824	297	826	38.6%	1.10 [0.90, 1.35]
Tajstra et al. 2020	89	299	116	301	17.1%	0.68 [0.48, 0.95]
Total (95% CI)		**2587**		**2580**	**100.0%**	**0.94 [0.83, 1.07]**
Total events	643		670			

Heterogeneity: Chi² = 7.13, df = 6 (P = 0.31); I² = 16%
Test for overall effect: Z = 0.92 (P = 0.36)



Bohm et al. 2016[38], Boriani 2017[40], Hansen 2018[17], Hindricks 2014[32], Luthje 2015[30], Morgan 2017[29], Tajstra 2020[22]

4.3.2.8 *Emergency Department Visits*

Ontario-HTA. Five studies were included.[30, 31, 35, 39, 40] There was no clear-cut evidence of a reduction in emergency department visits. Two studies reported a statistically significantly lower 24-month rate of emergency department visits per patient[40] or patient-year.[31] In this latter study the rate for emergency department/urgent in-clinic visits for HF, arrhythmias, or ICD-related events was 0.59 versus 0.93 events per year (Rate Ratio=0.65; (95%CI: 0.49; 0.88); p=0.005).[31] The other three studies did not observe a statistically significant difference in the mean number of visits between the two groups.[30, 35, 39]

KCE update. No additional data was retrieved.

Overall. The rate of emergency department visits could possibly be reduced in patients with remote monitoring compared to in-clinic monitoring in 2 studies.[31, 40] The level of evidence was considered very low because of the inconsistency and imprecision of results, and a potential publication bias.[2]

4.3.2.9 *Mortality*

Ontario HTA. Thirteen studies were included.[9, 25, 26, 28-32, 34, 35, 38-40] No statistically significant difference in all-cause mortality between the two groups was observed in the meta-analysis of 12 studies (RR=0.89; (95%CI: 0.78;1.02); p>0.05).[a] Results were similar for cardiovascular mortality (8 studies) (RR=0.89; 95% CI: 0.75; 1.05); p>0.05).[25, 26, 29, 30, 32, 34, 38, 40]

Our update. We retrieved two studies which reported on all-cause mortality and found no significant difference between groups, 6% vs. 6% (p=0.9) and 4.9% vs. 5.6% (p = 0.832), in study by Tajstra et al. 2020 and Hansen et al. 2018 respectively.[17, 22] Cardiovascular mortality was not reported separately in these 2 studies.

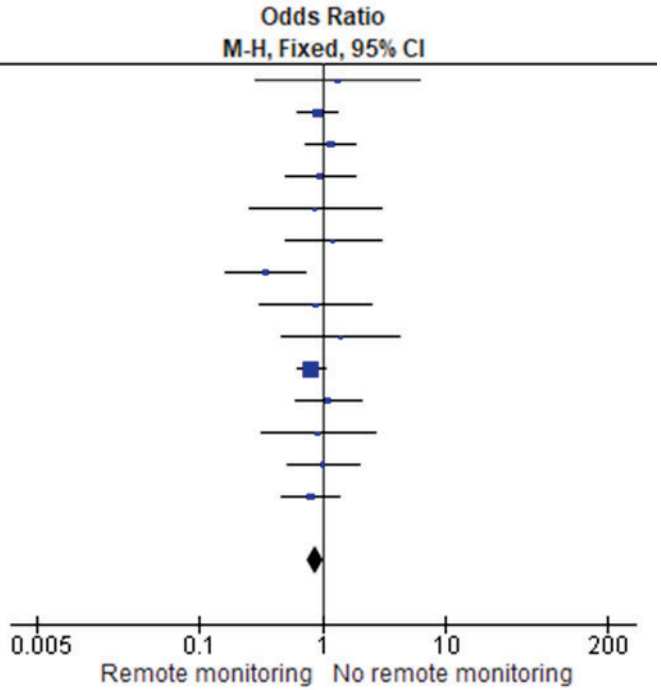
Overall. In our updated meta-analysis including 14 studies, with a follow-up between 12 and 37 months, and 7974 patients, no significant effect of remote monitoring on all-cause mortality or cardiovascular mortality was demonstrated (see Figure 10). However, there was a trend towards a risk reduction in all-cause mortality and results were marginally non statistically significant (RR for all-cause mortality=0.76; (95%CI: 0.76; 1.03); p=0.11). However, the quality of evidence was considered low because of imprecision and a likely publication bias.[2]

[a] The number of deaths in each group was not provided in study by Crossley et al.[35]

Figure 10 – Meta-analysis of the effect of remote vs. standard monitoring on all-cause mortality

Study or Subgroup	Remote monitoring Events	Total	No remote monitoring Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Al-Khatib 2010	4	76	3	75	0.8%	1.33 [0.29, 6.17]
Bohm 2016	59	505	63	497	15.5%	0.91 [0.62, 1.33]
Boriani 2017	40	437	34	428	8.6%	1.17 [0.72, 1.88]
Guedon Moreau 2013	20	221	20	212	5.1%	0.96 [0.50, 1.83]
Hansen 2018	5	102	6	108	1.5%	0.88 [0.26, 2.96]
Heibuchel 2015	12	159	9	144	2.4%	1.22 [0.50, 3.00]
Hindricks 2014	10	333	27	331	7.3%	0.35 [0.17, 0.73]
Landolina 2012	7	99	8	101	2.0%	0.88 [0.31, 2.54]
Luthje 2015	8	87	6	89	1.5%	1.40 [0.47, 4.22]
Morgan 2017	128	824	152	826	35.5%	0.82 [0.63, 1.06]
Osmera 2014	29	97	28	101	5.3%	1.11 [0.60, 2.06]
Sardu et al. 2016	7	89	8	94	2.0%	0.92 [0.32, 2.64]
Tajstra et al. 2020	18	299	18	301	4.7%	1.01 [0.51, 1.98]
Varma	36	908	21	431	7.6%	0.81 [0.46, 1.40]
Total (95% CI)		**4236**		**3738**	**100.0%**	**0.89 [0.76, 1.03]**
Total events	383		403			

Heterogeneity: Chi² = 10.04, df = 13 (P = 0.69); I² = 0%
Test for overall effect: Z = 1.59 (P = 0.11)



Al-Khatib 2010[39], Bohm 2016[38], Boriani 2017[40], Guedon-Moreau 2013[34], Hansen 2018[17], Heibuchel 2015[9], Hindricks 2014[32], Landolina 2012[31], Luthje 2015[30], Morgan 2017[29], Osmera 2014[28], Sardu 2016[26], Tajstra 2020[22], Varma 2010[25]

4.3.2.10 Adverse events

Ontario-HTA. Four studies were included.[25, 27, 33, 40] The definition of adverse events varied across studies. There was no evidence of a difference in adverse events between groups (see above sections for detailed analysis per outcome).

KCE update. Two additional studies were included.[17, 22] As explained in the above sections, no difference between groups in risk of stroke, worst NYHA functional class, hospitalisation or mortality was reported. Tajstra et al. 2020 also reported on myocardial infarction (3.6% vs. 2.3%; p=0.46),[22] and Hansen et al. 2018 on cardiac decompensation (p=0.915) and stored tachycardia (25% vs. 23%; p=0.58),[17] with no further differences between groups.

Overall. There was no evidence of difference in occurrence of adverse events among groups, as also demonstrated in our above analysis per outcome (stroke, hospitalisation, mortality, worsening of NYHA class).

4.3.2.11 Quality of life

Ontario-HTA. Four studies compared the changes in quality of life and the satisfaction with ICD care between patients in the remote and standard monitoring groups.[9, 31, 39, 40] No clear-cut effect of remote monitoring on quality of life could be demonstrated (see Table 7). Two studies did not find any statistically significant difference between groups in the change in quality of life from baseline.[9, 40] In the two other studies results were mixed.[31, 39] Landolina et al. 2012 found a statistically significant improvement in quality of life at 16 months of follow-up in the remote monitoring group compared with the standard monitoring group, using the Minnesota Living with Heart Failure questionnaire,[a] although statistical significance was marginal (p=0.03).[31] Al-Khatib et al. 2010 found a statistically significant improvement with remote monitoring only in the EuroQol-5D visual analogue scale (EQ-5D VAS) at six months, but not at 12 months nor in the EQ-5D at month 6 and month 12.[39]

KCE update. Four additional studies were included.[17, 22-24] In none of them a difference in quality of life was observed (see Table 7).

Overall. The instruments to measure quality of life were heterogeneous across the 8 studies included (see Table 7). There was overall no demonstrated effect of remote monitoring on the quality of life, both with disease-specific (that are claimed to be more sensitive to small changes in quality of life) or generic instruments (that can be used for all diseases).

[a] The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a self-administered, disease-specific questionnaire composed of 21 items, each with a 6-point scale [0 = no impact of heart failure on QoL, 5 = a great deal of impact]

Table 7 – Quality of life indicators in RCTs of remote vs standard monitoring of patients with ICDs and CRT-Ds

Study	Indicator	Type of instrument	Results (RM vs in-clinic)	P-value
Boriani 2017[40]	Median (IQR) change in MLHFQ at month 16	Disease-specific	-10 (-22; 0) vs -10 (-25; 0)	0.85
Heidbuchel 2015[9]	SF36	Generic	No difference	NR
Landolina 2012[31]	Median (IQR) change in MLHFQ at month 16	Disease-specific	-2 (-17; 8) vs 2 (-7; 10)	0.03
Al-Khatib 2010[39]	• EQ-5D VAS at month 6 • EQ-5D VAS month at 12 • EQ-5D at month 6 • EQ-5D at month 12	Generic	83 vs 75 80 vs 80 85 vs 80 85 vs 100	0.002 0.47 0.26 0.29
Hansen 2018[17]	Mean±SD change in MLHFQ at month 13	Disease-specific	-8.4 ± 20.3 vs. −10.5 ± 21.6	0.47
Leppert 2019[23]	EQ-5D changes at month 12	Generic	3.9 vs. 1.2	0.24
Tajstra 2020[22]	MLHFQ at month 12	Disease-specific	31.0 ±20.5 vs. 38.4±16.5	0.33
Versteeg 2019[24]	Change in KCCQ at month 24	Disease-specific	No difference	0.29

EQ-5D VAS: EuroQol-5D visual analogue scale; KCCQ: Kansas City Cardiomyopathy Questionnaire[a]; MLHFQ: Minnesota Living with Heart Failure questionnaire

4.3.3 *Outcomes in RCTs of remote monitoring vs. standard monitoring of PMs*

In the Ontario-HTA, six open-labelled randomized studies were included.[27, 42-46] Our update included two additional studies (4 papers), one of which had a very small sample size (Nordland trial, n=50) (see Appendix 7 for study description and quality appraisal).[19, 21] In all studies, the intervention group received remote monitoring in addition to in-clinic visits. In the control group, patients were seen in person at the clinic and did not receive remote monitoring, with the exception of one study where remote monitoring was compared to trans-telephonic monitoring.[43] Follow-up durations varied from 12 to 24 months. The frequency of follow-up visits (remote or in-clinic) and data transmission varied from study to study. In six studies, data were transmitted daily in the remote monitoring group. In one study, remote interrogation of the device occurred at 3, 6, and 9 months,[43] in another at 6, 12 and 18 months.[21] The frequency of scheduled in-clinic visits varied both within study groups and between studies. All studies were at low risk of bias, except the Nordland trial where the risk of a selection bias was high (see Appendix 7 for more details).[19] However, all studies were open-labelled trials and performance and detection bias could occur. Detection bias were unlikely for hard outcomes (e.g. hospitalisation) but plausible for self-assessed outcomes such as quality of life. Main outcomes from studies in the Ontario-HTA and in our update, and overall are presented in Table 8.

[a] The KCCQ is a 23-item, validated self-report questionnaire that quantifies physical limitations, symptoms, social functioning, and quality of life of patients with heart failure.

Table 8 – Overview of outcomes in RCTs of remote monitoring vs. standard monitoring of PMs

Outcome		Ontario-HTA 2018			KCE update 2021			Total studies after update	Meta-analysis update
		N° studies	n	Results	N° studies	n	Results		
1. Arrhythmias									
1.a. Patients with atrial tachyarrhythmia	**%**	2[42, 45]		**28% vs 22% (p=0.06)**[42] **24% vs 19.3% (p=0.36)**[45]	0		**NA**	2[42, 45]	**NA**
1.b. Daily atrial fibrillation burden	**% or mean (95%CI)**	2[42, 45]		**8% vs 28% (p=0.04)**[a 42] **16.0 (8.9;23.2) vs 51.2 (21.9;81.9) (p=0.028)**[b45]	0		**NA**	2[42, 45]	**NA**
2. Time to detection and treatment of arrhythmias (days)	**Median (IQR)**	3[42, 45, 46]		**114 (44;241) vs 224 (67;366) (p<0.05)**[42] **111 vs 196 (p<0.001)**[45] **17 (4;48) vs 139 (33;201) (p=0.001)**[46]	0		**NA**	3[42, 45, 46]	**NA**
3. Number of in-clinic visits	**Mean (±SD) or Median (IQR)**	2[27, 46]		Visits per year: **0.29 (±0.6) vs 0.53 (±0.5) (p<0.001)**[27] Visits per patient-year: **1.04 (±1.02) vs. 1.63 (±1.12) (p<0.001)**[46]	2[19, 21]		Visits per patient-year: **0.50 (0.50;0.62) vs. 2.00 (1.93;2.05) (p<0.01)**[21] Visits per year: **1.3 vs. 1.2 (p=0.30)**[19]	4[19, 21, 27, 46]	**NA**
4. Stroke	**RR (95%CI)**	3[27, 42, 45]	1010	**0.82 (0.30; 2.25) (p=0.70)**	1[21]	1327	**1.13 (0.41; 3.08) (p=0.82)**	4[21, 27, 42, 45]	**No**
5. Cardiovascular hospitalisation	**RR (95%CI)**	3[27, 42, 46]	1204	**0.97 (0.72; 1.31) (p=0.84)**	1[19]	50	**1.28 (0.58;2.86) p=0.54**	4[19 , 27, 42, 46]	**No**
6. All-cause mortality	**RR (95%CI)**	2[42, 46]	1089	**1.29 (0.78;2.13) p=0.32**	1[21]	1327	**1.11 (0.74;1.66) p=0.62**	3[21, 42, 46]	**No**

[a] Atrial tachyarrhythmia burden defined as mean percentage of time spent in a day at an atrial rate above the programmed value[42]

[b] Mean number of daily atrial fibrillation burden > 10% (2.5 hours) during the mean follow-up of 15.5 months[45]

Outcome		Ontario-HTA 2018		KCE update 2021		Total studies after update	Meta-analysis update
7. Adverse events (various definitions)	**HR (95%CI) or RD (95%CI)**	2[44, 46]	**HR=0.90 (0.59; 1.41)**[a46] **RD=−0.04 (-2.2; 10.4); p = 0.98**[b44]	2[19, 21]	**10.9% (8.8%; 13.1%) vs. 11.8% (9.5%; 14.1%)**[c21] **8.0% vs. 4.2% with at least 1 event (p=0.40)**[d19]	4[19, 21, 44, 46]	**NA**
8. Quality of life (various instruments)		2[44, 46]	**No difference**[e]	1[19]	**No difference**[f]	3[19, 44, 46]	**NA**

**: our own computation HR: hazard ratio; IQR: interquartile range; RD: risk difference; RR: risk ratio; SD: standard deviation*

4.3.3.1 Arrhythmias

Ontario-HTA. Two studies were included.[42, 45] The percentage of patients with atrial tachyarrhythmias was not significantly different between the two groups, although there was a trend for a greater percentage in the remote monitoring group particularly apparent in the study by Amara et al. 2017.[42] However, the mean percentage of time spent in a day at an atrial rate above the programmed value (i.e. atrial tachyarrhythmia burden)[42] or the mean number of daily atrial fibrillation burden > 10%[45] were statistically significantly lower in the remote compared to the standard monitoring group, although the tests were marginally significant (see Table 8).

KCE update. No additional studies were retrieved.

Overall. Remote monitoring did not decrease the proportion of patients with atrial tachyarrhythmias but may have an effect on the atrial tachyarrhythmia burden in the only two studies retrieved (follow-up duration between 12 and 24 months).[42, 45] The quality of evidence was judged high by the authors of the HAS-HTA.[2]

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[a] Major adverse events included death or hospitalisations for complications due to either the pacing system or a cardiovascular event occurring within 18 months of follow-up.[46]

[b] Major adverse events included death, prolongation of hospitalisation for peri- or postoperative complications, and readmission to hospital within 1 month of follow-up.[44]

[c] Adverse events included death, stroke, or cardiovascular surgical procedure over 24 months

[d] Adverse events included angina, lead dislodgement and percutaneous coronary intervention at month 6 and month 12[19]

[e] Measured with the SF36 instrument (generic instrument)

[f] The health-related quality of life was assessed through the Norwegian version EuroQol-5D and the self-rated HRQoL was assessed with the EQ-5D Visual Analogue Scale (EQ-5D-VAS) (generic instruments). The disease specific health-related quality of life was measured by the Minnesota Living with Heart Failure questionnaire (MLHFQ)[19]

4.3.3.2 *Time to detection and treatment of arrhythmias or medical intervention*

Ontario-HTA. Three studies were included.[42, 45, 46] The median time between the pacemaker implantation and the first treated atrial tachyarrhythmia (or undefined medical intervention in Mabo et al. 2012[46]) was shorter in the remote monitoring group compared to the standard monitoring group in the three studies (see Table 8).

KCE update. No additional studies were retrieved.

Overall. Remote monitoring reduced the time to detection and treatment of arrhythmias. The quality of evidence was judged high, although based on only 3 studies.[2]

4.3.3.3 *Number of in-clinic visits*

Ontario-HTA. Two studies were included.[27, 46] They both reported fewer in-clinic visits in the remote versus standard monitoring group (see Table 8). However, the absolute differences in means were small: -0.24 visit/year in Perl et al. 2013[27] and -0.59 visit/patient-year in Mabo et al. 2012.[46] Disaggregation in scheduled and unscheduled visits was not provided.

KCE update. Two studies were included.[19, 21] In Watanabe et al. (n=1327), the median in-clinic visits per year was 0.50 (IQR: 0.50; 0.63) vs. 2.01 (IQR: 1.93; 2.05) (p<0.001).[21] Between randomisation and 24-month follow-up, there were 201 in-clinic patient evaluations in the remote monitoring group (all unscheduled) versus 1775 in the standard monitoring group (sum of scheduled and unscheduled). Including the 24-month visit, 710 scheduled and unscheduled in-clinic visits were performed in the remote monitoring group (0.54 per patient-year) versus 2275 in the standard monitoring group (1.76 per patient-year) (p<0.01). This translates into a 69.5% reduction of in-clinic visits in the population. However, when inclusive of remote follow-ups, the difference was not anymore significant (1.85 follow-ups (remote + in-clinic) per patient-year in the RM group versus 1.76 in the standard monitoring group).[21] In the Nordland trial (n=50), there was no significant difference between groups in the mean number of in-clinic visits at month 6 (1.24 vs. 1.17 (p = 0.26)) or at month 12 (1.3 vs. 1.2 (p=0.30) after randomisation.[19]

Overall. Three of the four studies included reported fewer in-clinic visits in the remote versus standard monitoring group.[21, 27, 46] Given the heterogeneity of study design and indicators it was not possible to do a meta-analysis. However, Watanabe et al. reported that the difference between groups was not anymore significant when remote follow-up controls were accounted for.[21] The quality of evidence was judged moderate because of a likely publication bias.[2] In particular one unpublished RCT (Virtual clinic pacemaker follow-up (VIRTUE) (Identifier NCT00475124) was terminated because of the increased number of in-clinic visits in the remote monitoring group. Redundant in-clinic visits increased the workload in the RM group.[a]

4.3.3.4 *Stroke*

Ontario-HTA. Three studies were included.[27, 42, 45] There was no significant differences between groups (RR=0.82; (95%CI: 0.30;2.25); p=0.70).

KCE update. One study was included.[21] Watanabe et al. reported that during a follow-up of 24 months 1.4% (9/558) vs 1.3% (7/550) participants suffered a stroke (RR=1.13; (95%CI: 0.41; 3.08); p=0.82).[b]

Overall. There was no difference in the incidence of stroke between remote and standard monitoring groups. The quality of evidence was judged low because of a serious imprecision.[2]

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[a] https://www.clinicaltrials.gov/ct2/show/NCT00475124?term=virtual+clinic+pacemaker&rank=1

[b] Our own calculation

4.3.3.5 Cardiovascular hospitalisations

Ontario-HTA. Three studies were included.[27, 42, 46] There was no statistically significant difference between remote and standard monitoring in the percentage of patients with at least one cardiovascular hospitalisation within a mean follow-up of 12 to 18 months (RR=0.97; (95%CI: 0.72;1.31); p=0.84). All-cause hospitalisations were not reported.

KCE update. One study was included.[19] At month 6, 42.0% vs. 33.4% of patients had at least 1 hospitalisation (p=0.54), and at month 12 these numbers amounted to 44.0% vs. 36.0% (p=0.53).

Overall. There was no evidence of a difference in cardiovascular hospitalisations between the remote monitoring and standard monitoring groups in the 4 studies retrieved (mean follow-up of 12 to 18 months).[19, 27, 42, 46] Imprecision was high (moderate quality evidence)[2]

4.3.3.6 Mortality

Ontario HTA. Two studies were included.[42, 46] The was no statistical difference in all-cause mortality between groups after a mean follow-up of 12 to 18 months (RR=1.29; (95%CI:0.78;2.13); p=0.32).

KCE update. One study was included.[21] There was no significant difference in all-cause mortality between groups after 24 months (RR=1.11; (95%CI:0.74;1.66); p=0.62)

Overall. There was no difference in all-cause mortality between groups in the only 3 studies retrieved (follow-up duration between 12 and 24 months). Imprecision of results was very high (low quality evidence).

4.3.3.7 Adverse events

Ontario-HTA. Two studies were included.[44, 46] No significant difference in major adverse events was identified between groups. In Mabo et al. 2012 major adverse events included death or hospitalisations for complications due to either the pacing system or a cardiovascular event occurring within 18 months of follow-up. No statistically significant difference in the number of patients experiencing the composite end point was observed between the two groups (HR=0.90; 95% CI: 0.59; 1.41).[46] In Halimi et al. major adverse events included death, prolongation of hospitalisation for peri- or postoperative complications, and readmission to hospital within 1 month of follow-up. The was no significant difference between the two groups (RD= −0.041; (95%CI: -2.2; 10.4); p= 0.98).[44]

KCE update. Two studies were included.[19, 21] In Watanabe et al. 2020 the occurrence of adverse events including death, stroke, or cardiovascular surgical procedure was not significantly different between groups (10.9% (95%CI: 8.8; 13.1) vs. 11.8% (95%CI: 9.5; 14.1)) over 24 months.[21] In the NORDLAND study (n=50), cardiovascular adverse events including angina, lead dislodgement and percutaneous coronary intervention were not significantly different between groups at month 6 (8.0% vs. 4.2% had at least 1 event (p=0.40)) or month 12 (8.0% vs. 4.0% had at least 1 event (p = 0.39)).[19]

Overall. There was no evidence of a significant difference in the risk of adverse events between groups in the four RCTs retrieved.[19, 21, 44, 46]

4.3.3.8 Quality of life

Ontario-HTA. Two studies were included.[44, 46] Neither study observed a statistically significant difference between the two groups in the physical, psychological, and overall scores (SF36-generic instrument).

KCE update. One study was included (n=50).[19] The health-related quality of life was assessed through the Norwegian version of the EQ-5D instrument and the self-rated HRQoL was assessed with the EQ-5D Visual Analogue Scale (EQ-5D-VAS) (generic instruments). The disease specific health-related quality of life was measured by the Minnesota Living with Heart Failure questionnaire (MLHFQ). There was not significant difference in any of these indicators between remote monitoring and standard monitoring groups at month 6 and month 12.

Overall. There was no evidence of a difference in quality of life between remote monitoring and standard monitoring groups in the three studies retrieved.[19, 44, 46]

4.3.4 *Clinical outcomes of remote vs. standard monitoring of patients with implantable loop recorders (ILRs)*

This section relies entirely on the very recent systematic review carried out by the HAS on the clinical benefit of remote vs. standard monitoring (with data analysed during regular in-clinic visits every 3-6 months) of ILRs in the diagnosis of recurrent unexplained syncopal episodes and cryptogenic strokes.[10] Medline, the Cochrane Library and Lissa databases were searched. The websites of other HTA Agencies were also screened. The search strategy covered the period 01/2009 to 03/2020, with a bibliographic surveillance up to January 2021. The methodological quality of the review was appraised by applying the AMSTAR-2 grid (Appendix 3).[11] The HAS review presents two non-critical weaknesses (study selection and data extraction not done in duplicate; reasons for exclusion of eligible studies after full text appraisal are given globally and not per individual studies) and can be considered good quality.[10]

In total, the HAS identified 1538 documents, 181 of which were screened on full text. No RCT were retrieved. Five observational studies were included.[47-51] Only one of these had a comparative design (retrospective cohort).[47] All studies had a small sample size and presented high risk of bias. Moreover, they were relatively old with low applicability to the current practice.

Drak-Hernandez et al. 2013 was the only comparative study retrieved.[47] It included 109 patients with recurrent unexplained syncopes, who had to transmit manually data from their ILR monthly or in the 24 hours following the appearance of symptoms whereas the standard monitoring consisted of an in-clinic visit every 3 months. There was no difference between groups in the proportion of patients diagnosed with an arrhythmia (82.6%) during a mean follow-up of 64 weeks.[47] However a significantly shorter mean time between the implantation of the loop-recorder and the arrhythmia diagnosis (56 vs. 260 days; $p<0.001$) or start of the treatment (73 vs. 260 days; $p<0.001$) was reported between the remote vs. standard monitoring groups.[47] The proportion of unscheduled in-clinic visits was lower in the remote monitoring group (13.2% vs. 31.7%). No data on morbidity or mortality was reported. It should be noted that the period of evaluation differed between groups (June 2009-December 2010 for remote monitoring; March 2003-October 2010 for standard monitoring) and this is very likely to limit the validity of the comparison (e.g. the type of implanted devices or the clinical management of patients may differ between the two periods). The study also presented a number of other limitations (e.g. only 41 patients were recruited over 7 years in the standard monitoring group without any description of the selection procedure). The four other studies were very low quality and had no comparator. They could have been useful for assessing adverse events but these were not reported and at any rate their sample size was small.

4.4 Discussion and limitations

4.4.1 *Defibrillators and pacemakers*

Our review (19 RCTs) showed that remote monitoring of defibrillators plus in-clinic visits decreased the time from event onset to data review, reduced the risk of inappropriate shocks and resulted in less in-clinic visits, whereas no significant difference was detected in other outcomes (quality of life, stroke, all-cause or cardiovascular hospitalisation, all-cause or cardiovascular mortality) including major adverse events. This is consistent with the results of other recent systematic reviews.[14, 15] For pacemakers (8 RCTs), our findings were fairly similar to those on defibrillators. The time to detection and treatment of atrial arrhythmias was reduced, which could explain a lower burden of atrial arrhythmias, and the number of in-clinic visits was reduced. We discussed hereunder the case of defibrillators but the arguments are also valid for pacemakers.

One benefit of the remote monitoring of CIEDs is the earlier detection of technical or cardiac events. First, this early detection would allow rapid defibrillators programming optimization to prevent inappropriate shocks.[15] Inappropriate shocks can cause discomfort, anxiety and depression.[33] Therefore their prevention is likely to improve the well-being of patients. However, evidence is lacking to confirm this plausible benefit, as only one of the four studies reporting on the reduction of inappropriate shocks also measured quality of life, and the results were ambiguous with an improvement of the EQ-5D VAS at month 6, but not at month 12, and no improvement in EQ-5D.[39] It is also important to note that the risk of inappropriate shocks in the included studies was relatively low (8%) and the

absolute risk reduction related to RM was thus also limited (4%; (95%CI: 1%; 7%); p=0.01) (4 studies, moderate quality evidence).

Second, an earlier medical intervention in case of alerts may also prevent further deterioration of patients' health status and subsequently reduce emergency department visits and hospitalisations. There was however no clear-cut evidence of a reduction in emergency department visits (2 studies over 5) and our updated meta-analysis including seven RCTs showed no significant difference in hospitalisations.[17, 22, 29, 30, 32, 38, 40]. The all-cause mortality and cardiovascular mortality was not significantly different in the remote monitoring group, although a trend towards risk reduction was observed, and the statistical significance was marginally non-significant in our updated meta-analysis including 13 RCTs. Whether more positive results could have been observed with a more intensive follow-up of the telemonitored patients is an interesting hypothesis. One single study (Tajstra et al. 2020[22]) reported a decrease in hospitalisation due to cardiovascular reason (37.1% vs. 45.5%; OR=1.25; (95%CI: 1.0;1.57) p=0.045) and heart failure (29.8% vs. 38.5%; RR=0.77 (95%CI: 0.62;0.97); p=0.024), although marginally statistically significant. The follow-up was seemingly more intensive than reported in other studies. The monitoring staff included two physicians (a cardiology resident and a cardiology consultant) and two electrophysiology nurses, who daily analysed data derived from remote monitoring online systems and undertook adequate actions if necessary. A clinical response to remote alerts was triggered at the discretion of the monitoring staff.[22] In the only study which reported a significant decrease in cardiovascular mortality in the remote monitoring group (Hindricks et al. 2014), in-clinic visits were scheduled according to the physician's discretion in contrast to all other studies and the total number of follow-up controls was higher in the remote monitoring group.[32] In a pooled analysis of the three trials using a specific remote monitoring system with daily verification of transmission (Biotronik Home Monitoring),[25, 32, 34] the risk of all-cause mortality was reported to become marginally significant.[52] However, this review suffered a severe selection bias as other published studies with daily monitoring were not included.[9, 22, 26-29]

Another benefit of the remote versus standard monitoring would be the reduced number of in-clinic visits. This result was not unexpected as the study protocols imposed that in-clinic visits be scheduled less frequently in the group with remote monitoring. In contrast, the number of unscheduled visits was higher in the remote monitoring group in 4 studies over 8.[9, 22, 25, 40] The reduced number of in-clinic visits is often presented as a key advantage of the remote monitoring. However, two important drawbacks can be noted. First, the total number of follow-up controls (i.e. in-clinic visits plus remote interrogations) in the remote vs. standard monitoring group was not reported in most studies. The monitoring of alerts on top of the scheduled remote interrogations may increase considerably the burden of health professionals and a fair comparison between groups should account for that dimension. For example, in their study on ICDs and CRT-Ds (n=664) Hindrix et al. reported that the rate of follow-up controls in the remote monitoring was higher than in the standard monitoring group (3.13 versus 2.86 follow-up controls per patient-year; no statistical test reported).[32] A similar observation was reported in the RCT by Watanabe et al. (n=1327) about pacemakers.[21] In that study, the remote monitoring translated into a 69.5% reduction of in-clinic visits compared with standard monitoring. However, the difference was not anymore significant when all follow-up controls were considered.[21] Second, it is unclear how the research protocols imposing a reduced number of in-clinic visits for telemonitored patients would translate in real-life practice. For example, clinicians could use remote monitoring to ensure a closer follow-up of their patients, particularly those suffering heart failure, without necessarily reducing the number of in-clinic visits. This point was clearly emphasised during the stakeholder meeting that was held at KCE in June 2021 (see chapter 3). Therefore, the remote monitoring of implanted cardiac devices could result in an increased workload for medical staff in some situations, and strategies to overcome this difficulty might be needed. For example, it was recently proposed that relying exclusively on alert transmissions could be a valid strategy to reduce the workload of medical staff as the ability of scheduled transmissions to detect clinically relevant events was low.[53] Another approach would be to safely cancel in-clinic visits of telemonitored cardiac patients. As an example a RCT comparing outcomes in patients exclusively telemonitored (remote monitoring + remote interrogations) versus telemonitored patients with in-clinic visits every 6 months reported non-inferior results, whereas the time a physician/nurse spent per patient/follow-up was significantly reduced.[54] Other strategies may

include task-shifting (e.g. specialised nurses being in charge of monitoring alerts), increasing the medical workforce, or limiting reinforced monitoring to specific categories of frail patients. Assessing the feasibility and effectiveness of such strategies was beyond the scope of this report.

Evidence on the remote monitoring of both defibrillators and pacemakers present some limitations. First, methods were heterogeneous across studies. For example, the frequency of data transmission and review by the clinic varied widely, from once a day to once every 6 months, as well as the number of scheduled in-clinic visits, and duration of follow-up. Definition of some outcomes (adverse events, quality of life) could also differed substantially across studies. Standard of care may also vary between countries, hospitals and treating physicians, and the benefit of remote monitoring ultimately depends on the adaptation of the treatment according to parameters measured.[14] These sources of heterogeneity make it difficult to draw conclusions that would be valid for all patients and all settings.

Second, for most of the outcomes except the number of in-clinic visits, the number and size of studies were relatively limited, and this was particularly true for pacemakers' evaluation. Moreover, most of the primary studies were not powered to detect outcomes such as hospitalisation, stroke or mortality. Even in meta-analyses, numbers were quite limited for many outcomes. For example, in our updated meta-analysis on stroke incidence in patients with ICDs or CRT-Ds, only 3 studies accounting for 2 122 patients and 21 events were included. This said, although the statistical power was much better for heart failure hospitalisation, no difference was detected between groups neither. To detect an effect on mortality would have required bigger sample sizes and/or longer study duration. For example, some observational studies based on patient registries reported a reduction in all-cause mortality in patients with remote monitoring of their implanted cardiac devices.[55, 56] However, these studies are prone to bias, and particularly patient characteristics and clinical follow-up may have differed significantly between groups.

Third, authors of the Ontario-HTA reported that 8 studies on remote monitoring of ICDs or CRT-Ds were not published in peer-reviewed literature, two of which were terminated early.[2] Among these 8 studies, only one was published since the Ontario-HTA was published (Versteeg et al. 2019)[24] and included in our update. These unpublished studies could result in a significant publication bias, and the direction of this bias on our results is unknown.[2, 14]

Finally, a big proportion of studies were relatively old, and the performance of devices and clinical practice may have evolved meanwhile. For example, a recent study reported that a new algorithm for early detection of impending decompensation in heart failure patients allowed a significant reduction in hospitalisation for decompensated heart failure.[57] However, the results of this small size (n=74; 8% lost to follow-up) non-blinded single-arm trial with historical comparison need to be confirmed.

4.4.2 Implanted loop recorders

For ILRs, no RCTs were retrieved and the 4 observational studies included in the HAS-HTA had a small size and presented a high risk of bias.[10] The clinical benefit of remote monitoring of patients with ILRs is thus not substantiated by direct scientific evidence.[10] However, experts consulted by the HAS inferred that remote monitoring of ILR would minimize the risk of patients being lost to follow-up, reduce time to event detection and allow an earlier start of treatment. This would be particularly important for the early detection of auricular fibrillation in patients with cryptogenic strokes. This line of arguments makes sense as time reduction from event onset to detection was also observed for defibrillators and pacemakers, although confirmatory scientific evidence is lacking. It has also been proposed that the frequent upload of data by remote monitoring could reduce the risk of data loss due to memory saturation of the device.[49] However, the HAS-HTA report mentioned it is unclear if this applies to most recent ILR models with advanced programming options.[10]

5 COST-EFFECTIVENESS OF REMOTE MONITORING

5.1 Introduction

This chapter provides an overview of economic evaluations on remote monitoring of adults implanted with cardioverter defibrillators (ICDs), cardiac resynchronization therapy without (CRT-Ps) or with defibrillation (CRT-Ds), permanent pacemakers (PMs), or implantable loop recorders (ILRs). The aim is to evaluate the potential cost-effectiveness of this monitoring method, as an alternative to in-clinic visits.

5.2 Methods

5.2.1 Search strategy

A two-step process was pursued to ensure that good quality HTA reports (including an economic component) on our topic of interest would be considered. First, the websites of Health Technology Assessment (HTA) institutes listed on the EUnetHTA (European Network of Health Technology Agencies) and the INAHTA (International Network of Agencies for Health Technology Assessment) websites were searched (search date: July 2020, updated in March 2021) via their respective databases[a] to capture recent (published from 2010) reports on remote monitoring for patients implanted with cardiac devices. Search terms used in the INAHTA database were: "(cardiac) AND ((monit*) OR (remote) OR (tele*))". In the EUnetHTA database, a broad search using the MESH term "C14 - Cardiovascular Diseases" was applied.

If any relevant, recent HTAs were identified (i.e. HTAs including a review of economic evaluations and/or an original economic model), a quality appraisal was performed and only high to moderate quality assessments (according to the AMSTAR 2 tool[11]) were retained. Such HTAs were then, considered as the starting point of the review, but all original evaluations included in them were revisited to ensure consistency in the data extraction, and no results or appraisal were taken directly from the HTA.

A second step consisted of a systematic search for relevant economic evaluations carried out from the search date of any relevant HTAs identified during the first step. This approach was thought to be a valuable method to avoid a duplication of efforts and focus instead on updating the existing research base. If no relevant HTAs were found, this systematic search was carried out for the period 2000-July 2020.

Medline (through OVID), EMBASE, COCHRANE, CINAHL, NHSEED (CRD) and NHSHTA (CRD) were searched to retrieve primary full economic evaluations (studies comparing at least two competing alternatives in terms of both costs and outcomes) and systematic reviews of economic evaluations (i.e. secondary economic evaluations). An overview of the search strategy is given in the appendix to this chapter.

No restrictions were imposed for language. The search strategy was performed by an expert information analyst and checked by a second researcher.

5.2.2 Selection procedure

To identify potentially relevant studies for our analysis all titles and abstracts were checked, in order to exclude any obvious studies that did not match our research subject. All articles that appeared to be interesting, or for which there were some doubts, were read in full in order to select those pertinent for inclusion in our review.

Reference lists of the selected evaluations found via our search were checked for additional studies worth adding to our analysis.

Study selection was completed by one researcher but any doubts that came up during the exercise were discussed and solved in collaboration with a second reviewer.

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[a] INAHTA: https://database.inahta.org/
EUnetHTA: https://eunethta.eu/pop-database

The critical appraisal of all individual studies included in our review was based on the checklist designed by Drummond et al.[58]

5.2.3 Selection criteria

All full economic evaluations focusing on remote monitoring as a potential method for following-up patients implanted with cardiac devices were included in our review. Cost descriptive analyses or cost comparisons not taking into consideration effectiveness, as well as cost consequences analyses (considering costs and effects separately), were excluded from this review.

Similarly, a decision was made to exclude publications in the form of letters, editorials or notes and abstracts, since these would not offer enough information to include them in our analysis and critically appraise their findings. An overview of the inclusion/exclusion criteria is given in Table 9.

Table 9 – Selection criteria for economic evaluations

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Patients implanted with: ICDs; CRT-Ps; CRT-Ds; PMs or ILRs	Any other patient.
Intervention	Remote monitoring or a combination of remote and in-clinic visits	Non-remote monitoring systems
Comparator	In-clinic visits only	Combinations or remote + in-clinic monitoring systems
Design	High or moderate quality HTAs; CUAs; CEAs; CMAs	Low quality HTAs; cost descriptive analysis; cost comparisons and CCAs
Type of publication	Articles or reviews	Letters; editorials; notes; abstracts and posters

CCA: Cost consequences analysis; CEA: Cost-effectiveness analysis; CMA: Cost-minimisation analysis; CRT-D: Cardiac resynchronization therapy with defibrillation; CRT-P: Cardiac resynchronization therapy without defibrillation; CUA: Cost-utility analysis; HTA: Health technology assessment; ICD: Implantable cardioverter defibrillator; ILR: Implantable loop recorder; PM: Pacemaker

5.2.4 Results

5.2.4.1 Search for HTAs

The search for HTAs in the INAHTA returned 43 reports, while the search in EUnetHTA POP database identified 63. Only 4 reports focused on the relevant topic and included a review of economic evaluations and/or an original economic model. From these, one published in 2012,[59] did not identify any economic evaluations at the time of their search. From the remaining three, two were carried out by the same agency,[60, 61] the more recent of them consisting of a partial re-submission of the former. These two proved to be short reports offering little detail regarding their methods and results. The last one, a more recent study of high quality (according to AMSTAR 2[11] – See the appendix) by Health Quality Ontario (HQO)[2] was finally used as the starting point of our literature review. This report did not include ILRs and focused instead on ICDs, CRT-Ps, CRT-Ds and PMs.

One HTA on remote monitoring of ILRs was identified in the EUnetHTA POP database (performed by the HAS, as mentioned in the chapter on clinical evidence), but it did not include a review of economic evaluations or an original economic model, and therefore, it could not be considered in this chapter.

5.2.4.2 Search for primary and secondary economic evaluations

For PMs, ICDs, CRT-Ps and CRT-Ds, the search for primary studies was carried out from the search date of the Canadian HTA identified during the first step of this review (i.e. June 2017).[2]

Given the lack of relevant high or moderate HTAs on ILRs including economic evaluations, the search for primary studies for ILRs was carried out separately, for the period 2000-January 2021.

Primary and secondary economic evaluations on ICDs, CRT-Ps, CRT-Ds and PMs

Our systematic search for primary and secondary economic evaluations for ICDs, CRT-Ps, CRT-Ds and PMs returned 98 citations, after eliminating duplicates. Of those, 88 did not meet our inclusion criteria based on a review of their title and/or abstract. Of the 10 citations left, 5 were excluded after reading their full text because of the study design (3), publication type (1) and focus (1), which left us with 5 relevant studies to be considered in our review, including the Canadian HTA report. To these, the 4 studies identified in the latter, were added. Further exploration of the references of the selected articles did not result in the identification of any additional study that could be of interest to our research. Therefore, overall, 9 full economic evaluations for ICDs, CRT-Ps, CRT-Ds and PMs were included in our review. Out of these, one consisted of an HTA report, which included the development of an original cost model,[2] while a further one published in 2014, provided a review performed by the Australian Medical Services Advisory Committee on the basis of a model completed by the industry.[60, 61]

Primary and secondary economic evaluations on ILRs

The systematic search for primary and secondary economic evaluations for ILRs (search period 2000-January 2021), returned 318 studies, after eliminating duplicates. Of those 294 did not meet the inclusion criteria based on title and abstract. Of the 24 citations left, and after having read their full text, 1 was excluded based on the publication type (i.e. abstract), a further one based on its focus (i.e. wrong intervention), while the study design was the reason for exclusion for 4 studies. The remaining 18 were also excluded because they compared ILRs with other non-implantable monitors or diagnostic tools. They, therefore, did not focus on the remote monitoring aspect.

Our literature selection process is illustrated in two flow charts (see Figure 11 and Figure 12).

Figure 11 – Flow-Chart Selection Process Economic Evaluations on ICDs, CRT-Ps, CRT-Ds or PMs

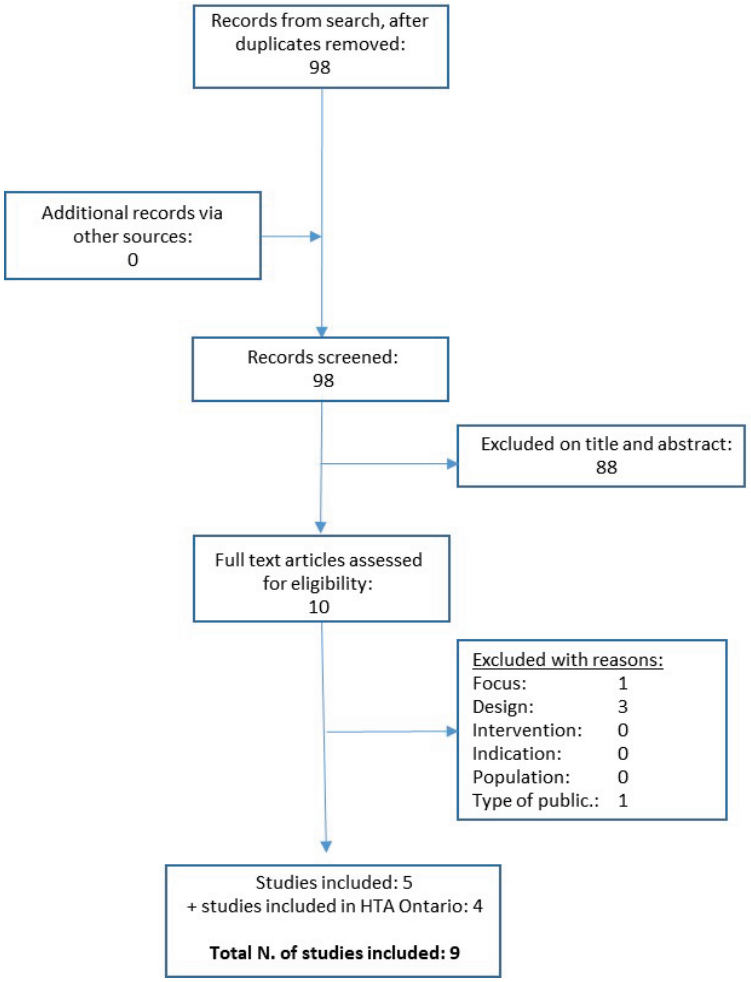
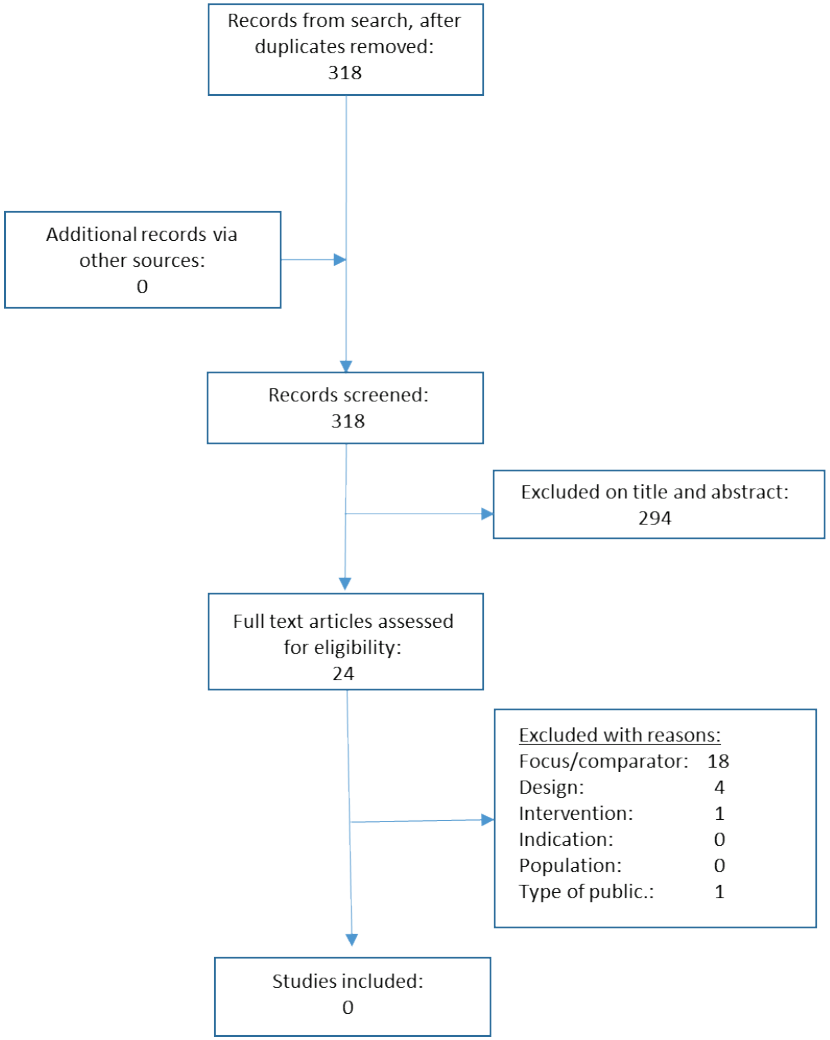


Figure 12 – Flow-Chart Selection Process Economic Evaluations on ILRs



5.3 Overview of economic evaluations on PMs, ICDs, CRT-Ps and CRT-Ds

As shown in Table 10, four studies were undertaken in Western Europe: two in Italy,[62, 63] one in Spain[64] and one in France.[15] A further study was undertaken in Eastern Europe, and more specifically in Poland,[65] one more in the USA,[66] one in Canada,[2] and two in Australia.[60, 61] However, the Australians were counted as one single study, since the most recent of them[61] provided a partial re-submission of the same CMA presented in the original application.[60] A final international study was carried out in five different countries, including the USA, and four European countries (France, Germany, Italy and the UK).

All studies were published after 2010, and six of them[2, 15, 62, 64-66] in 2017 or after, reflecting the importance that the topic has gained in recent years. Four studies[2, 15, 66, 67] were model-based (decision-tree and/or Markov models). Three studies were trial-based.[62-64] The evaluation by Curila et al.[65] consisted of a retrospective data analysis, while the Australian study by the MSAC,[60, 61] did not offer any details on the analytic technique used.

5.3.1 Type of economic evaluation

Table 10 illustrates that five of the studies performed cost-utility analyses (CUA),[2, 15, 62-64] all of which expressed their clinical outcomes in terms of quality-adjusted-life-years (QALYs). Two[60, 61, 65] carried out a cost minimisation analysis (CMA), one of which[4] also pursued an exploratory cost-effectiveness analysis (CEA). Finally, two[66, 67] carried out both cost-utility and cost-effectiveness evaluations with results reported as cost per QALY and cost per life-years saved (LYS) respectively.

5.3.2 Perspective

Five studies were performed from a third party payer perspective,[2, 60, 61, 65-67] and one from a health care system perspective.[15] The remaining three considered also a patient or carer perspective in addition to a health care system[64] or a third party payer[62, 63] perspective. (See Table 10 for details).

5.3.3 Modelling

Only two studies consisted of Markov models and both considered 1-month cycles in their evaluations. The first of these evaluations, published in 2020 by Sequeira et al.,[15] focused on ICDs with or without re-synchronisation (ICDs and CRT-Ds), and kept the structure of their model simple, with only three mutually-exclusive health states: 1. stable outpatient (initial state); 2. hospitalisation due to a cardiovascular event; and 3. death. The second study, carried out by the Ontario group,[2] performed two separate models, one for ICDs/CRT-Ds, and another for PMs. Both models used four health states. In the ICD/CRT-D model, these were: 1. stable heart failure; 2. NYHA functional classes (from I to IV); 3. year 1 post-hospitalisation and 4. death. In the PM model, they were: 1. stable arrhythmia; 2. year 1 post-hospitalized non-stroke related; 3. post stroke and 4. death.

Two of the remaining models consisted of decision-analytic models;[66, 67] while a further by the MSAC[60, 61] did not offer a detailed description of the models they received from the industry. The remaining offered either trial-based evaluations, for which no modelling was performed,[62-64] or retrospective data analyses.[65]

5.3.4 Time frame of analyses and discounting

Table 10 also summarises the time frame of the economic evaluations included in this review, as well as the type of discounting applied. Three out of the four model-based evaluations identified[2, 15, 66] looked at costs and outcomes over a time period longer than one year, and amongst them, only Hummel et al.[66] considered a patient's lifetime, with two others,[2, 15] limiting the analysis to 5 years, and justifying it as reflecting the mean lifespan of the battery of the implanted devices.

The least recent of all model-based analyses, studied costs and outcomes over 1 year.[67] This was the same time frame used by two of the three trial-based evaluations,[62, 64] with the third one, looking at a slightly longer time frame of 16 months.[63] Finally, the retrospective data analysis looked at cases registered between the year 2002 and the 2015, although the study did not give any details on the mean follow-up per patient or the number of patients who went missing during the study.[65]

All three evaluations presenting a time frame longer than a year, discounted costs and outcomes and gave information on the rates used. The study by Ontario[2] used 1.5% for both costs and outcomes in their base case scenario, reflecting Canadian recommendations.[68] Hummel et al.[66] used 3% following the most recent USA guidelines[69] and Sequeira et al.[15] referred to discount rates of 4% for both costs and outcomes, in accordance with the recommendations of the Haute Autorité de Santé (HAS) at the time of their publication,[70] although the latter have since, been updated and changed.[71]

Table 10 – Characteristics of selected economic evaluations

Author	Year	Country	Type of evaluation	Perspective	Analytic technique	Discount rate; both costs and outcomes (%)
Sequeira	2020	France	CUA	Health care system	Markov Model	4%
Hummel	2019	USA	CEA/CUA	Health care payer	Time to event simulations	3%
Lopez-Villegas	2019	Spain	CUA	Health care system and patient/family carers	Trial based (PONIENTE)	NA
Curila	2018	Poland	CMA	Health care payer	Retrospective data analysis	NA
Ontario	2018	Canada	CUA	Health care payer	Markov model	1.5%
Ricci	2017	Italy	CUA	Health care payer and patient	Trial based (TARIFF)	NA
MSAC (application n°1197 and 1197.1)	2014	Australia	CMA/CEA	Health care payer	Not specified	NA
Zanaboni	2013	Italy	CUA	Health care payer and patient	Trial based (EVOLVO)	NA
Klersy	2011	USA, Italy, France, Germany, UK	CEA/CUA	Health care payer	Decision-analytic model	NA

CEA: Cost-effectiveness analysis; CMA: Cost-minimisation analysis; CUA: Cost utility analysis; MSAC: Medical Services Advisory Committee; NA: Not applicable (since time horizon of study ≤1 year).

5.3.5 Population

Table 11 summarises the populations reflected in the different evaluations. Overall, four studies identified in our review focused on patients implanted with ICDs and CRT-Ds,[15, 62, 63, 67] while the evaluation by Hummel et al.[66] made no specific reference to resynchronisation and mentioned only patients implanted with ICDs compatible with remote monitoring, without a clear, detailed description of the types of ICDs covered.

Two studies focused on patients implanted with PMs,[64, 65] while a further two, included both patients implanted with ICDs or CRT-Ds, and patients implanted with PMs.[2, 60, 61] No economic evaluations were found specifically on patients implanted with CRT-Ps.

All studies which reported the gender of patients showed to have a large majority of males.

The mean age mentioned in the trial or registry-based evaluations varied from 69 to 78 years.[62-65] reflecting the fact that most cardiac devices are implanted in older populations.

5.3.6 Intervention and comparator

A description on the interventions studied and the comparators used is offered in Table 11. Overall, four evaluations did not specify or define in detail the intervention (i.e. remote monitoring), while a further four, described remote monitoring as a combination of remote interrogations combined with more or less frequent in-clinic visits. The least recent of all studies,[67] did not define any frequencies, and included within the remote monitoring arm, not just technology-assisted monitoring but also telephone monitoring.

In addition to the scheduled remote monitoring interrogations or in-clinic visits, all evaluations also considered unscheduled in-clinic visits prompted by the remote monitoring interrogations.

The comparator was in all cases described as in-clinic visits only, which were also linked to specific annual frequencies.

5.3.6.1 Frequency of remote interrogations and in-clinic visits

For patients implanted with ICDs or CRT-Ds:

The frequency of in-clinic visits accounted for in the RM arm, varied from one annual visit in three of the studies[2, 60-62] to one every eight months.[63] The evaluations that specified the timing of the remote interrogations, varied from one per year[2] to every three months,[60-62] with Zanaboni et al.[63] foreseeing a RM interrogation every 8 months.

The frequency of the in-clinic visits used as comparators (in-clinic visits only), ranged from a low of one visit every six months,[2] to a high of one visit every three months[60-62]

For patients implanted with PMs

The two studies that focused purely on PMs[64, 65] did not offer any detailed definition of the intervention, but two studies including both ICDs/CRT-Ds and PMs assumed a lower frequency of remote interrogations for PMs (every 6 months to every 2 years) than for ICDs (every 3 months to every year).[2, 60, 61] These remote interrogations were combined in the case of PMs with in-clinic visits every one[60, 61] to two years.[2]

The frequency of in-clinic visits used as a comparator (in-clinic visit only) ranged from one every 6 months[60, 61] to one every year.[2]

Table 11 – Population and Intervention/comparator in selected economic evaluations

Author	Implanted device	Intervention/Comparator	Population
Sequeira 2020	ICD/CRT-D	RM/CM (as described in the studies considered in their Meta-analysis)	Patients with ICD with or without resynchronization. Mean age: 54.7 to 69.5. Majority males. LVEF: 20.4% to 40%
Hummel 2019	ICD	RM/ CM	Medicare patients with RM-capable ICDs; (from PREDICT RM database)
Lopez-Villegas 2019	PM	RM/CM (hospital follow-up)	82 patients with an internet-based transmission PM. Mean age: 77.57. Mostly males
Curila 2018	PM	RM/CM (outpatient follow-up)	217 patients (mean age 75), with a PM replacement in 2002-2015. 34% with coronary artery disease. 1/2 single chamber device
Ontario 2018	ICD/CRT-D and PM	ICD/CRT-D: RM interrogations alternated with in-clinic visits every 6 months/ in-clinic visits-only (every 6 months) PM: RM interrogations alternated with in-clinic visits every 12 months/in-clinic visits-only (every 12 months)	ICD or CRT-D: Adult patients with HF, 3 months after implantation. Mean age: 65; 70% males; NYHA class II. PM: Adults with arrhythmia. Mean age: 70 years; 65% males.
Ricci et al. 2017	ICD/CRT-D	RM (interrogations at 3,6,9 months and in response to alerts) + 2 in-clinic visits (at baseline & 12 months) vs in-clinic visits-only (at 3, 6, 9, & 12 months)	Mean age 69. Implanted with St. Jude Medical implants (single chamber ICD, dual chamber ICD, CRT-D). 85% male
MSAC 2014	ICD/CRT-D and PM	RM (one annual in-clinic visit + RM interrogations every 3 months for ICR/CRT-Ds and every 6 months for PM + response to alerts/in-clinic visit-only (every 6 months for PM; every 3 months for ICD or CRT-D)	Patients implanted with Biotronik CardioMessenger implants (PM, ICD, CRT-D). Included patients at risk for sudden cardiac death, & patients with chronic HF (except NYHA IV)
Zanaboni et al. 2013	ICD/CRT-D	RM (in-clinic visits at 8 & 16 months + RM interrogations at 4 & 12 months)/in-clinic visits-only (at 4, 8, 12, & 16 months)	HF implanted with Medtronic CareLink home monitor defibrillators (ICD, CRT-D) Median age: 66-69; 79% male
Klersy et al. 2011	ICD/CRT-D	RM: frequency of interrogations not defined; included: telephone monitoring and technology-assisted monitoring/in-clinic visits-only: frequency not defined.	HF patients (from RCTs) with ICD and CRT-D

CRT-D: Cardiac resynchronization therapy with defibrillation; HF: Heart failure; ICD: Implantable cardioverter defibrillator; PM: Pacemaker; RM: Remote monitoring; CM: Conventional monitoring (i.e. in-clinic visits only).

5.3.7 Cost and outcome inputs

Costs were derived from different sources depending on the study, including health insurance administrative data, reimbursement claims or hospital accounting. Only one evaluation[60, 61] did not specified their source, although they were probably derived from DRGs and tariffs. The three studies that included the patient's perspective, captured relevant patient costs via questionnaires.[62, 64]

With regard to cardiovascular events and mortality outcomes, all studies used for their models data obtained from the literature, or specific trial data, with the exception of the study by Hummel et al.[66] which used data from a US patient registry (the PREDICT RM database). The most recent evaluation,[15] captured data from the trials included in their own MA, which considered 17 RCTs overall. However, the outcomes used as inputs in their analyses referred mostly to two trials: the ECOST[33] and the EVOLVO (n=200).[63]

The three trial-based evaluations captured their outcome data during their studies.[62-64] All of these trials were short-term studies with relatively small sample sizes, (n < 210 patients overall) and only one, was randomised.[63]

The remaining three evaluations considered data from their own Meta analyses (MAs),[2, 67] or from one specific trial (the IN-TIME trial) in the case of the Australian evaluation,[60] for which a model was provided by the industry to the authorities. Unfortunately, the latter, only considered outcomes in an explorative CEA and did not offer enough detail to appropriately assess the validity of their evaluation.

Quality of life is an important factor to bear in mind when studying chronic conditions. QoL values for the three trial-based studies[62-64] were captured during the studies by means of the EQ-5D questionnaire,[a] while the remaining four cost-utility evaluations[2, 15, 66, 67] based their utility assumptions on literature. From the three studies published after 2013, two focusing on ICDs,[2, 15] based their assumptions on the cost utility study of the EVOLVO trial,[63] while the remaining,[66] a USA based study, based their assumptions on a less recent manuscript on preference-based EQ-5D scores for chronic conditions in the USA.[72] The Canadian model specifically designed for PMs,[2] derived their utilities from Comoretto et al.,[73] who used a visual analogue scale (VAS) to capture their values in elderly patients who had been implanted with PMs. The least recent study[67] based their assumptions on a cost-utility study published in 2008 by Herbert at al.,[74] during which the Health Utilities Index Mark 3 (HUI3)[b] was used.

5.3.8 Results

5.3.8.1 Incremental costs:

Table 12 shows the incremental costs obtained in the nine studies included in our review. Comparisons between studies are difficult primarily because of the different costs borne in mind but also due to the different time horizons used for the calculations.

a https://euroqol.org/eq-5d-instruments/

b http://www.healthutilities.com/hui3.htm

Table 12 – Incremental costs in selected economic evaluations

Author	Costing year	Time horizon (years)	Costs included	Cost source	Mean incremental cost (CM vs RM) over study period
Sequeira 2020	NA	5	RM unit, ambulatory follow-ups; transport; CV treatments and procedures; hospital costs (CV disorders)	Health insurance billing	€4142.32
Hummel 2019	2016	Lifetime	Hospital costs, outpatient costs, physician (specialists and GP) costs	DRGs (hospital) and claim costs (outpatient)	-US$6914 (-€5684); (CM: US$99 815; RM: US$106 729)
Lopez-Villegas 2019	NA	1	To the NHS: hospital staff time, consultation room, ambulance and hospitalisation. To patients and carers: Income lost (patients and carers) on office visits & transport costs.	Accounting and questionnaires	€104.94 (CM: €183.27; RM: €78.33; p<0.001)
Curila 2018	2015	NA	RM unit; RM costs; outpatient check-ups & unscheduled outpatient in-clinic visits	Reimbursed medical procedures (weighted codes)	-CZK25 787.66 per patient; (≈-€1013.20/patient)
Ontario 2018	2017	5	Scheduled and unscheduled in-clinic visits; reimbursement of remote interrogations; ED visits; Hospitalisation; RM costs (home transmitter hardware and connection accessories); post stroke care; battery replacement & transport.	Insurance admin data. Discussions with the MoH, nurses associations and industry	ICD/CRT-D: -CAN$4354.10 (-€2959.05); (CM: CAN$ 55 137.74; RM: CAN$ 59 491.84); PM: CAN$ 2370.14 (€1610.75); (CM:CAN$ 32 766.66 CM vs RM: CAN$ 30 396.52)
Ricci et al. 2017	NA (from Dec 2009 to March 2011)	1	To health care system: Urgent and non-urgent clinic visits, scheduled and unscheduled remote follow-up examinations, ED visits, hospitalisations, & diagnostic tests. To patients: Transport, productivity loss, impact on daily activity; assistance.	To health care system: Reimbursement rates and tariffs. To patients: costs captured during study (TARIFF)	Health care payer: €562.02; p <0.0001 (CM: €1044.89 ± SD 1990.47 per person per year; RM: €482.87 ± 2488.10 per person per year); Patient: €112.62; p <0.0001 (CM: 169.49 ± 189.50; RM: 56.87 ± 80.22)
MSAC 2014	NA	1	RM unit, scheduled and unscheduled visits. Not reported in detail.	Probably from DRGs and tariffs, but not specified.	ICD or CRT-D: AU$349 (≈€227.08); (CM: AU$8960; RM: AU$8611). PM: AU$0.71 (€0.45)
Zanaboni et al. 2013	2010	1.33	Payer perspective: Urgent and non-urgent in-office visits, scheduled and unscheduled remote follow-ups, ED visits, hospitalisations, and diagnostic examinations. Cost of RM assumed to be equal to a clinic visit. Patient perspective: transport to in-office and ED visits and productivity losses.	Reimbursement tariffs. RM assumed to cost the same as a clinic visit.	Payer perspective: €167.23/year; p = 0.80. (CM:€2130.01 vs RM: €1962.78; P=.80).; Patient perspective: €89.98/year (CM: €381.34 vs RM: €291.36; p=0.01)

Klersy et al. 2011	NA	1	Hospitalisation	Based on DRGs (in some EU countries and the US)	€451.49 (CM: €1458.66; RM: €1007.17)

CM: Conventional monitoring; CRT-D: Cardiac resynchronization therapy with defibrillation; CV: Cardio vascular; DRG: Diagnostic related groups; ED: Emergency department; GP: General practitioner; ICD: Implantable cardioverter defibrillator; MoH: Ministry of health; NA: Not available; NHS: National health system; PM: Pacemaker; RM: Remote monitoring.

Most studies included scheduled and unscheduled in-clinic visits and hospitalisation or ED costs, while the oldest study by Klersy et al.[67] focused purely on hospitalisation costs. The cost of the monitoring unit was made explicit in few studies.[2, 15, 61, 65]

The three studies offering a patients' perspective included transport costs for patients as well as productivity losses.[62-64]

The majority of the included studies showed savings linked to RM use compared with in-clinic visits only. The mean annual savings ranged from € 167[63] to € 828[15] for ICDs and CRT-Ds, and from € 0.45[60] and € 322[2] for PMs, depending on the costs considered, while three studies out of the nine found RM to be more expensive than in-clinic visits only.[2, 65, 66]

Two of the four studies looking at PMs showed that RM for these implants would be cost-saving,[2, 64] while a third evaluation showed it to be practically cost-neutral.[60, 61] The last study, found RM to be cost-additive, with a cost difference of CZK 25 787.66 per patient (≈€ 1013.20).[65] It is important to mention that the later consisted of a CMA, in which only costs were considered, and which was based on a retrospective review on a limited number of patients (n=217) registered over a considerably large time period (2002-2015), over which remote monitoring practices may have evolved.

When looking at the evaluations on ICDs, five out of the seven evaluations found RM to be cost-saving, with the remaining two[2, 66] finding an incremental cost of US$ 6914 ≈€ 5684 for RM over the study period (25 years) in the case of Hummel et al.[66] and of CAN$ 4354.10 (≈€ 2959), over a 5 year period, in the Canadian study.[2] It is important to note, that these two studies, were, together with the study by Sequeira et al.,[15] (which found annual savings of ≈€ 828) linked to RM), the only three studies which considered a time horizon longer than one year.

Some of these studies assumed the costs of a RM interrogations to be equal to that of a clinic visit.[2, 63, 65] However, others, did not include such costs,[15, 62, 67] or their inclusion remained unclear (no details offered).[60, 61, 66] Even in those cases where equivalence in costs was assumed, less time was assumed to be required during remote interrogations,[2] or reductions in costs were assumed in case there was no need to follow the remote interrogation by a call to the patient.[63]

The costs of remote monitoring units, as well as transmitters were made explicit only in a few of the studies included in this review.[2, 61, 65] When included, they ranged from a min of € 450 (specifically for PMs) or € 864 (for ICDs), to a high of ≈€ 1900 for both devices. Only one of the studies considering a longer time horizon, included these costs in their base line calculations,[15] although a further, examined different scenarios for line items and home transmitters.[2] In these two recent, longer time horizon evaluations, the RM unit costs and services used were of € 1150 and € 864 for ICDs and of € 450 for PMs.

Table 13 summarises the incremental outcomes obtained in the different studies included in this review. All studies which considered outcomes (i.e. CUA or CEA), reported positive clinical effects for RM when compared to in-clinic visits only.

Table 13 – Incremental outcomes in selected economic evaluations

Author	Outcomes	Source of outcomes	Incremental LYG RM vs CM	Incremental QALYs RM vs CM
Sequeira 2020	QALYs	Trials included in MA (mainly ECOST and EVOLVO)	NA	0.29
Hummel 2019	LYG/QALYs	From literature (Sullivan 2006)	0.77 (RM: 7.62; CM: 6.85)	0.64 (RM: 6.29; CM: 5.65)
Lopez-Villegas 2019	QALYs	Trial (PONIENTE); EQ-5D questionnaires	NA	0.09 (RM: 0.87; CM: 0.78; p=0.173)
Curila 2018	NA	NA	NA	NA
Ontario 2018	QALYs	Trials and published literature	NA	ICD/CRT-D model: 0.19 (RM: 2.56; CM: 2.38); PM model: 0.12 (RM: 2.76; CM: 2.64)
Ricci et al. 2017	QALYs	Trial (TARIFF); QoL: EQ-5D at baseline and 12 months	NA	0.02; p=0.53 (RM: 0.87 ± SD 0.13 QALYs; CM: 0.85 ± SD 0.17)
MSAC 2014	LYG	IN-TIME trial (ICDs-CRT-Ds) and COMPASS trial (PMs). Safety from other trials.	0.11	NA
Zanaboni et al. 2013	QALYs	From trial (EVOLVO); QoL: EQ-5D	NA	0.065 (RM: 1.032; CM: 0.966; p=.03)
Klersy et al. 2011	QALYs	Data from the literature: Utility from Herbert et al. 2008. Mortality from a MA (Klersy et al. 2009)	NA	0.06

CM: Conventional Monitoring; CMA: Cost minimisation analysis; CRT-D: Cardiac resynchronization therapy with defibrillation; ICD: Implantable cardioverter defibrillator; LYG: Life years gained; MA: Meta-analysis; NA: Not available; PM: Pacemaker; QALYs: Quality adjusted life years; QoL: Quality of life; RM: Remote monitoring.

The seven studies looking at ICDs, showed gains in QALYs ranging from a low of 0.02; (p=0.53),[62] to a high of 0.64.[66] However, it is important to note that only three of these studies considered medium to long time horizons,[2, 15, 66] while the remaining, including the study by Zanaboni et al.[63] limited their analyses to the short term.

Looking at the clinical outcomes obtained in the four studies carried out on patients implanted with PMs, one of the studies[65] did not considered outcomes, since it consisted of a CMA, while the other three (2 CUAs and 1 CEA), all showed positive results for the RM option, with Lopez-Villegas et al.,[64] reporting an incremental gain in QALYs of 0.09 (p=0.173), and the Canadian study,[2] showing gains of 0.12 QALYs. The remaining study,[60] provided an explanatory CEA that showed an increment in LYG of 0.11 in favour of RM.

5.3.8.2 *Incremental cost-effectiveness ratios (ICERs)*

Table 14 shows that overall, five studies from the eight that calculated ICERs, reported RM to be the dominant strategy.[15, 62-64, 67] Two CUAs found ICERs well below the countries' specific willingness to pay thresholds, with the US study by Hummel et al. reporting an ICER of US$ 8 966 per QALY[66] and the Canadian evaluation[2] showing an ICER of CAN$ 23 374 per QALY. Finally, an Australian CEA, resulted in an ICER of AU$ 26 269.70 per LYG. Nevertheless, it is important to highlight that given the purely exploratory nature of this study, the lack of detail and description makes it hard to evaluate the validity of their results. When separating the results per intervention, we can observe that the two only evaluations estimating ICERs for PMs,[2, 64] both showed RM to be the dominant strategy, despite basing their outcomes data on different trials and covering different costs. From the studies covering ICDs or CRT-Ds, four found RM to be dominant, while a further three reported the previously mentioned ICERs: from ≈€8847 to ≈€15 248 per QALY in the two CUAs[2, 66] and from ≈€7377 to ≈€17 081 per LYG in the CEAs.[60, 66] All evaluations which calculated ICERs considered RM to be a cost-effective alternative to conventional in-clinic-based follow-ups.

5.3.8.3 *Sensitivity Analyses*

Three of the studies included in this review did not perform any sensitivity analysis (SA).[60, 61 , 64, 67] The CMA by Curila et al.,[65] carried out a one-way SA testing the impact that changes to the different costs (including that of the monitoring unit), as well as to the number of controls and checks, could have on their results and confirmed the robustness of their findings, showing that RM for PM would be cost-additive when compared to and exclusively in-clinic visit-based follow-up. Two studies focussed on ICDs with or without re-synchronisation and limited their SA to testing just one scenario. First, Ricci et al.[62] who assumed a zero cost for scheduled and unscheduled RM interrogations in their base case scenario (and justified it by the fact that no reimbursement for these were available in Italy at the time of their study), run a further analysis, assuming an equivalent tariff to that of an in-clinic visits follow-up, for the RM interrogations and transmissions, which resulted in an annual per patient cost of €128, still representing savings for the RM group, since the main cost driver in this non randomised, retrospective analysis study proved to be CV hospitalisations. Zanaboni et al.[63] tested a one-off device fee to manufacturers of €900 per patient, to cover for renting the remote monitoring unit, the network server, and the website. This scenario also confirmed their base case findings (RM is a dominant strategy).

Only two evaluations performed probabilistic SA. These were the study by Sequeira et al.[15] which focused on ICDs or CRT-Ds and the Canadian study[2] which looked at both ICDs/CRT-Ds and PMs. A further study[66] also on ICDs/CRT-Ds pursued a one-way SA and a scenario analysis. All of these three evaluations confirmed their results and found RM to be a cost-effective option when compared to clinic visits only (see Table 14 for more details).

5.3.8.4 *Conflict of interest*

All nine studies included in their manuscripts a declaration of conflict of interest for their authors. From these, only three[2, 64, 65] reported no conflict. Looking in more detail to the three longer time horizon studies, only one, the Canadian study, reported no conflict of interest.[2] The existence of conflicts of interest may introduce a bias which could affect the validity of the study results, although there is, up to date, no hard evidence on this.

Table 14 – Incremental cost-effectiveness ratios in selected economic evaluations

Author	Intervention	ICER RM (vs CM)	Prob. Of RM being cost-effective	Sensitivity analysis performed or not	Result of sensitivity test
Sequeira 2020	ICD/CRT-D	RM dominant	RM dominant in 70% of cases	Probabilistic	ICERs: RM dominant in 70% of simulations
Hummel 2019	ICD	US$ 8966/LYG (≈€7377.35) ; US$ 10752 (≈€8846.90) /QALY	NA	Scenario analysis, one-way	Robust results
Lopez-Villegas 2019	PM	RM dominant	NA	NA	NA
Curila 2018	PM	NA	NA	One-way	Robust findings. RM more expensive than CM
Ontario 2018	ICD/CRT-D & PM	ICD/CRT-D: CAN$ 23 373.70 (≈€15 247.67) /QALY; PM: RM dominant	ICD/CRT-D: RM CE in 71% of cases at a WTP CAN$50 000 (≈€32 662.53) PM: RM dominant in 53% of cases.	Scenario analysis, one-way and probabilistic	Robust results
Ricci 2017	ICDs or CRT-D	RM dominant	NA	Scenario analysis	Robust results. RM still cost saving
MSAC 2014	ICDs or CRT-D & PM	2014 exploratory CEA: AU$ 26 269.70 (≈€ 17 081.44) /LYG	NA	NA	NA
Zanaboni et al. 2013	ICDs or CRT-D	RM dominant	NA	One scenario analysis	Robust results. RM dominant
Klersy et al. 2011	ICDs or CRT-D	RM dominant	NA	NA	NA

CEA: Cost-effectiveness analysis; CRT-D: Cardiac resynchronization therapy with defibrillation; ICD: Implantable cardioverter defibrillator; LYG: Life years gained; NA: Not available; PM: Pacemaker; RM: Remote monitoring; SA: Sensitivity analysis; CM: Conventional monitoring.

5.3.9 Discussion and limitations

Overall, the economic evaluations here considered appear to show a high level of consistency indicating that RM (in combination with in-clinic-based visits) is likely to be cost-effective compared to in-clinic visits only for ICDs, CRT-Ds and PMs (no studies on CRT-Ps were identified). However, despite this consistency there is a number of important points worthwhile considering that will be discussed in this section. Table 15 summarises key assumptions (for costs) and weaknesses liked to the data from which utilities have been derived for these evaluations, to highlight the importance of considering all these factors when appraising the existing evidence.

Table 15 – Key assumptions linked to costs and weaknesses linked to utility estimates

Author	Weaknesses linked to utility estimates	Key assumptions regarding costs of RM interrogations
Sequeira 2020	Point estimates for utility. taken from **EVOLVO, (non sig. differences).** From 1-16 months: assumed utility of the EVOLVO for both groups at baseline. After 16 months, the utility of EVOLVO at week 16.	Professional or physician fees for RM interrogations not included (based on ECOST trial)
Hummel 2019	Utility for chronic comorbidities from **Sullivan et al 2006.** Utility for rehospitalisation assumed 0 during length of stay.	Unclear. No detailed information offered
Lopez-Villegas 2019	Utility from **PONIENTE** trial (single centre non-randomised study (n=83)). Differences **non sig. in EQ-5D utility scores**, but **sig in EQ-5D VAS scores**.	Only physician time considered. Monitoring, data capturing and management and storage not considered. Patient's data in the RM arm reviewed daily. In-clinic visits left to physicians' discretion.
Curila 2018	NA	Assumed to be equal to normal in-clinic visits
Ontario 2018	ICDs/CRT-Ds - Point estimates for utility from **EVOLVO**, (**non-sig differences)**. PMs: **Comoretto** 2017 (non-randomised small sample study; n=42). **Non sig differences** on **EQ-5D**. **Sig diff** in 2 subscales of **Aquarel Scales**	Assumed equal to in-clinic visits (in cost/min), but less time assumed to be required for interrogations
Ricci 2017	From **TARIFF** study (observational; n=209). **Non sig differences** in utility.	Costs assumed to be 0, since not reimbursed. Only time to review transmissions considered
MSAC 2014	NA	Unclear. No detailed information.
Zanaboni et al. 2013	Point estimates for utility from **EVOLVO,** (**non-sig differences)**	Same cost as office-visit and 50% less if RM not followed by a call to the patient
Klersy et al. 2011	Point estimates for utility taken from a study looking at "nursing management" versus "usual management care". **Estimates not related directly to RM**	Unclear. Probably not considered

5.3.9.1 Sources of clinical data

Three of the evaluations were trial based, from which only one study was randomised. The remaining used trial data from the literature to populate their models. Overall, the existing trials, involved a limited number of patients and were carried out over short time horizon (i.e. 16 months or less), for all but three of the evaluations. From the latter, the only study considering the patient's lifetime, used observational data with patients being mostly followed for a limited time (mean of 2,5 years). Therefore, modelling these data required extrapolations, which were based on parametric survival fits to Kaplan-Meier curves. This showed most of the clinical benefits to be gained during the extrapolation period, and thus, being subject to important uncertainties. The two other model-based studies used mid-time horizons (i.e. 5 years). Although ideally, economic evaluations for chronic treatment/interventions should consider the entire lifespan of the patients, the authors of these two evaluations justified their approach, by the fact that 5 years represents the mean lifespan of the battery of these implanted cardiac devices, and that therefore, after such a period, other costs should come into consideration.

Despite the consistency in the findings, showing RM to be cost-effective, it is important to highlight that the estimates of utilities used to calculate QALYs in all CUAs included in this review, were derived from the numerical, but non-significant differences between RM and in-clinic visits only, from the RCTs reviewed in the clinical chapter of this research (see Table 15 and

chapter 4 for more details). This fact makes for the usual uncertainties linked to any modelling exercise to be even greater in this case.

5.3.9.2 *Model structure and assumptions*

The model structure was not explained in detail in some cases, and a number of important assumptions were made that may have had an important impact on the results of these studies. Thus, the number and frequency of RM interrogations as well as in-clinic visits was protocol imposed and, in some cases, they were not well explained or justified. In addition to this, the differences in these parameters from one evaluation to another, raise the question on how representative these would be of real clinical practice.

An important number of studies did not consider the cost of remote interrogations, and some, justified this by the fact that no reimbursement was available for such interrogations at that time[15, 62] (see Table 15 for more details). In addition to this, two out of the three studies assuming equal costs per equal time, assumed remote interrogations to take less time than in-clinic visits, therefore, favouring RM, and did not attempt to assess how realistic these assumptions would be.

Only three evaluations considered in their costing the price of the monitoring unit and some important costing factors appeared not to be considered in some of the models with the longer time horizons (e.g. Sequeira et al. did not considered staff time to manage alerts raised by RM).

All studies assumed that no additional staff would be needed to handle RM. However, one study (Lopez-Villegas et al) considered that RM data would be reviewed by a physician every day, while all others referred to specific timings for the RM interrogations.

5.3.9.3 *Transferability to the Belgian context*

No Belgian studies were identified and as a consequence, none of them evaluated remote monitoring from the perspective of the Belgian health care system.

Five studies were carried out in Europe (four in Western Europe and one in Eastern Europe).

Aside from the different perspectives and costs considered, the different definitions of RM used across studies, pose a particular challenge when it comes to assessing the generalisability of the results found to the Belgian context. Thus, while some studies did not provide detailed information on their definition of “remote monitoring”, most considered remote monitoring as a combination of remote interrogations and clinic visits. Frequencies of both clinic visits and remote interrogations varied greatly from one study to the other, (from one interrogation or clinic visit every 3 to 6 months for ICDs/CRT-Ds, and from 6 to 12 months for PMs). To these, responses to alerts need to be added but the frequency of these was most often not detailed in the studies here included. A further uncertainty is linked to the continuity or frequency of remote monitoring, since the studies appeared to include remote interrogations at specific points in time as an alternative to in-clinic visits. However, the “ideal” frequency of such interrogations was not explored and instead the frequencies were mainly imposed by protocols.

The assumption on additional resources is also a point worthwhile highlighting. In view of the results obtained in the survey carried out in Belgian hospitals, (see chapter 3 of this report) it appears that additional resources would be necessary to implement RM appropriately in this country. These were, nevertheless, not considered in the economic evaluations here described.

Finally, the great uncertainties previously discussed in the chapter on the review of the clinical evidence, with differences in key outcomes (i.e. mortality, hospitalisation rates, utilities, etc) not reaching clinical significance, despite generally favouring RM, make it necessary to interpret the results here presented with great caution.

6 EVOLUTIONS OF THE LEGAL FRAMEWORK IN BELGIUM

6.1 Introduction

Over the last ten years, eHealth technologies further developed in all care sectors, changing care organization and increasing significantly the scale of data collection and sharing. To cope with these challenges, European legislator modernized the former legal frameworks on personal data protection and on medical devices. In addition, the European Commission is currently working on the creation of a European Health Data Space to promote better exchange and access to different types of health data (e.g. registries) to support healthcare delivery, health research and health policy making.

In Belgium, after several pilot projects in different areas, Belgian authorities are working to define the general principles for the reimbursement of the use of eHealth technologies in health care delivery, including the use of remote monitoring.

Several legal frameworks apply to cardiac remote monitoring such as rules regarding products safety and performance, privacy, quality of care, liabilities, patient's rights etc. In 2010, a previous KCE report analysed in detail the numerous legal issues affecting the particular issue of remote monitoring for patients with implanted defibrillators. [1] At this time, cardiac remote monitoring systems were emerging, and the applicable legal frameworks did not address specifically eHealth technologies and services. This report pointed out the lack of specific rules for emerging technologies, as well as the diversity of liability rules as major difficulties for the implementation of cardiac remote monitoring and recommended the adoption of legal and clinical guidelines.

The aim of this chapter is not to duplicate this extensive analysis but to identify the changes in the legal frameworks affecting cardiac remote monitoring and to discuss the most debated issues in this sector. Therefore, the focus of this chapter will be the impact of the new medical devices regulations (section 6.3) and of the new personal data protection rules (section 6.4) on the further implementation of cardiac remote monitoring. Changes in the Belgian rules applicable to health care delivery also deserve to be discussed in this context (section 6.5).

Liabilities (e.g. In case of missing an alarm?; Or in case of defect in the functioning of the remote monitoring system?; …), professional secrecy (e.g. Which information can be shared between various actors?) and patients' rights (e.g. What information must be given to the patient?; How can the patient access the collected data?) are also critical issues for the successful implementation of cardiac remote monitoring. These frameworks have however not been subject to further developments since our last analysis. Therefore, we refer to our previous report in this respect. Reimbursement and related legal issues are dealt with in chapter 7 and 8 and compared with reimbursement schemes in other countries.

6.2 Methodology

To update our previous legal analysis, this chapter used traditional legal research methods, consisting of the following elements:

- **Analysis of European and Belgian legislations**: the Official European legal database Eur-Lex, the Belgian Monitor and the official databases of the European and Belgian Parliaments were consulted to describe the applicable legal rules and their context. Guidelines and policy papers from European authorities regarding the implementation of these rules were also consulted.
- **Analysis of the European and Belgian courts decisions:** the European Court of Justice database (CURIA) and the Belgian public legal database (JURPORTAL) and the Belgian database JURA were consulted to check possible relevant court's decisions.
- **Non-systematic review of the legal literature**: keyword searches were used in European and Belgian database (Eur-Lex and Jura) and in Google and Google Scholar to find grey literature identifying the main legal issues, bottlenecks and policy options.

- **Discussion during a stakeholder meeting and direct questions** addressed in written or orally to the Belgian public authorities and to the manufacturers of CIEDs remote monitoring systems were used to cross validate and complete the topics addressed and identified in this chapter.

6.3 Regulation of CIEDs remote monitoring technologies

Remote monitoring of CIEDs relies on several technologies including not only the CIED itself but also the transmitter (also called communicator or in-home/bedside/portable monitor) and several software and telecommunications devices or apps (see chapter 2). CIEDs and most of the components of cardiac remote monitoring systems are medical devices certified under the previous European Directives on medical devices and active implantable medical devices (see infra 6.3.1). Non-medical technologies such as telecommunication technologies and services used to transmit information in the context of cardiac remote monitoring are also regulated. Section 6.3.2 briefly describes these rules but only to the extent that they impact on the medical service.

6.3.1 Regulation of the medical components of CIEDs

6.3.1.1 Introduction

In accordance with the general European policy for consumers products[a], medical devices can circulate freely on the European market via a certification system. The compliance of medium and high-risk medical devices with European general safety and performance requirements is assessed prior to their market entry by Notified Bodies which are usually for-profit and private organisations. After their entry on the market, these products are monitored by their manufacturers, under the surveillance of the national competent authorities (see infra Box 2).

To meet major safety concerns affecting certain devices and to reflect the technological and scientific progress in the medical devices sector, the former three medical devices Directives on medical devices[b], in vitro diagnostic medical devices[c], and active implantable medical devices[d] are progressively replaced since 2017 by two Regulations[ef] which, in contrast to Directives, do not need to be transposed into national law. The Regulation 2017/745 (hereafter "MDR"), which is relevant for the present study[g], replaces the Directives 90/385 on active implantable medical devices and the Directive 93/42 on medical devices (hereafter "MDD" and "AIMDD").

These new rules largely contain the same basic regulatory requirements for manufacturers and devices than the former Directives (see Box 2). The MDR adds however clarifications of the already existing safety and performance

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a European Commission 'Blue Guide' on the implementation of EU products rules 2016. O.J. C272/1, 26/07/2016.

b Directive 93/42/EEC concerning medical devices. O.J. L169, 12/07/1993.

c Directive 98/79/EC of 27 October 1998 on in vitro diagnostic medical devices. O.J. L331, 07/12/1998.

d Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices. O.J. L189, 20/07/1990.

e Regulation 2017/745 of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. O.J. L117, 5/05/2017.

f Regulation 2017/746 of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. O.J. L117, 5/05/2017.

g The Regulation on in vitro diagnostic medical devices is not applicable in the context of our study and will therefore not be analysed.

requirements regarding connected devices and more stringent rules in terms of risk classification, oversight provided by notified bodies and control of these entities by the public authorities. The MDR also places more emphasis on clinical evidence required to place high-risk medical devices on the market and on post-market monitoring ("post-market vigilance" and "post-market surveillance").

The MDR entered into force in May 2017 and became applicable during the drafting of this report, on 26 May 2021. However, transitionally[a], CE markings delivered under the MDD and AIMDD remain valid until the expiry date of the certificate or until 26 May 2024 at the latest[b]. During this transitional period, medical devices certified under the MDD and AIMDD, called "legacy devices", will be subject to a mixed regime.

All CIEDs and related remote monitoring systems available in Belgium were approved under the former MDD or AIMDD. New post market surveillance and vigilance obligations are already applicable to their manufacturers but new rules on clinical evidence, risk classification or transparency (for instance the drafting and publication of a Summary of Safety and Clinical Performance - see infra section 6.3.1.8.) are not applicable yet.

Box 2 – CE marking

Regardless of the risk classification of a device, its manufacturer must, in order to obtain a CE marking, demonstrate that this device is **safe and perform as intended** and that the risks which may be associated with its use constitute acceptable risks when weighed against the benefits to the patient (acceptable benefit-risk balance).

Depending on the risk classification of the device, specific, usually for-profit, entities called Notifies Bodies will audits the manufacturer's quality system and, depending on the type of device, perform a review of the evidence provided by the manufacturer before delivering a CE mark.

Once placed on the market, the device is the responsibility of the manufacturer who markets it. However, the CE marking has a limited period of validity and the Notified Body must periodically reassess the relevance of the evidence and the organisation of the manufacturer. The manufacturer must monitor the performance and safety, check that the benefit-risk balance remains acceptable and, if necessary, take preventive or corrective actions. The national competent health authorities are responsible for market surveillance and the designation and control of notified bodies.

6.3.1.2 Medical devices qualification and classification

The MDR marginally rephrases the MDD definition of medical device and defines it as "*any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for specific medical purposes, including the following purpose:*

- *diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,*
- *investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,*
- *providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,*

[a] Article 120 MDR.

[b] Some medical device will have to comply with the new regulation by 2022 (if they obtained their CE mark under a specific EC verification procedure).

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means."[a]

Active device means any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy. Software shall also be deemed to be an active device.

The manufacturer can decide to have its whole CIED remote monitoring system validated or to have the different parts validated separately (the manufacturer must nevertheless verify the compatibility between the different parts and the safety and performance of the whole system[b]). Each component qualifying as medical device independently has to comply with the medical devices' rules and, from 26 May 2021, will receive a specific identification code (UDI or equivalent code applicable to legacy devices) to ensure its traceability.

Once a product qualifies as a medical device, its manufacturer must determine its classification in order to identify the applicable conformity assessment procedure (to assess the compliance with the essential requirements under the MDD or AIMDD or the general safety and performance requirements under the MDR).

Box 3 – Risk classification

Medical devices are divided into classes I, IIa, IIb and III, taking into account their intended purpose and their inherent risks. Classification shall be carried out in accordance with Annex VIII of the MDR[c] or annex IX of the MDD.

Class I - generally regarded as low risk

Class IIa - generally regarded as medium risk

Class IIb - generally regarded as medium risk

Class III - generally regarded as high risk

The MDR (and the MDD) foresees that a medical software which drives a device or influences the use of a device, shall fall within the same class as this device[d]. However, the MDR adds several sub-classification rules that could impact the current classification of software used in remote monitoring of CIEDs[e].

- Rule 9 : All active devices (including software) that are intended for controlling, monitoring or directly influencing the performance of active implantable devices are classified as class III.
- Rule 11: Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause:
  - death or an irreversible deterioration of a person's state of health, in which case it is in class III; or
  - a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.

[a] Article 2 (1) of the MDR.

[b] Annex I of the MDR, Chapter II, specifically paragraphs 10.1 (c); 14 ; 17; 18 and 19.

[c] Article 51 of the MDR.

[d] Annex VIII of the MDR – Implementation rule 3.3. and Annex IV of the MDD.

[e] The classification criteria (classification rules) are set out in Annex VIII of the Medical Devices Regulation (EU) 2017/745 (MDR).

- Rule 11: Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb.

  All other software is classified as class I

Except for clearly non-medical components, such as cell-phones or connectivity adapters, all components of cardiac remote monitoring systems are medical devices. All CIEDs qualify as Class III medical devices falling under the category of active implantable medical devices both under the AIMDDs and the MDR[a]. In principle, transmitters also fall in this category as well as software within implanted electronic devices used to detect and treat arrhythmias [b]. Some differences in classification can however exist for certain software. Some manufacturers look at the system as a whole and classify all components, including software, as class III medical devices (eventually in application of different classification rules). In that case, the evaluation of the clinical evidence for the implant / transmitter covers also the integrated algorithms. Based on a different architecture, other manufacturers see their software as standalone software and classify them as class IIa or IIb. If several rules apply to the same device or software the strictest rule resulting in higher classification applies[c].

Qualification as medical device and classification can be disputed by third parties, including notified bodies or competent authorities and brought before national courts or before the Court of Justice of the European Union. Only the European Court can, ultimately, give binding interpretations of European Union law.

In case of interpretation issues, the European Commission or the Member States can ask a specific coordination group composed of representatives of all the Member States, including the Federal Agency for Medicines and health products (FAMHP), called the Medical Devices Coordination Group ("MDCG") to publish a guidance[d]. MDCG guidelines are not binding as such but their interpretation represents a common position of the Member States.

6.3.1.3 General safety and performance requirements

Remote monitoring systems for CIEDs are used to monitor both the implant functioning and some patient health parameters. Differences exist in functionalities and used technologies. Certain functionalities offered by remote monitoring systems are included in the general safety and performance requirements of the MDR[e]. Indeed, where some risks cannot be eliminated, the MDD and MDR require that alarms systems must be foreseen. In addition, MDD and MDR also require that when the safety of the patient depends on an internal power supply, the device must be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical. Devices intended to monitor one or more clinical parameters of a patient shall be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health[f]. The MDR states that if a device is intended to be used in combination with other devices or equipment, the whole system (including the interoperability and compatibility with the external environment) must be safe and shall not impair the specified performance of the device. Any restrictions on use applying to such

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[a] These implants are active implantable medical devices under rule 8, subpart 6 of the MDR and under the former Active Implantable Medical Devices Directive (90/385/EEC).

[b] Annex VIII MDR - Rule 9 and definition of accessories under the Directive on active implantable medical devices.

[c] Annex VIII MDR - Implementation rule 3.5.

[d] Article 103 MDR.

[e] These requirements were already included in the MDD and AIMDD but were less extensively and explicitly developed.

[f] Paragraph 18.4 of Annex I, Chapter II MDR.

combinations shall be indicated on the label and/or in the instructions for use[a].

All elements that impact the performance or safety of cardiac remote monitoring, including conditions and limitations linked to the IT environment or to the patient behaviour shall be mentioned to the healthcare professionals and patients. Based on these instructions, healthcare professionals and patients should be able to clearly understand what is expected of them to ensure the proper functioning of their CIED. If, for example, the exposure of the implanted cardiac device is affected by proximity to certain sources of radio frequencies, patients should be aware of this in order to adapt their behaviour[b].

Under the MDR, manufacturers must also ensure that all claims of clinical benefit mentioned for instance on their website or communicated to the users / patients do not overstate the clinical benefits of their devices; such claims usually involve indirect benefits, such as ease of use, atraumatic use, reliability, and patient comfort, and must be supported adequately by objective evidence. [75] If manufacturers of cardiac remote monitoring systems claim for instance that the use of their systems reduces the number of in-clinic visits, this must be supported by objective evidence. The same applies to the claim of better clinical follow up of the cardiac condition.

6.3.1.4 Clinical evaluation and investigations

Like the previous Directives, the MDR requires the confirmation of conformity with relevant general safety and performance requirements under the normal conditions of the intended use of the device and an acceptable risk - clinical benefit ratio (see above, Box 2). While the previous Directives were relatively vague, the new MDR specifies that clinical benefit means the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health. In the context of CIEDs remote monitoring systems, this means that the manufacturer will need to provide evidence of the utility and safety of accessing and using the collected data.

Confirmation of this conformity shall be based on clinical evaluation (assessment) of the clinical data pertaining to the device and which shall include, under the new MDR, “consideration of currently available alternative treatment options for that purpose, if any” (article 61.3 MDR).

This does not necessarily mean that clinical investigations (trials) have to be performed for all devices or that these clinical investigations must have a specific study design. Under the former MDD / AIMDD, the choice to perform clinical investigations was left to the manufacturer. Under the new MDR, clinical investigations are required for implantable and Class III medical devices (MDR Article 61.4). Clinical investigations shall be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims regarding the safety, performance and aspects relating to benefit-risk of devices as referred to in Article 62(1). The rationale for the design and chosen statistical methodology shall be presented. The endpoints shall be determined and assessed using scientifically valid methodologies. The primary endpoint shall be appropriate to the device and clinically relevant (annex XV of the MDR).

However, clinical investigations are not required for a class III device which have been lawfully placed on the market in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation is based on “sufficient clinical data”. Ultimately, the notified bodies will evaluate whether these data are sufficient. A clinical investigation is also not required when the applicant modifies its own devices or when the applicant claims that a new medical device is equivalent to an existing device from another manufacturer. In this case, it shall be clearly demonstrated that the applicant

[a] Paragraph 14.1 and 14.5 of Annex I, Chapter II MDR.

[b] See for instance the 2016 report of the French authority in charge of radiofrequencies http://www.radiofrequences.gouv.fr/dispositifs-medicaux-implantables-actifs-a14.html

has sufficient levels of access (for instance via a contract) to the data relating to devices with which equivalence.

The methodology and the extent of the evidence used by the manufacturers of CIEDs to place these medical devices on the market are only held by manufacturer and notified bodies and are not publicly accessible. Unfortunately, it is currently not possible to know which clinical investigations were conducted to place medical devices on the market or whether new clinical investigations are ongoing for regulatory purposes because there is no comprehensive public database containing this information. This will, in principle, improve when the new version of Eudamed developed to implement the MDR requirements become fully operational (which is not expected before 2024) (see section 6.3.1.8).

6.3.1.5 Cybersecurity requirements

The use of Bluetooth, radiofrequencies or internet by CIEDs remote monitoring systems and reliance of these systems on established platforms or apps pose particular threats. This topic has come under the spotlights after the reporting of existing vulnerabilities of CIEDs remote monitoring systems to cyber-attacks in the USA and in Europe. The FDA and the American agency for cybersecurity issued notices regarding the cybersecurity vulnerabilities of CIEDs and their remote monitoring systems (e.g. in 2017[a], 2019[bc], 2021[d]). In the context of post-market vigilance, manufacturers have issues field safety notices containing similar issues in Europe (see infra section 6.3.1.7).

Despite those notices, no concrete cyber-attacks against any CIEDs have been reported so far and the possibility of an active reprogramming of CIEDs by cyber-attacks seems to be extremely low. [76]

For devices using new technologies, such as CIEDs and their remote monitoring systems, the MDR contains specific provisions on cybersecurity. In theory, these are not new but only more explicit requirements, as manufacturers were already required to guarantee the security and performance of their systems under the MDD and AIMDD[e]. Under these rules, manufacturers are required to develop and manufacture their products in accordance with the "state of the art" taking into account the principles of risk management, including information security, as well as to set out minimum requirements concerning IT security measures, including protection against unauthorised access. Any restrictions on use of a medical device linked to other systems or networks vulnerabilities must be indicated on the label and/or in the instructions for use[f].The Medical Device Coordination Group has recently issued a Guidance on cybersecurity explaining in detail how manufacturers can meet all relevant essential requirements with regard to cybersecurity[g]. In addition, several international[h] and national guidance are available such as e.g. ASIP certification in France, or NEN 7510 in the Netherlands.

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a https://wayback.archive-it.org/7993/20201222110125/https://www.fda.gov/medical-devices/safety-communications/firmware-update-address-cybersecurity-vulnerabilities-identified-abbotts-formerly-st-jude-medicals.

b https://wayback.archive-it.org/7993/20201222110056/https://www.fda.gov/medical-devices/safety-communications/cybersecurity-vulnerabilities-affecting-medtronic-implantable-cardiac-devices-programmers-and-home.

c https://www.fda.gov/medical-devices/safety-communications/cybersecurity-vulnerabilities-affecting-medtronic-implantable-cardiac-devices-programmers-and-home

https://www.fda.gov/medical-devices/safety-communications/fda-alerts-providers-and-patients-check-premature-battery-depletion-certain-medtronic-pacemakers-fda

d See for instance https://us-cert.cisa.gov/ics/advisories/ICSMA-19-080-01

e Annex I - section II, 9 AIMDD and article 12 and Annex I – Chapter II – paragraph 12 of the MDD.

f Paragraph 14.1 of Annex I MDR.

g https://ec.europa.eu/docsroom/documents/41863.

h http://www.imdrf.org/workitems/wi-mdc-guide.asp

To demonstrate compliance with these requirements, the manufacturer must include evidence of cybersecurity for the device in the technical file that is submitted to a notified body. In practice, a recent study of submissions to the Food and Drug Administration (FDA) in the USA implies that that such evidences are rarely available in the USA. [77] In Europe, this information lies in the hand of the notifies bodies and is not made public. Competent authorities can ask all documents/results (including for instance the source code) related to a medical device. If the manufacturer does not cooperate or the information provided is incomplete/incorrect, the competent authorities can take all possible measures to restrict or prohibit the placing on the market and to recall the devices on the market[a].

In fact, concrete evaluation of cybersecurity of these devices is extremely complex, especially for systems that includes several components. A recent report of the German authority for cybersecurity in 2020 showed no major vulnerabilities but also underlined that authorities are only able to perform very limited evaluations of these issues due to the complexity of the system and absence of available information[b].

To find effective IT solution to reduce the risk of CIEDs' cybervulnerability and increase patient safety, several experts call for political, regulatory, scientific, and clinical cooperation and propose several measures such as the use of open source operating systems and the disclosure source code, the limitation of the distribution channel for monitors and transmitters, the use of secured access to transmitters and programmers for instance with fingerprints or the conduct of vulnerability testing's or hackathon. Patients should also be aware of good cybersecurity practices, including use of strong Wi-Fi passwords at home, restricting access of strangers to their home monitor, and informing the physician's office regarding any malfunction of their home monitor. [78] [79]

Cybersecurity is not only a challenge for manufacturers and the authorities that control them. In Belgium, the manufacturer but also the healthcare professionals using the device are responsible for reporting incidents (see infra section 6.3.1.6), including cybersecurity incidents, affecting medical devices to the competent authorities (FAMHP in Belgium)[c]. However, some cybersecurity incidents should also be notified by hospitals under the consumers protection law to the Belgian Centre for cyber security (see Box 4). If those incidents involve personal data breaches, a specific notification procedure is also foreseen by the GDPR (see infra section 6.4).

For health professionals the complexity of these laws and the overlapping of different reporting obligations may make compliance with these obligations particularly complicated.

In Belgium, political discussions are ongoing to improve and fund the improvement of cybersecurity in hospitals[d].

Box 4 – Cybersecurity: Other relevant legal frameworks

Other legislative frameworks are also relevant to the cybersecurity of medical devices or to operators dealing with protecting or processing of personal data stored in medical devices.

The **NIS Directive**[e], implemented in Belgian law by the NIS law[f] provides for legal measures to increase the general level of cyber security in the EU. It requires the member States to be appropriately equipped, e.g. via

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a Article 10.14 and articles 95,97,98 of the MDR.

b https://www.bsi.bund.de/SharedDocs/Downloads/DE/BSI/DigitaleGesellschaft/ManiMed_Abschlussbericht_EN.pdf?__blob=publicationFile&v=1

c Article 87 MDR.

d https://organesdeconcertation.sante.belgique.be/sites/default/files/documents/cfeh_d_536-2_-_avis_bmuc_et_cybersecurity_-_fr.pdf

e Directive on security of network and information systems. O.J. L194, 19.7.2016,

f Law of 7 April 2019 establishing a framework for the security of networks and information systems of general interest for public security, *M.B-B.S* 03/05/2019. See also for more information: https://ccb.belgium.be/fr/actualit%C3%A9/transposition-de-la-directive-nis-en-droit-belge

a Computer Security Incident Response Team (CSIRT) and a competent national NIS authority. In certain area identified by the Directive, Member States shall also identify operators of essential services who will have to take appropriate security measures and to notify incidents of significant impact to the relevant national authority. Also, key digital service providers (search engines, cloud computing services and online marketplaces) will have to comply with the security and notification requirements under the new Directive. In Belgium, hospitals are designated as essential services.[a]

In addition, the **EU Cybersecurity Act**[b] contains rules for the certification of cybersecurity for ICT products, services and processes.

Cybersecurity issues are also addressed in the GDPR (General Data Protection Regulation) that regulates and protects the processing of personal data by a person, company or organisation relating to individuals in the EU (see infra section 6.4)

6.3.1.6 Interoperability

According to Article 1 (26) of the MDR 'interoperability' is the ability of two or more devices, including software, from the same manufacturer or from different manufacturers, to: (a) exchange information and use the information that has been exchanged for the correct execution of a specified function without changing the content of the data, and/or (b) communicate with each other, and/or (c) work together as intended.

Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe[c].

Interoperability is mentioned in the medical devices legislation. However, is up to the manufacturers decide whether their devices are "intended to function with" other devices or products. They decide if they want their devices to interoperable with those placed on the market by other manufactured or with the devices or systems used by the health care systems (patient record etc.). The diversity and incompatibility of current data sources is a barrier to high-quality, patient-centred care. [80]

Therefore, some experts have developed vendor-neutral exchange standards to manage data from CIEDs. These data elements and definitions have been endorsed by the Institute of Electrical and Electronics Engineers. If these standards are implemented, data exchange across proprietary vendor environments (e.g., from a CIED programmer to an electronic medical record) would be made possible. [80].

Interoperability is also mentioned in recital 68 of the GDPR linking to the data subject right to data portability (see infra section 6.4.4). Recital 68 GDPR indicates that data controllers are encouraged to develop interoperable formats that enable data portability. Up to today, there are no standardized technical requirements for interoperability that are put forward in this regard.

One manufacturer reported to have developed remote monitoring systems allowing hospitals to automatically import data into their Electronic Health Record systems in 3 different formats. However, as reported by hospitals, the level of interoperability with systems developed by other manufacturers and patient health records is relatively low in Belgium (see 3.6.5).

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[a] Annex I of the law of 7 April 2019 establishing a framework for the security of networks and information systems of general interest for public security, M.B-B.S 03/05/2019.

[b] Regulation (EU) 2019/881 of the European Parliament and of the Council of 17 April 2019 on ENISA (the European Union Agency for Cybersecurity) and on information and communications technology cybersecurity certification and repealing Regulation (EU) No 526/2013. O.J. L151,07/06/2019.

[c] Annex I, 14.5 of the MDR.

6.3.1.7 Post-market vigilance and surveillance

The “market surveillance” (performed by the national competent authorities) covers the set of activities carried out and the measures taken to verify and guarantee that the devices that are on the market are compliant with medical devices rules and do not endanger health and safety.

“Post-market surveillance” (performed by the manufacturer) is a proactive and systematic process, designed to monitor the safety and performance of a medical device by collecting and analysing information relating to its use in the field. Under the new MDR, the post-market surveillance is based on a PMS plan which should include the post-market clinical follow-up plan. Manufacturer of middle and high risks devices must submit a Periodic Safety Update Report (PSUR) to the notified body that issued the certificate for its device, at least every 2 years (class IIa) or at least every year (class IIb & III). For class III & implantable devices these PSURs need to be submitted through Eudamed and the notified body should add its assessment in the Eudamed database. Only competent authorities and notified bodies have access to these documents.

Finally, “vigilance” (performed by the manufacturer and the national competent authority) is a reactive process and consists in reporting serious incidents and field safety corrective actions (FSCA) to the Competent Authorities involved. FSCA is a corrective action (e.g. a recall, software-update, etc.) while a serious incident is a specific failure event causing harm to a specific patient. Under the MDR, manufacturers must also report side effects trends, as well as trends of expected unwanted accidents that are not classified as serious. Notification obligations are broader in Belgium since they require also healthcare professionals, and professionals that use device to notify incidents with medical devices[a].

All FSCAs in which Belgium is concerned (affected devices or in which manufacturer, or authorized representative is located in Belgium) need to be reported by the manufacturer to the FAMHP, the Belgian’s national competent agency. Based on the FSCA, the manufacturer shall draw up a Field safety notice for user **(FSN)** summarizing the identified problem, the potential risks that may arise for patients and users and/or actions to be taken by user to minimize the risks. It should also include the actions taken by manufacturer to resolve the problem and/or minimize the risks. Only FSN are “public”. However, unlike in other countries (UK, Germany), FSN are not systematically classified in a specific database allowing product or key-word researches in Belgium. Therefore, they are not easily accessible. In the future Eudamed database, the FSNs will be publicly available through Eudamed. Additionally, also a limited dataset of the reported serious incidents will be available to the public.

In the US, the MAUDE[b] database summarizes some data-elements of the reports made by manufacturers and mandatory reporters. Occasionally, the FDA publishes recommendations on specific safety issues affecting medical devices[c]. Due to time constraints, we did not investigate the MAUD database. We did however look at the recalls and noticed that several recalls and corrective actions for CIEDs and related remote monitoring devices have been issued in the USA in 2020 and 2021[d]. A similar database exists in Australia[e]. Based on key words searches of the FAMHP website, we also

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a These definition were taken from https://www.thema-med.com/en/what-is-the-difference-between-market-surveillance-post-market-surveillance-pms-and-vigilance/

b https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm

c https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm

d See for instance https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=180403, https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=179535 (Merlin 2020); https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=183949 (Latitude 2020) ; https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=186464 (Care link)

e https://www.tga.gov.au/database-adverse-event-notifications-daen.

identified several FSN concerning the available remote monitoring systems of CIEDs[a].

Examples of issues raised include:

- cybersecurity vulnerabilities requiring updates;
- problems in the transmitter or software configuration resulting in an overestimation in the displayed longevity of the device or to overconsumption followed by loss of pacing and sensing capabilities of the implants;
- defect in the connection to cellular network;
- …

These examples only give an idea of the possible safety issues affecting CIEDs remote monitoring but does not give information on their scale or frequency.

6.3.1.8 Transparency and access to information

Under the MDD, most of the information related to medical devices is confidential. Confidentiality extends to data resulting from clinical investigations of medical devices as well as claims submitted by manufacturers to notified bodies, assessment reports, and evaluation of the device by notified bodies. [81] [82]

Information contained in the current version of Eudamed is only for accessible for national competent authorities in charge of the implementation of the medical devices' legislation. This platform works currently as a platform for information exchange and storage (vigilance, manufacturer information's, National Competent Authority Reports) but the content of this database is rather limited.

This situation does not only make it very difficult for physicians to fulfil their duty of informing their patients, and for patients to make a well-informed decision but also hinders the good cooperation between Members States and with the European Commission.

Overall transparency will improve with the MDR and the further development of the public database Eudamed[b], which will include certain data on registration, certificates, clinical investigations and vigilance and a system on market surveillance. Once the new version of Eudamed will be available, the general public will also be able to access, for each implantable medical device and class III, a Summary of Safety and Clinical Performance (SSCP) drawn up by the manufacturer. This summary must contain general information on the devices and specifically a description of the clinical evaluation and the possible diagnostic or therapeutic alternatives. For all CIEDs this summary shall be written in a way that is clear to the intended user and, if relevant, to the patient. For other components of remote monitoring systems, the MDR allows the manufacturers to assess the relevance and the need to communicate certain information.

The MDR clarifies that patients should be fully informed about their devices. Therefore, for CIEDs, this information should include not only information on the CIEDs but also the details of the system of remote monitoring [77], including, for instance clear and objective explanation on what are the follow-up alternatives, the residual risks and the possible side-effects of this specific follow-up.

In addition, the new version of Eudamed database is not functional yet and has been repeatedly delayed. As a consequence of this delay, the registration obligation is postponed to a later date (Art. 123(3) and 122 4th indent). This notice is estimated to be published in mid-2023. Actors will therefore only be obliged to register at the end of 2023. As far as DMs are concerned, there is still an additional delay of 18 months, which means there will be no obligation before 2025.

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[a] https://www.afmps.be/sites/default/files/fsn_20265_fr.pdf ; https://www.afmps.be/sites/default/files/downloads/FSN%2016850%20fr.pdf

[b] Article 33 of the MDR.

Box 4 – Databases containing information on CIEDs in Belgium

In Belgium, a specific database is hosted by the FAMHP for the reimbursement authorities[a]. The distributors, importers and manufacturers are required to notify implants and long-term invasive devices for reimbursement. This database only includes basis information (name, reference, price, etc.) on implants and long-term invasive devices that are reimbursed by the NIHDI and do not give any information on the number of implanted patients. In addition, cardiac remote monitoring systems are not notified in this database as they are not reimbursed.

For the purpose of traceability, health care professionals have to register implants, including cardiac implants, in another database called the Central Traceability Register (mandatory since 1st May 2021)[b]. This obligation does not cover remote monitoring systems (software, transmitters, apps, …) that are not implantable.

The Qermid©Cardiac Defibrillators and Qermid© Pacemakers databases are online registries for registering individual patient medical data as well as material data from heart implants and operations. Currently, remote monitoring is not mentioned as a mandatory field in these databases[c]

6.3.1.9 Key points

- **All CIEDs qualify as Class III medical devices. Most of the components of related remote monitoring systems also fall under this classification but slight differences can exist for certain software, depending on the architecture chosen by the manufacturer.**
- **CIEDs and related remote monitoring systems, previously governed by European Directives (MDD and AIMDD), are being progressively covered by the Medical devices Regulation (MDR) which introduces more stringent evidence and transparency rules, particularly for class III medical devices.**
- **CIED remote monitoring systems must be seen as a whole. The whole system must be safe and performant (including with regard to the interoperability and compatibility with the external environment) and have an acceptable risk-benefit balance. Any restrictions on use applying to the used combinations or interactions with the environment shall be indicated on the label and/or in the instructions for use.**
- **All claims of clinical benefit mentioned by the manufacturers, including indirect benefits, must be supported adequately by objective evidence and this evidence must be explained in the information provided to user and patients. Information provided must also include clear and objective explanations on what are the follow-up alternatives, the residual risks and the possible side-effects of this specific follow up. Alarms offered by remote monitoring systems regarding the implant battery and certains critical health incidents are included in the general safety and performance requirements of the MDR (and were already implied in the essentials requirements of the MDD and AIMDD). Manufacturers are for instance required to equip their CIEDs with systems monitoring the power supply capacity and critical health incidents and containing appropriate alarm systems**

[a] Arrêté royal du 7 avril 2019 portant exécution de l'article 35septies de la loi relative à l'assurance obligatoire soins de santé et indemnités, coordonnée le 14 juillet 1994. *M.B.-BS.* 26/04/2019.

[b] https://www.afmps.be/fr/humain/produits_de_sante/dispositifs_medicaux/registre_central_de_tracabilite_rct

[c] Règlement du 15 avril 2015 modifiant le règlement du 16 juin 2014 fixant les formulaires relatifs aux procédures de demande en matière d'intervention de l'assurance obligatoire soins de santé et indemnités dans le coût des implants et des dispositifs médicaux invasifs, repris dans la liste des prestations des implants et des dispositifs médicaux invasifs remboursables.

- **Interoperability with other manufacturer's devices and with patient health records is not a market access requirement. Diversity and incompatibility of current data sources have been identified years ago as a barrier to high-quality, patient-centred care but Belgian hospitals report that this problem is not solved in Belgium.**
- **The new regulation requires, in principle, clinical investigations for all Class III devices and insist on appropriate study design. These new requirements might help to generate more evidences on remote monitoring of CIEDs.**
- **However, the requirement to perform clinical investigations does not apply to implantable devices and class III devices: which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation is based on sufficient clinical data. Equivalent devices might also, in some circumstances, escape this requirement.**
- **At this stage, it is difficult to have a complete overview of which clinical evidence is used by the manufacturers to place the current remote monitoring systems of CIEDs on the market and if new clinical trials will be necessary because this information lies in the hands of the manufacturers and notified bodies and is not made public.**
- **Some safety issues affecting CIEDs remote monitoring systems, including cybersecurity vulnerabilities, have been identified. However, no public information on their scale or frequency is publicly available.**
- **Transparency and accessibility of information regarding the level of evidence and the safety issues will improve via the new version of the European database (Eudamed). This database will include several public information, including field safety notices and a patient-friendly summary of the product containing information on the scientific evidence and possible treatment alternatives. However, the implementation of this database has been considerably delayed and its complete functionality is not expected before the end of 2023 and 2025 for devices related information.In Belgium, health care professionals or their hospitals must notify incidents with medical devices to the competent authorities (FAMHP), but are also required to notify cybersecurity incidents to the Belgian Centre for cyber security. If incidents involve personal data breaches, a specific notification procedure is also foreseen by the GDPR. The complexity of these laws and the overlapping of different reporting obligations can make compliance with these obligations particularly complicated.**
- **• While legal rules on medical devices require CIEDs and related remote monitoring systems to be protected against cyber-attacks, the concrete compliance with this requirement and the possible impact (for instance on the implant battery) remain one of the biggest challenges not only for manufacturers but also for hospital and different controlling authorities.**

6.3.2 Regulation of non-medical components and services

Patient information is transmitted from the monitor to the datacentre and from the datacentre to the technicians and physicians via mobile phones or monitors, using different communication networks (fix or mobile Internet networks, worldwide reserved radio frequencies etc.) (see chapter 2).

Under the MDR, connection system shall be safe and shall not impair the specified performance of the CIEDs and other medical devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use[a]. Manufacturers shall therefore be

[a] 14.1 of Annex I of the MDR.

explicit on the required network coverage and connectivity conditions. CIEDs remote monitoring components shall be designed and manufactured in such a way as to eliminate or reduce as far as possible any risk associated with a possible negative interaction between the software and the computer environment in which it operates and with which it interacts[a].

The specific regulation of telecommunication services allowing the transmission of data falls outside the scope of this HTA. However specific rules applicable to these areas are relevant for the appropriate functioning of remote monitoring of CIEDs.

6.3.2.1 Inapplicability of priority rules in the telecommunication sector to CIEDs remote monitoring

The use of CIEDs remote monitoring systems requires access to Internet/ telephone network. The lack or limited access thereto[b] can cause inequal access to this care organization and must also be taken into account in the discussions on the implementation of remote monitoring and its reimbursement[c].

In addition, it must be taken into account that, since 15 June 2017, commercial operators are bound by certain rules concerning the access of the higher number of people to all the potentialities of the Internet and cannot unfairly block or slow down certain uses of the internet, while granting extra-fee based priority treatment to a small number of users (principle of "net neutrality"[d] in EU legislation). Patients who use commercial remote monitoring services to monitor their cardiac condition cannot have priority over other users for the use of Internet/ telephone network.

Priority access is reserved for emergency services and networks and "priority users", the list of which is determined by the King[e]. This legislation does not aim at protecting individual commercial services such as cardiac remote monitoring.

In addition to the fact that medical staff is not available 7/7 24/24 to scrutinize alarms from these systems, these legal frameworks also make it impossible for such services to work as an alarm emergency system. Appropriate disclaimers and warnings shall consequently always be included in the information given to the patient and health care professional involved in cardiac remote monitoring.

6.3.2.2 Absence of liability of the telecommunication operator

Since remote medicine is a service frequently provided by Internet, it also falls (partly) under Directive 2000/31/EC on certain legal aspects of information society services, in particular electronic commerce, in the Internal Market, also known as the E-Commerce Directive, implemented in Belgian legislation by the Law of 11 March 2003 concerning certain legal aspects of information society services.

According to this law, information society providers operating communication networks are not liable in case of illegal acts initiated by others when they act as intermediaries. This exemption from liability cover only cases where the activity of the information society service provider is limited to the technical process of operating and giving access to a communication network over which information made available by third parties is transmitted or temporarily stored, for the sole purpose of making the transmission more efficient; this activity is of a mere technical, automatic

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[a] 14.2.d of Annex I of the MDR. See also paragraphs 17 and 23.4.

[b] https://statbel.fgov.be/fr/nouvelles/isolement-numerique-pres-dun-quart-des-personnes-seules-nont-pas-acces-internet-la-maison.

[c] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7428456/.

[d] https://eur-lex.europa.eu/legal-content/FR/TXT/?uri=celex%3A32015R2120. European Regulation 2015/2120. Belgian legislation see : https://www.ibpt.be/operateurs/net-neutrality#:~:text=En%20Belgique%2C%20la%20neutralit%C3%A9%20de,acc%C3%A8s%20%C3%A0%20un%20internet%20ouvert.

[e] Article 4/1 of the « Loi du 13 juin 2005 relative aux communications électroniques, *M.B.*, 20.06.2005 ».

and passive nature, which implies that the information society service provider has neither knowledge of nor control over the information which is transmitted or stored.

In remote monitoring applications appeal is often made to intermediaries, e.g. for the storing of health data or provision of internet access. If for instance a webserver hosts a website or database of a third party containing medical information, the webserver cannot be held liable for wrong information.

6.3.2.3 Key points

- **Patients who use commercial remote monitoring services to monitor their cardiac condition do not have priority over other users for the use of Internet/ telephone networks.**
- **Information society providers operating communication networks are not liable in case of illegal acts initiated by others when they act as mere intermediaries with no knowledge nor control over the information which is transmitted or stored.**

6.4 Regulation of the data

CIEDs remote monitoring systems collect important amounts of data concerning the patient health status but also concerning the devices functioning. Personal data, and specifically health data, enjoy a specific protection from the European General Data Protection Regulation (hereafter "the GDPR")[a] which came into effect in May 2018 and repealed the former Directive (hereafter the Personal data Directive)[b]. In Belgium, this legal framework is completed by a law of 30 July 2018[c].

Like the previous Directive[d], the European Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (hereafter referred to as General Data Protection Regulation – GDPR) aims at protecting the rights and freedoms of persons with respect to the processing of personal data. The Regulation was adopted to reduce the fragmentation in different national systems[e] and to adapt the data protection rules to the new challenges linked to digital technology development[f].

The GDPR preserves many of the principles enshrined in the Data Protection Directive but introduce several changes, including the insertion of particularly high sanctions in case of breaches of the GDPR, stricter consent requirements, reinforcement of the rights of the data subjects etc. It is beyond the scope of this study to examine all these changes. The new Regulation also provides a margin of appreciation for Member States to specify their own rules for the processing of special categories of personal

a Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). O.J. L119, 4.5.2016.

b Council directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data, O.J. L281/31 1995.

c Law of 30 July 2018 regarding the protection of natural persons regarding the processing of personal data, *M.B.-B.S.* 05.09.2018.

d Council directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data, O.J. L281/31 1995.

e Divergent implementations the older Directive between Member States of were mentioned in the KCE report 2010 as hampering uniformity in data protection modalities.

f See whereas 5, 6 and 7 of the Regulation.

data ('sensitive data'). To that extent, this Regulation does not exclude Member State law that sets out the circumstances for specific processing situations, including determining more precisely the conditions under which the processing of personal data is lawful.

Therefore, the next sections summarise the mains principles and actors of the GDPR in relation to remote monitoring of CIEDs (section 6.4.1). Despite the changes introduced by the GDPR, debates are still taking place on the concrete application of the GDPR provisions to remote monitoring of CIED's, particularly regarding the identification of the legal ground for the data processing and regarding the distribution of roles under the GDPR between the different actors involved (sections 6.4.2 and 6.4.3). Another debate concerns the extent of patients' rights over the data collected and their effective exercise (6.4.4).

6.4.1 GDPR actors and principles applied to remote monitoring

6.4.1.1 Field of application and territorial scope

The GDPR protects personal data regardless of the technology used for processing that data. It also applies regardless on how the data is stored – in an IT system, through video surveillance, or on paper.

The EU GDPR has a wide territorial scope. It applies to the processing of personal data in the context of the activities of an establishment of a controller or a processor in the Union, regardless of whether the processing takes place in the Union or not (Art. 3(1)). Furthermore, it may apply even to companies not established in the EU, in cases in which they process the personal data of subjects who are in the EU and the processing activities are related to the targeted monitoring of their behaviour as far as their behaviour takes place within the Union (Articles 3(2)(b) and 4(1)).

Data rendered irrevocably anonymous in such a way that the data subject is not or no longer identifiable are not affected by GDPR. Therefore, if manufacturers of the CIEDs remote monitoring systems only collect and process anonymous data, for instance for research or post-market surveillance purpose the GDPR is not applicable to this part of the treatment.

6.4.1.2 Definitions

Personal data under the GDPR are "*any information relating to an identified or identifiable natural person* ('data subject')" (Art. 4(1)). An identifiable natural person is a person "*who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person*" (Art. 4(1)). Different pieces of information, which collected together can lead to the identification of a particular person, also constitute personal data.

Data concerning health are "*personal data related to the physical or mental health of a natural person, including the provision of health care services, which reveal information about his or her health status*" (Art. 4(15)).

Personal data concerning health should include all data pertaining to the health status of a data subject which reveal information relating to the past, current or future physical or mental health status of the data subject. This includes information about the natural person collected in the course of the registration for, or the provision of, health care services to that natural person; a number, symbol or particular assigned to a natural person to uniquely identify the natural person for health purposes; information derived from the testing or examination of a body part or bodily substance, including from genetic data and biological samples; and any information on, for example, a disease, disability, disease risk, medical history, clinical treatment or the physiological or biomedical state of the data

Two types data are collected by CIEDs remote monitoring devices: data related to the integrity and proper functioning of the implant and components of the remote monitoring systems (battery status, electrode impedance, detection and pacing thresholds) and clinical data related the patient health status such as the detection of arrhythmias, therapies delivered (e.g. administration of a shock).

Unless it is made completely anonymous, information regarding the health status of the patient collected by the implant and transmitted via CIEDs remote monitoring systems are health data protected by the

GDPR. In addition, the information linked to the implant and remote monitoring system functioning that is coded and transmitted via the datacentre to the hospital for each particular patient to be able to alert him and protect his health, are also health data.

According to an analysis of a joint Task Force of the European Heart Rhythm Association (EHRA) and the Regulatory Affairs Committee of the European Society of Cardiology (ESC), most of the manufacturers using the collected data for research or statistical purposes anonymise them beforehand. However, the exact extent and nature of collected data remain unclear and this Task force recommends the development of consensus recommendations concerning which data can be collected and exchanged. [77]

Personal data that have been de-identified, encrypted or pseudonymised but can be used to re-identify a person remain personal data and fall within the scope of the GDPR.

Personal data that have been irrevocably rendered anonymous in such a way that the individual is not or no longer identifiable are no longer considered personal data. For data to be truly anonymised, the anonymisation must be irreversible.[a]

Data collection on the CIEDs or remote monitoring systems performance that are irrevocably anonymised do not qualify as personal data. However, encrypted information received from the datacentre of the manufacturer are not anonymised but pseudonymized in order to be sent to the treating physician who must be able to identify the patient (see chapter 2). Complete anonymisation seems not possible as manufacturer is required to investigate the circumstances of any possible incidents reported and to analyse them (see 6.3.1.7). [77]

[a] Article 29 Working Party Opinion 05/2014 on Anonymisation Techniques https://ec.europa.eu/justice/article-29/documentation/opinion-recommendation/files/2014/wp216_en.pdf

Processing under the GDPR is "*any operation or set of operations which is performed on personal data or on sets of personal data, whether or not by automated means*," including collection, use, disclosure by transmission, storage, structuring, and erasure (Art. 4(2)).

The broad notion of data processing applies to different steps in the trajectory of remote monitoring of cardiac implants. For instance, the data transfer from the bedside monitor to the server as well as the consultation of the data by the treating physician (or other persons having access to the data) is perceived as data processing to which the dispositions of the privacy legislation apply.

Box 5 – GDPR actors

- **Controller** is "*the natural or legal person, public authority, agency or other body which, alone or jointly with others, determines the purposes and means of the processing of personal data*" (Art. 4(7)).
- **A processor** is "*a natural or legal person, public authority, agency or other body which processes personal data on behalf of the controller*" (Art. 4(8)).
- **Data subject :** Depending on whom the data can be linked to, the patient, the treating physician or other persons involved in the data processing can be considered as the data subject and thus benefits from the rights included in the GDPR.
- **Third party** means a natural or legal person, public authority, agency or body other than the data subject, controller, processor and persons who, under the direct authority of the controller or processor, are authorised to process personal data.

In order to identify who has to comply with the obligations and who benefits the rights stipulated in the GDPR, the concepts of data subject, processor and data controller have to be interpreted. In the remote monitoring application, different actors are eligible for one or more roles depending on the concrete actions on data.

The GDPR acknowledges that there may be more than one controller, and it reconfirms the concept of joint controllers where two or more controllers together determine the purposes and means of processing data. In case of joint controllers (Article 26) or in case of a controller and a processor (Article 28) contracts must formally determine their respective responsibilities with regard to compliance with the GDPR, as in case of any breach both parties will need to justify their accountability. The GDPR does not address data sharing between independent controllers, and in most cases, such relationships are also set out in a contract. [77]

6.4.1.3 Principles

According to the Regulation, the **data controller** (or joint controllers) is (are) responsible for being able to demonstrate GDPR compliance with the following principles:

- Data must be collected for the legitimate purposes specified explicitly to the data subject when the data are collected and not further processed in a way incompatible with the initial purposes;
- Personal health data used in remote monitoring applications must be processed fairly and lawfully;
- The collection must be transparent to the data subject;
- The data collected must be adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed (‘data minimisation’);The controller should therefore balance the necessity of the personal data against the purpose;
- Personal data must be accurate and, where necessary, kept up to date;
- Moreover, data must be kept in a form that permits identification of data subjects for no longer than is necessary for the specified purpose;
- Processing must be done in such a way as to ensure appropriate security, integrity, and confidentiality (e.g. by using encryption).

The **data processor** processes personal data only on behalf of the controller. The duties of the processor towards the controller must be specified in a contract or another legal act. For example, the contract must indicate what happens to the personal data once the contract is terminated. A typical activity of processors is offering IT solutions, including cloud storage. The data processor may only sub-contract a part of its task to another processor or appoint a joint processor when it has received prior written authorisation from the data controller.

An entity can be a data controller, or a data processor, or both.

6.4.1.4 Data breaches

A data breach occurs when the data for which an entity or a person is responsible suffers a security incident resulting in a breach of confidentiality, availability or integrity. If that occurs, and if it is likely that the breach poses a risk to an individual’s rights and freedoms, the entity or person has to notify the supervisory authority without undue delay, and at the latest within 72 hours after having become aware of the breach. If the entity or person is a data processor it must notify every data breach to the data controller.

If the data breach poses a high risk to those individuals affected then they should all also be informed, unless there are effective technical and organisational protection measures that have been put in place, or other measures that ensure that the risk is no longer likely to materialise.

6.4.2 Distribution of roles in CIEDs remote monitoring

In CIEDs remote monitoring, the question of who determines the purpose and methods of the personal data processing (and therefore who is responsible as data controller) is crucial. According a survey of the joint Task Force of the European Heart Rhythm Association (EHRA) and the Regulatory Affairs Committee of the European Society of Cardiology, the majority of the manufacturers considers that the entire purpose of the data processing is defined by the hospital/cardiology service who are the data controllers and that manufacturers only act as data processors. This position

is not shared by the joint Task Force who considers, depending on the architecture put in place by the manufacturer, both the manufacturers and the hospitals (cardiology service) as joint controllers.

Manufacturers are indeed not only processor on behalf of the hospitals because they establish, at least partly, the objectives ('purposes') for remote monitoring of their devices, determine which data should be collected, and determine the methods ('means') for obtaining those data.

This position is consistent with the regulatory requirements applicable to the manufacturers under the medical device regulations. Manufacturers are indeed explicitly required to equip their CIEDs with systems allowing to determine the capacity of the power supply and alert the user in case this power supply becomes critical[a]. CIEDs must also be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health[b]. These two objectives are defined by the legislation but the concrete data to be collected and means to do so are defined by the manufacturer. In addition, in the context of their post-marketing surveillance obligations, manufacturers must implement a specific plan prior to the placing on the market to monitor their devices (see supra 6.3.1.7). The specific content of this plan is defined by the manufactured who must define which measures (including, for instance which data) need to be collected to monitor the safety, performance and benefit risk balance of their CIEDs and remote monitoring device. However, legal guidance from the European Commission and European Data Protection Board is needed clarify this issue.

Indeed, manufacturers may also act as data processors when analysing and storing the data collected.

Hospitals as well as self-employed physicians working in private practice or as private/independent practitioners in a hospital are indeed also data controllers since they determine the clinical indications for collecting data remotely from CIEDs, the details of the procedure, and which data are collected and analysed from individual patients. It is uncertain whether it should be considered that they are the ones requiring to collect data regarding the implant power supply or implant functioning.

For the Task force EHRA-ESC, the most appropriate model is thus that of two joint controllers. This requires a legal contract between the joint controllers that specifies their respective responsibilities and liabilities.

Finally, third-party providers are data processors if they function under delegated authority from a data controller to collect, analyse, and transmit data acquired from remote monitoring of CIEDs. An agreement between the controller and the processor must also be drafted [77]

6.4.3 Legal ground for data processing of CIEDs

The controller or the joint controllers determine the primary purpose of the data collection. A specific and legitimate reason is needed for any personal data that are collected. Personal data can only be used for the specified reasons.

According to article 6(1)(a)-(f), processing of data (not health data) shall be lawful only if and to the extent that at least one of the following applies:

- The data subject has given consent to the processing of his or her personal data for one or more specific purposes;
- Processing is necessary for the performance of a contract to which the data subject is party or in order to take steps at the request of the data subject prior to entering into a contract;
- Processing is necessary for compliance with a legal obligation to which the controller is subject;
- Processing is necessary in order to protect the vital interests of the data subject or of another natural person;

[a] Paragraph 18.2 of Annex I, Chapter II MDR.18.2

[b] Paragraph 18.4 of Annex I, Chapter II MDR.

- Processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller;
- Processing is necessary for the purposes of the legitimate interests pursued by the controller or by a third party, except where such interests are overridden by the interests or fundamental rights and freedoms of the data subject which require protection of personal data, in particular where the data subject is a child.

In addition, in principle, the processing of sensitive data, such as health data, is prohibited (Article 9.1). However, article 9.2.a allows the processing of health data on the basis of explicit consent of the person concerned. Processing of sensitive data is also allowed if it is necessary for the provision of health care or treatment, or for management of health or social care systems and services, on the basis of Union or Member State law or pursuant to contract with a health professional. Finally, health data can also be processed for reasons of public health such as ensuring 'high standards of quality and safety of medical devices, on the basis of EU or Member State law which provides for suitable and specific measures to safeguard the rights and freedoms of the data subject, in particular professional secrecy' (Article 9.2.i). [77]

When data are processed to treat the patient, the processing must happen under the responsibility of a professional or another person subject to the obligation of professional secrecy. Manufacturers claim that their obligations under the medical device regulation, and in particular, the requirement to conduct post-market surveillance, could constitute and acceptable legal ground to collect a whole range of health personal data. This would potentially allow them to collect data without informing the patient.

According to the European Data Protection Board[a], article 6 c) can, in the context of the application for the Clinical Trial Regulation (applicable to **interventional clinical trials** on human persons with medicines) provide a legal basis for the processing of personal data in the context of safety reporting of incidents within a trial. Therefore, this legal ground (article 6 c)) can be rely on in the context of an inspection of the trial by a national competent authority and for the retention of clinical trial data in accordance with archiving obligations set up by the EU Clinical Trials Regulation, as they are necessary to comply with legal obligations to which the sponsor and/or the investigator are subject to. The controller should however not have an undue degree of discretion on how to comply with the legal obligation.

It is doubtful that this reasoning can be applied to the processing of personal health data collected in the context of CIEDs remote monitoring (article under art. 9, 2, i) and j). Some manufacturers argue that post-market vigilance obligations under the MDR would constitute an appropriate legal basis for the collection of certain data (therefore allowing them not to request consent). Indeed, under their post-marketing surveillance obligations, manufactures must implement a specific plan they should have prepared prior to the placing on the market to monitor their devices. The specific and precise content of this plan is not detailed and the manufactured shall defines which measures (including, eventually a clinical trial) will be done. The margin of appreciation of the manufacturer is very important. He defines what need to be followed up, how its needs to be done and if a clinical trial is envisioned, what are the comparators and endpoints (and consequently which data are needed). As mentioned above (section 6.3.1.7), post market surveillance obligations of the manufacturer have to be read in the context of the specific system for market access of medical devices based on a certification demonstrating a priori the conformity of a devices and strong post-market surveillance obligations. In a recent report ordered by the European Commission, it is concluded that the European legislation does not allow medical devices companies or even authorities to process personal data for post market surveillance. Therefore, unless the national

[a] Opinion of the European Data Protection Board 3/2019, recitals 12 and 13.

rules allow that, these data need to be either fully anonymised or their processing must be based on consent[a].

Given the above-mentioned uncertainties, consent of the patient should always be asked by the manufacturers for processing heath data of remotely monitored patients. Under the GDPR, consent must be freely given, specific, informed, unambiguous, and where consent is used as a justification for processing special categories of data, such as health data, such consent must be explicit (Article 9(2) (a) GDPR). Data controllers should pay particular attention to the condition of a "freely given" consent. As stated in the Working Party 29 Guidelines on consent, this element implies real choice and control for data subjects. When data are collected for scientific purposes (which could be the case even in the context of post market vigilance), it is not always possible to identify all the purposes for which the collected data will be processed for scientific research at the time of data collection. Therefore, data subjects should be able to give their consent with regard to certain areas of scientific research, in accordance with recognised ethical standards for scientific research. Data subjects should be able to give consent only in relation to certain areas of research or parts of research projects, insofar as the purpose allows.

Box 6 – Consent[b]

The basic requirements for the effectiveness of a valid legal consent are defined in Article 7 and specified further in recital 32 of the GDPR. Consent must be freely given, specific, informed and unambiguous. In order to obtain freely given consent, it must be given on a voluntary basis. The element "free" implies a real choice by the data subject. Any element of inappropriate pressure or influence which could affect the outcome of that choice renders the consent invalid. In doing so, the legal text takes a certain imbalance between the controller and the data subject into consideration.

For consent to be informed and specific, the data subject must at least be notified about the controller's identity, what kind of data will be processed, how it will be used and the purpose of the processing operations as a safeguard against 'function creep'. The data subject must also be informed about his or her right to withdraw consent anytime. The withdrawal must be as easy as giving consent. Where relevant, the controller also has to inform about the use of the data for automated decision-making, the possible risks of data transfers due to absence of an adequacy decision or other appropriate safeguards.

The consent must be bound to one or several specified purposes which must then be sufficiently explained. If the consent should legitimise the processing of special categories of personal data, the information for the data subject must expressly refer to this.

There must always be a clear distinction between the information needed for the informed consent and information about other contractual matters.

Last but not least, consent must be unambiguous, which means it requires either a statement or a clear affirmative act. Consent cannot be implied and must always be given through an opt-in, a declaration or an active motion, so that there is no misunderstanding that the data subject has consented to the particular processing. That being said, there is no form requirement for consent, even if written consent is recommended due to the accountability of the controller. It can therefore also be given in electronic form.

While consent is being relatively frequently used in the context of CIEDs remote monitoring, this choice has important consequences. Indeed, if a controller chooses to rely on consent for any part of the processing, he must be prepared to respect that choice and stop that part of the processing if an individual withdraws consent. Strictly interpreted, this means the controller is not allowed to switch from the legal basis consent

a https://ec.europa.eu/health/sites/default/files/ehealth/docs/ms_rules_health-data_en.pdf.

b https://ec.europa.eu/health/sites/default/files/ehealth/docs/ms_rules_health-data_en.pdf.

to legitimate interest once the data subject withdraws his consent. This applies even if a valid legitimate interest existed initially.

6.4.4 Primary vs. secondary purpose

Primary purpose is not defined by the GDPR. However, secondary use is defined as processing of personal data for purposes "*other than those for which the personal data were initially collected"* (original, primary purposes) (recital 50 if the GDPR).

In the context of cardiac remote monitoring, the initial *vs.* secondary purpose of the processing depend on how you interpret the situation. It could be argued that the whole data processing happens for the purposes of provision of health care by health and care providers to the patient concerned and that the data processing by the manufacturer for the purpose of control of the implant or remote monitoring system for the purpose of ensuring high standards of quality and safety of healthcare and of medical products and medical devices is a secondary purpose [a].

Secondary use allowed only where the processing is compatible with the original purposes. In this case, no separate legal basis (other than that which originally allowed the collection of the personal data) is required.

The following should be taken into account, inter alia[b]:

- Any link between the original, primary purposes (for which the personal data have been collected) and the secondary purposes of the intended further processing;
- The context in which the personal data have been collected: relationship between data subjects and the controller, the reasonable expectations of data subjects;
- The nature of the personal data: data concerning health is a special category;
- The possible consequences of the intended further processing for data subjects;
- The existence of appropriate safeguards, e.g. encryption or pseudonymisation of data further processed.

Secondary use is lawful when:

- Processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller Union or Member State law may determine and specify the tasks and purposes for which the further processing should be regarded as compatible and lawful.
- Further processing for scientific research purposes are considered to be compatible lawful processing operations.
- The legal basis provided by Union or Member State law for the processing of personal data may also provide a legal basis for further processing.

However, if the manufacturer has collected the data on the basis of consent or following a legal requirement, no further processing beyond what is covered by the original consent or the provisions of the law is possible. Further processing would require obtaining new consent or a new legal basis.

The data protection regulations provide for a number of relaxations for the benefit of scientific research activities (possibility of re-using data initially collected for other purposes, possibility of processing sensitive data, possibility of derogating from the rights of the data subjects, possibility of

a https://ec.europa.eu/health/sites/default/files/ehealth/docs/ms_rules_health-data_en.pdf

b https://www.ema.europa.eu/en/documents/presentation/presentation-32-electronic-health-record-access-share-expand-project-secondary-use-healthcare-data_en.pdf

keeping data for a longer period of time, exception to the duty to inform and the right to erasure, etc.).

In Belgium specific restrictions to data subjects' rights are foreseen in the Law of 30 July 2018 on the protection of individuals with regard to the processing of personal data (Article 186 to 208) in the context of scientific research. In principle, in case of research, only anonymised or pseudonymised data can be used and the choice for pseudonymized data must be justified by the DPO prior to the data collection.

6.4.5 Debate regarding the patient rights

Individuals are granted the right to obtain information from the data controller about the nature and use of the data stored, and they have the right of access to their own data. With certain exemptions (such as when the security of the state must be protected) they have the right to be forgotten and to have their data erased from a particular database (Article 17). Data subjects also in general have the right to 'data portability' which means that they can receive their personal data in a 'structured, commonly used and machine-readable format', thereby allowing them to transmit those data to another controller without hindrance from the controller to which personal data have been provided (Article 20).

The question of which rights patients have to the data collected remotely by these devices beyond what is summarised in their medical records and the question of what format they can claim for this data (raw or granular format) are not defined in the texts and are not widely explored in the literature.

The Data Protection Working Party explicitly mentions in its guidelines that the right to data portability "may also include other raw data such as the heartbeat tracked by a wearable device". The right of data portability complements the right of access under Art. 15 of the GDPR. 31 Art. 20(1) of the GDPR states that the personal data concerning the data subject should be received "*in a structured, commonly used and machine-readable format*."

The Data Protection Working Party's guidelines also clarify that "where the personal data requested are processed by a data processor, the contract concluded in accordance with Article 28 of the GDPR must include the obligation to assist '*the controller by appropriate technical and organizational measures, … to respond to requests for exercising the data subject's rights.*'"

The requirement for manufacturers to monitor the performance of their devices, for which they need to collect data, appears incompatible with the right given to individuals by the GDPR that they can require their personal information to be removed from a database (unless the processing is required for compliance with certain legal obligations). In practice, if a patient withdraws consent, then no future data will be collected but information that has already been collected may be retained by the company.

No specific legal advice has been published by the European Commission concerning this question, however, and it would not arise if manufacturers stored only anonymised or de-identified data (see Article 4.5 of the GDPR). Manufacturers of CIEDs state that this will be impossible because they need to know the site and date of any implant. [77]

companies seem to invoke several reasons to refuse to transfer data collected. Patient associations advocates that there is no legal ground for such refusal. In fact, this information could even be useful in order to improve patient awareness of his health [a].

[a] https://www.wsj.com/articles/SB10001424052970203937004578078820874744076. 2012

6.4.6 GDPR certifications and Guidelines

The five remote monitoring companies have confirmed their compliance with the GDPR. Currently, this compliance in not certified. Indeed, while the GDPR explicitly provides the *possibility* of GDPR certification (article 42), there is however no official EU- certification process yet.

Article 43 of the Regulation provides that certification shall be issued and renewed by a certification body with an appropriate level of expertise, after informing the supervisory authority so that the latter can exercise its powers under Article 58(2)(h).

It is up to each Member State to determine which of the competent national supervisory authority or the national accreditation body will be competent to approve certification bodies (§ 1(a) and (b)).

Once accredited, the certification body is responsible for carrying out the proper assessment for certification or withdrawal of certification. Approval is granted for a maximum period of five years and may be renewed under the same conditions as long as the body meets the requirements. It must then systematically communicate to the supervisory authority the reasons for issuing or withdrawing the requested certification.

In Belgium, article 18 the law of 30.07.2018 on the protection of individuals with regard to the processing of personal data requires certification bodies to be accredited in accordance with EN-ISO/IEC 17065 and the additional requirements established by the supervisory authority by the national accreditation body designated in accordance with Regulation (EC) No 765/2008 of the European Parliament and of the Council of 9 July 2008 setting out the requirements for accreditation and market surveillance relating to the marketing of products and repealing Council Regulation (EEC) No 339/93.

6.4.7 Key points

- **Several duties, rights and responsibilities are linked to the different roles (data controller, data processor, data subject) defined in the Data Protection Act. Therefore, contracts between the respective parties involved, clarifying and defining the roles and responsibilities of the different parties are necessary.**
- **As far as CIEDs remote monitoring is concerned, the question of who determines the purpose of the personal processing (and therefore who is responsible as data controller) is crucial.**
- **The majority of the companies considers that the entire purpose of the data processing is defined by the hospital. This position is not shared by the joint Task Force of the European Heart Rhythm Association (EHRA) and the Regulatory Affairs Committee of the European Society of Cardiology who considers, in principle, both the manufacturers and the hospitals (cardiology service) as joint controllers.**
- **This position is consistent with the requirements applicable to the manufacturers under the medical device regulations prior and after the market access. However, guidance from the European Commission and the Data protection advisory Board would be useful to clarify the relationships between these two legal frameworks (GDPR – Medical devices).**
- **The legal grounds for the data processing are also debated. The consent of the patient seems however the most used ground for the collection and processing of data collected remotely by CIEDs.**
- **The use of current guidelines and consent templates issued by experts independent from the companies should be promoted to provide the greatest possible clarity for the patient.**
- **It should be remembered that even if this right is not often exercised, the patient should have the right to access all his or**

her data. If he/she requests it, he/she should also be able to access all the raw data concerning his/her health and the functioning of his/her implant.

6.5 Regulation of health care services

In contrast with the European regulations on medical devices and data protection, the regulation of health care delivery falls entirely in the hands of the Member States.

CIEDs remote monitoring implies a different way of organizing care and interacting with patients. In Belgium, legal rules regarding medical liability, professional secrecy or patient's rights are the same regardless of the physical or remote contact between the patient and the health care professionals and collaborators. However, as detailed in our 2010 report, the specific context of cardiac remote monitoring requires certain precautions[1].

6.5.1 Summary of (unchanged) medical liability, patient rights and professional secrecy rules

In terms of **medical liability** of the treating physicians, as far as adding remote monitoring to regular follow-up can be considered to be the standard of care, it is arguable that if a patient is eligible for remote monitoring, the physician should inform the patient on remote monitoring as part of the aftercare. However, patient information on the benefits and limitations is crucial and particularly broad in this case.

Some guidance [80] [77] were published since our last report. In this regard the situation is thus better than in 2010 when we wrote our first report. However, their number remain limited, and physicians shall balance the fact that while the potential benefits to the patient can be valuable (fewer hospital visits, faster response to alerts, etc.), high quality evidence on clinical outcomes is limited. In addition, the clinical organization of the health care professional and the patient own behaviour or living environment might affect the service delivered by CIEDs remote monitoring. If remote monitoring is applied for continuous follow-up or for disease management, patients need to be informed orally as well as in writing on the modalities (frequency of viewing the data, during specific hours etc.) and the limitations and financial consequences of the system.

Information to the patient must also stipulate that the remote monitoring application for continuous follow-up or for disease management is not an emergency system. Functioning and limitations of alert functionalities shall be clearly explained to the patient as well. Specific contracts shall be signed with the remote monitoring provider specifying the maximum response time and other modalities and protocols shall be in place in hospitals implementing these alerts systems. Such protocols must be reviewed by the competent authorities in the context of hospitals inspections.

In addition to medical liability of the physicians, the hospital is in principle responsible for actions of its employees and the manufacturer is liable for damages caused by defective product, for instance the decision- supporting software, the implanted device, the bedside monitor,(for further details see our previous report).

Once appropriately informed, **the patient can give his consent**. In principle, oral patient consent suffices for care delivery and exchange of health data by health care providers in the context of health care. For the remote monitoring application, however, an integrated approach using a written consent containing information elements regarding data processing as well as the information linked to the remote monitoring as medical intervention is preferable.

Under the law on patient's rights, the patient has a **right to access his patient file**. The health data (or the derived results) revealed by the remote monitoring application are part of the patient file filled by the physicians. In theory, the whole raw data set is part of the information to which the patient is entitled. However, the question of the patient's actual access to this type of data is not settled (see above section 6.4.4).

Finally, **professional secrecy** also applies to remote monitoring. As a general rule, health care professionals involved in the remote monitoring application cannot disclose health data they have been entrusted by virtue of their profession. Exceptions exist in legislation and in jurisprudence.

Health data within the remote monitoring application can be shared between the treating physician, his/her (para)medical team and the referring physician if the addressee is also bound by the duty of professional secrecy; if the sharing of the confidential information must be necessary to ensure continuity and quality of care and if the patient has to give his explicit or tacit consent or the disclosure should at least be in his/her best interest (shared professional secrecy).

The necessity of the intervention of ICT staff and other experts in the treatment of personal data of the patient necessitates to consider them as "collaborators" of the health care professionals and thus justifies the sharing of certain secrets in accordance with the theory of shared professional secrecy. Technical staff, administrative support and other persons involved in the remote monitoring process should however be subjected to strict rules stipulated in contracts with regard to privacy and confidentiality of the respective health data.

6.5.2 The new law on the quality of health care practice

Under the law on patient's rights[a], the patient is entitled **to** qualitative care. On 22 April 2019, the Belgian legislator adopted a new law relating to the quality of the care delivery (that will, in principle, enter into force in 2022)[b]. This law intends to transpose certain patient's rights in more specific correlative obligations for all healthcare practitioners. In other words, it sets specific behaviour rules for all healthcare practitioners. This law applies wherever the concerned practitioners' practices (hospital ward, private practice), to all care provisions (reimbursed or not) and to all patients (Belgian or foreigners). The relationship between a patient and a health care professional in the context of telemedicine also falls within the scope of the text. A physical contact between the patient and the health care professional for the requirements of this law to apply.[c]

Article 8 of this law states that health care professionals shall only provide health care for which they have the necessary demonstrable competence and experience. This rule is already implied by medical liability rules (see supra 6.5.1). However, the law on the quality of health care practice provides here a quality requirement that might be sanctioned by a withdrawal of the license to practice (visa) by the competent health authority.

The health care professional must also be able to proof his competence and experience. In Belgium, cardiology is recognised as one of the 51 physician **specialisations**[d]. There is currently however no official specialisation title or qualification for physicians performing remote monitoring of cardiac devices (specialization in electrophysiology). Specialisation in electrophysiology does also not exist for the nurses.

Under the new law, a new possibility[e] to proof competencies will lie in the requirement for all health care professionals to maintain a, preferably electronic, portfolio containing evidence to demonstrate that he is sufficiently trained to in order to be able to provide quality care (article 8).

In addition, article 4 states that "*the health care professional shall be guided in his or her therapeutical choice by relevant scientific evidence and expertise, taking into account the patient's preferences*." Consequently, unnecessary (expensive) services must be avoided[f] and the recommendations accepted by national scientific associations must be considered. The health care professional should always be able to justify his or her choice, referring in particular to the recommendations he or she has applied. It is also his responsibility to be informed of the latest scientific

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a Law on patient rights of 22 Augustus 2002. *M.B.- B.S.*, 26.09.2002.

b Law on the Quality of Healthcare Practice. *M.B. – B.S.*14.05.2019.

c *Doc. Parl.*, Chambre, 54 3441/001, p. 15.

d https://www.health.belgium.be/fr/sante/professions-de-sante/medecins-dentistes-et-pharmaciens/medecins-specialistes

e This provision is in line with recital 39 of Directive 205/36/EC of the European Parliament and of the Council of 7 September and of the Council of 7 September 2005 on the recognition of professional qualifications.

f This is also required by article 73 of the Law of 14.07.1994 on health and disability insurance.

developments and recommendations, primarily issued by professional and scientific associations. The fact that a particular recommendation has not been brought to the attention of health care professionals by the authority cannot constitute an excuse for non-compliance.

Article 14 stipulates that the provider must ensure that the necessary working environment is present to enable him to perform qualitative health. This includes logistical, technical, architectural and hygienic conditions. The health care professional therefore has an obligation of means and bears responsibility for the choice of rules, recommendations, etc. that he must follow in a concrete situation. In addition, the doctors involved in remote monitoring and the hospitals are also responsible for ensuring cybersecurity. In application of the new law on the quality of health care practice of 22 April 2019, which will be applicable from 2022 onwards, the health care professional must ensure that he/she works in an appropriate environment and has the necessary support to deliver qualitative care. This includes the logistic, technical, or architectural as well as hygienic conditions. Hospitals must also ensure this as part of their accreditation. In this respect, a financing from the federal authorities is still under discussion in order to provide hospitals with additional means to ensure cybersecurity.

In addition, different quality requirements (‘*agrément-erkenning*’) apply to hospitals. However, the health care professional still remains responsible for delivering qualitative care. This means, for example, that he will have to consult with the hospital or other care facility and if the conditions are not met, refuse to perform a specific care.

Finally, the law of 22 April 2019 also regulates the access of health care professionals to patient personal data. The health care professional shall only have access to personal data relating to the health of patients with whom he/she has a therapeutic relationship. A therapeutic relationship is any relationship between a patient and a health care professional in which health care is provided. (article 37).

The health care professional who has a therapeutic relationship with the patient only has access to personal data relating to the patient's health under the following conditions:

1. The purpose of the access is to provide health care.
2. The access is necessary for the continuity and quality of the health care provided.
3. The access is limited to data that are useful and relevant to the provision of health care.

6.5.3 eHealth

Since 2008, the eHealth platform permits the electronic exchange of secured data between health actors in Belgium. A national eHealth plan (2013–2018) was also launched, with the objectives to develop data exchanges between care providers, increase patient involvement and their knowledge related to eHealth, develop common terminology, simplify administrative procedures and create a transparent structure of governance with all involved actors.

In hospitals, a recurrent accelerator budget is agreed for the faster implementation of electronic health records. In addition, a specific budget is also currently discussed to allow hospital to implement cybersecurity measures[a].

Since 2018, patients can access personal information about their health (both medical and administrative) and other general health related information through an online portal (Personal Health Viewer: mijngezondheid.be; masante.belgique.be).

While interoperability with these systems (or with other devices) is not a market access requirement (see supra section 6.3.1.6), interoperability and connectivity to the basic services of the eHealth platform is, in principle, a

[a] https://organesdeconcertation.sante.belgique.be/sites/default/files/documents/cfeh_d_536-2_-_avis_bmuc_et_cybersecurity_-_fr.pdf

requirement for health applications to access reimbursement stage (M2 requirement)[a].

6.5.4 Key points

- **In Europe, the regulation of health care delivery falls entirely in the hand of the Member States.**
- **CIEDs remote monitoring implies a different way of organizing care and interacting with patients. In Belgium, legal rules regarding medical liability, professional secrecy or patient's rights are the same regardless of the physical or remote contact between the patient and the health care professionals and collaborators implementing cardiac remote monitoring. However, as detailed in our 2010 report, the specific context of this technology requires certain precautions.**
- **Specific protocols shall be in place in hospitals using CIEDs remote monitoring and clear and specific consent documents must be signed. In contrast to 2010, some specific guidelines issued by scientific societies are available and can support the drafting of these protocols.**
- **The Belgian legislator adopted a new law relating to the quality of the care delivery (that will, in principle, enter into force in 2022) setting specific behaviour rules for all healthcare practitioners. This law applies in an identical way to the physical or remote therapeutic relationship between a patient and a health care professional.**
- **Under this law, health care professionals shall only provide health care for which they have the necessary demonstrable competence and experience. All health care professionals will have to prove their competencies by maintaining a, preferably electronic, portfolio containing evidence to demonstrate that they are sufficiently trained to in order to be able to provide qualitative care.**
- **Infringements to these quality requirements might be sanctioned by a withdrawal of the license to practice (visa) by the competent health authority.**
- **As there is currently no official specialisation title or qualification for physicians or nurses performing remote monitoring of cardiac devices (specialisation in electrophysiology), the portfolio will have to be filled with proofs of specific trainings.**
- **Health care professional shall also be guided in his or her therapeutical choice by relevant scientific evidence and expertise, taking into account the patient's preferences.**
- **Since 2018, patients can access personal information about their health (both medical and administrative) and other general health related information through an online portal (Personal Health Viewer: mijngezondheid.be; masante.belgique.be).**
- **In hospitals, a recurrent budget is agreed for the faster implementation of electronic health records (EHRs). At the beginning of 2019, only 15% of general hospitals had EHRs. A specific budget is also currently discussed to allow hospitals to implement cybersecurity measures.**

[a] https://mhealthbelgium.be/ and https://mhealthbelgium.be/images/downloads/Criteria-mHealth-apps-ENv5.pdf

6.6 Discussion

Since the publication of our last KCE report, several new rules were modified to taking into account the existence of eHealth technologies. However, these new rules did not solve all the legal debates affecting the successful implementation of cardiac remote monitoring.

Unlike the previous Directives, the new Regulation on medical devices require, in principle, pre-market clinical trials for all Class III devices such as CIEDs and (the main components of) related remote monitoring systems. However, the requirement to perform clinical investigations does not apply to implantable devices and class III devices: which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation is based on sufficient clinical data.

In Europe, the evaluation of appropriateness of these data and, more generally, the compliance of remote monitoring systems with the general safety and performance requirements is in the hands of the notifies bodies.

Improvements regarding transparency will be brought by the new version of Eudamed but should not be expected before the end of 2025. This lack of transparency is regrettable not only in terms of respect for patients' rights (right to information in particular) but also for doctors to better understand their medical responsibility when delivering these services.

With the adoption of the GDPR and its very important sanctions, operators involved in the data collection and processing have been put under the spotlights. Citizens, including patients, are now more and more concerned about what will be done with their data and the authorities can sanction non-compliance with the GDPR. As far as CIEDs remote monitoring is concerned, the question of who determines the purpose of the personal processing (and therefore who is responsible as data controller) is crucial. The majority of the companies consider that the entire purpose of the data processing is defined by the hospital. This position is not shared by the European Society of cardiology who consider, in principle, both the manufacturers and the hospitals (cardiology service) as joint controllers. This position is consistent with the role of the manufacturers under the medical device regulations. Indeed, in the context of their post-marketing surveillance obligations, manufacturers must implement a specific plan prior to the placing on the market to monitor their devices. The specific content of this plan is defined by the manufactured who must define which measures (including, for instance which data) need to be collected to monitor the safety, performance and benefit risk balance of their device. In any case, the use of current guidelines and consent templates issued by experts independent from the companies and official certifications, where they exist, should be promoted to provide the greatest possible clarity for the patient. Finally, it should be remembered that even if this right is not often exercised, the patient should have the right to access all his or her data. If he/she requests it, he/she should also be able to access all the raw data concerning his/her health and the functioning of his/her implant.

In contrast with the European regulations on medical devices and data protection, the regulation of health care delivery falls entirely in the hand of the Member States. The health care professional implementing remote monitoring of CIEDs must be able to proof his competence and experience. To this end, a new Belgian law that will enter into force in near future, requires health care professionals to maintain a, preferably electronic, portfolio containing evidence to demonstrate that he is sufficiently trained to in order to be able to provide quality care. Only the actual implementation of this law will show whether this requirement is sufficient or whether a new specialisation recognised by the law (currently non-existent) should be created to offer this type of care.

Ten years after the first KCE report, legal frameworks have evolved but the technology is so specific that guidelines are still needed.

7 REIMBURSEMENT AND ORGANIZATIONAL ASPECTS IN SELECTED COUNTRIES

7.1 Introduction and method

The aim of this chapter was to analyse reimbursement practices and related organizational aspects in a selection of countries, i.e. France, the Netherlands, and Germany. These countries were selected because of their geographic proximity with Belgium (neighbouring countries) and their comparable living standard.

More precisely, the following aspects were analysed:

- What type of funding is available for remote monitoring (RM) activities provided by health care professionals?
- What type of funding is available for the equipment and services delivered by RM systems' providers?
- Which quality criteria, organizational aspects, or legal aspects are included in the reimbursement conditions?
- Who is involved in the process, including the question of responsibilities?

The description was based on information obtained from national official websites related to health care and contacts with national official institutions (see the appendix related to this chapter for details on the sources consulted).

7.2 Coverage of health care professionals' activities

In France, temporary reimbursement is currently provided through experiments known as the ETAPES programme ("*Expérimentations de Télémédecine pour l'Amélioration des Parcours en Santé*"). These experiments concern RM procedures for 5 pathologies, including implantable cardiac prostheses (i.e. heart failure, renal failure, respiratory failure, diabetes, and implantable cardiac prostheses). The objective of this programme is twofold, i.e. "to give rise to experimental approaches that will encourage innovative initiatives" and "to foresee what a telemedicine organisation could represent in the future".[83] During these experiments, specific tariffs for the RM of patients with ICDs and PMs by health care professionals have been defined (see Table 16). A yearly lump-sum of €130 (paid in two times) covers remote data interrogation according to a time schedule recommended by professional associations (every three to six months, at least every six months) and the management of alerts (reorientation of the patient, treatment adaptation, etc.). This payment is expected to cover the following aspects of RM: informing the patient, assessing its suitability, obtaining the patient's informed consent, performing the initial set-up of the RM system, analysing the data transmitted at scheduled calendar intervals, verifying and analysing alerts and associated data transmissions, updating the medical profile and system settings, intervening (e.g. by calling the patient) if required, drawing up a medical report in case of intervention and/or additional procedure, and informing other medical professionals involved in the patient's cardiac care. This lump sum also covers centre-specific requirements, i.e. implementing a RM programme, assessing the technical feasibility of the application, training patients, verifying the correct activation and use of the system by the patient, and implementing a telephone access for patients. For in-clinic visits (also if brought up by an alert), the traditional amount is paid (see Table 16). The final decision in terms of funding and organization and the potential entry of RM into common regulation will be based on the evaluation of these experiments. It is also important to note that the ETAPES programme only concerned cardiac devices for therapeutic purposes. The RM of ILRs, with a diagnosis purpose, is currently not reimbursed (not included in the ETAPES programme) but such request is currently under evaluation (see the HAS report 2021 for more details).[10]

In the Netherlands, characterized by a (regulated) private market (see the appendix to this chapter for more details), health care provision is the result of negotiations between health insurers and health care providers. Specialized medical care, including cardiology, is paid by means of a Diagnosis-Treatment Combination (Diagnose Behandeling Combinatie - DBC) care product, covering the entire care episode (in- and outpatient care activities). Health insurers negotiate with the hospital, the outpatient clinic or other forms of certified health care institutions, which care services (i.e. care activities – "*zorgactivities*") can be registered and declared for a specific diagnosis and a specific care episode, and at which price. The prices of the DBC-care products can either be freely determined (in about 70% of DBC - free segment) or be determined within the limit of a maximum price defined by the Dutch Health Care Authority ("Nederlandse Zorgautoriteit"-NZa) (in about 30% of DBC - regulated segment). For the monitoring of patients with ICDs, the prices of the related DBC-care products are freely negotiated but an estimation of the national average price is provided on the website of the NZa (see the average tariffs in Table 16). Since 2019, remote monitoring is a declarable health care activity that can be used for all medical specialties if agreed by the health insurer. It is nevertheless important to note that the same DBC care product is used for both remote and standard in-clinic monitoring. This is usual in the Netherlands. Health care products are described as functionally as possible and it is especially the care activity that is described, but not who provides the care or in which setting (in-clinic or remotely) it is performed. This gives health care providers and health insurers a lot of room to make their own choices about the use of digital care. This also allows health care providers to change the process of care within the existing product by partially replacing face-to-face care with digital care, without changing the negotiated price. While the price is the same between remote and standard monitoring, the cost related to RM activities can nevertheless be taken into account in the definition of the DBC price if the health insurer wants to promote the use of RM. After having contacted all health insurers listed on the website of the association representative of Dutch health insurers (*Zorgverzekeraars Nederland*)[84], it should nevertheless be noted that the only two health insurers having responded to our questions does not consider RM activities to determine the DBC prices for the monitoring of patients with CIEDs.

In Germany, the monitoring of patients with cardiac implantable electronic devices (CIEDs) is considered as an outpatient service and must therefore be included in the catalogue for outpatient services (Einheitlicher Bewertungsmaßstab, or EBM) to be reimbursed. Since 2015, scheduled remote data interrogations (functional analyses) of ICDs, CRT-Ps and CRT-Ds are included in the EBM, and are reimbursed at the same tariff as the standard in-clinic monitoring (functional analyses) of these devices, with a maximum of 5 controls per year. Such functional analyses of ICDs and CRTs are scheduled at specific dates to replace standard in-clinic visits; and consist in remotely checking the battery condition, checking and documenting the collected parameters and measured values, and controlling the functionality of the electrode(s). Other RM activities such as the (unscheduled) management of alerts are currently not covered yet (but such coverage is under discussion for patients with heart failure). There is also no reimbursement for the RM (neither for the remote date interrogations nor for the management of alerts) of single chamber and double chamber PMs and ILRs.

Table 16 – Coverage of RM activities provided by health care professionals

France	The Netherlands	Germany

• **ICD (ETAPES programme):**
  ○ RM: 2 x €65 (€130) per patient per year (**lump sum**)
  ○ In-clinic visit: €70.48 per visit (at least 1x per year and any additional if and when required, e.g. due to an alert) (**FFS**)
• **PM (ETAPES programme):**
  ○ RM: 2 x €65 (€130) per patient per year (**lump sum**)
  ○ In-clinic visit: €60.41 per visit (at least 1x per year and any additional if and when required, e.g. due to an alert) (**FFS**)
• **ILR: Currently not reimbursed (under evaluation)**
	• **Whole care episode** covered by the **DBC system** (with tariffs freely negotiated):
	  ○ ICDs: mean 2019 price of €175 if 1 – 2 (e)visits, and of €365 if > 2 (e)visits
	  ○ PMs: mean 2019 price of €170 if 1 – 2 (e)visits, and of €300 if > 2 (e)visits
	  ○ ILRs: mean 2019 price of €190 if 1 – 2 (e)visits, and of €390 if > 2 (e)visits for impulse and conduction disorders
	• Telemonitoring is a declarable activity but must be agreed by the health insurer
	• Same DBC tariffs are applied whatever the place of the activity (in-clinic or remotely) (see the appendix for details)
	• Not considered by all insurers
		• **ICD, CRT-P, CRT-D:** same EBM fee for both in-clinic monitoring and scheduled RM (and same maximum number of controls per year)
		  ○ **ICD:** €44.5 (maximum 5x/year) (**FFS**)
		  ○ **CRT-P, CRT-D:** €54.73 (maximum 5x/year) (**FFS**)
		  ○ Other RM activities (management of unscheduled alerts): not reimbursed yet
		• **PM (single and double chambers):** RM not reimbursed
		• **ILR**: RM not reimbursed

Tariffs applicable at the time of writing this report, i.e. May 2021; CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; DBC = Diagnosed-treatment combination (Diagnose Behandeling Combinatie); EBM = German catalogue for outpatient services (Einheitlicher Bewertungsmaßstab); ETAPES = Expérimentations de Télémédecine pour l'Amélioration des Parcours en Santé; FFS= Fee-for-service; ICD= implantable cardioverter-defibrillator; ILR = Implantable Loop Recorder; PM= Pacemaker; RM = Remote Monitoring

7.3 Coverage of the RM system and related services delivered by the system's provider

In France, a separate tariff (one-time amount) has been set for the RM system of ICDs, covering both the transmitter and other services such as data storage and transmission. The tariffs differ according to the implant (e.g. double or triple chamber ICDs) but not according to the trademark (see Table 17). For PMs and ILRs, no separate tariff has been set. The cost for the RM system is covered by the tariff set for the implant (also varying according to the implant characteristic but not to the trademark). For pacemakers, it should be noted that a higher tariff (a bonus) has been set for some implants (triple chambers or rate adaptive single/double chambers) when they are combined with a RM system (see Table 17) but such a bonus is conditional, i.e. more than 50% of the patients with PMs in the year (per sector) must be remotely monitored, otherwise the manufacturer must reimburse the surplus received (e.g. if only 45% of patients with PMs are remotely monitored, they must reimburse 5% of the received bonus).These tariffs serve as basis for the reimbursement and also determine the maximum selling price.

In the Netherlands, medical devices used in the context of RM are paid for as part of the DBC care product (see also section 7.2).

In Germany, RM systems are paid together with the implant by the G-DRG system and an additional procedure classification ('Operationen- und Prozedurenschlüssel' - OPS) code can be declared for implants compatible with a RM system. Such additional OPS code has no impact on the G-DRG tariff. Nevertheless, some health insurers have concluded contracts with RM systems' providers for a better funding. It should also be noted that a new law reinforcing the funding of RM activities is in progress. The aim is to better cover transmission devices and the infrastructure required for their use, in particular IT-related services for wireless data transmission or data backup.

In all countries, the RM system must be free of charge for the patient.

Table 17– Coverage of the RM system and related services delivered by the RM systems' providers

France	The Netherlands	Germany

• **ICD:** Included in the list of reimbursed products (LPP) separately from the implant. Reimbursement basis:
  ○ €864 for RM systems of single or double chambers ICDs (One-time amount)
  ○ €972 for RM systems of triple chambers ICDs (One-time amount)
• **PM:** No separate tariff (only implants are included in the LPP) but higher tariffs for some implants if combined with a RM system. Increase in the reimbursement basis:
  ○ + € 500 for rate-adaptive single or double chambers pacemakers and a RM device if 50% of patients are under RM
  ○ + € 700 for triple chamber and resynchronisation pacemakers and a RM device if 50% of patients are under RM
• **ILR:** No separate tariff (only implants are included in the LPP)
	• Covered by the DBC system (no separate tariff)	• Additional OPS code for RM-enabled implants (no impact on reimbursement)
		• RM infrastructure and support services usually not reimbursed (currently only selective contracts with local health insurances) but under discussion: draft Digital Supply and Care Modernization Act – DVPMG – adopted on 21/01/2021

Tariffs applicable at the time of writing this report, i.e. May 2021; DBC = Diagnosed-treatment combination (Diagnose Behandeling Combinatie); ICD= implantable cardioverter-defibrillator; ILR = Implantable Loop Recorder; LPP = List of reimbursed products and services ('Liste des produits et prestations remboursables'); OPS = German Procedure Classification ('Operationen- und Prozedurenschlüssel'); PM= Pacemaker; RM = Remote Monitoring.

7.4 Reimbursement conditions: quality criteria, organizational, and legal aspects

In France, specific criteria are specified in the reimbursement conditions (see a summary in Table 18). For the RM of patients with ICDs, these criteria are based on an assessment done by the HAS in 2017.[3] In this assessment, minimum requirements have been defined for the RM system providers, for the centres, and for the health care providers (see the appendix for this chapter). The centre must for example provide a telephone access for patients on working days and hours to answer patients', their families' and carers' clinical questions and must ensure patient education and proper functioning of the system. The RM system providers must for example provide a hotline for patients, their families and carers, as well as a technical assistance for health professionals, accessible via a free phone number on working days (9am-6pm). Additionally, according to the specificities of the ETAPES Programme, patients must suffer from a chronic condition which requires prolonged treatment (long-term illness – ALD status). Specific exclusion criteria have also been defined in the ETAPES programme, i.e. patients with a co-morbidity that imply a life expectancy inferior to 12 months (based on the opinion of the physician), with usual therapeutic compliance or adherence estimated to be low (based on the opinion of the physician), or with no fixed place of residence. Moreover, health professionals, health establishments, and RM systems providers must fill out a standard declaration of telemedicine activity which specifies the respective missions of each. This declaration must be sent to the regional health authorities and to the departmental council of the order of physicians. The RM system provider must also send to the Ministry of Health's Directorate-General for Health Care Services a CE marking certificate for medical devices and a statement on honour that he complies with the specifications for telemedicine experiments. Good clinical practice guidelines have also been elaborated.[85]

In the Netherlands, every declared RM activity (Zorgactiviteit code 039133 – Telemonitoring) in a care episode must be combined with a consultation, that can either be done in-clinic or by phone or video conference. Additionally, data must be recorded in the patient file. To obtain additional information on requirements imposed by the health insurers, all health insurers mentioned on the website of the association representative of Dutch health insurers (Zorgverzekeraars Nederland) were contacted without success.[84] Only two insurers that do not consider RM of CIEDs patients responded. Nevertheless, in the Netherlands, compliance with guidelines and consensus are required. In 2011, the Netherlands Society of Cardiology published an expert consensus on the standard care for the RM of patients with CIEDs including quality, technical and legal aspects (see Table 18 and the appendix to this chapter).[86] It should also be noted that the Netherlands funds a program (called 'MedMij) that develops specific standards and a label confirming that health data can be exchanged in a safe and reliable way (see the KCE report on teleconsultations for details).[87]

In Germany, the reimbursement conditions impose at least 1 in-clinic visit prior RM and limit the reimbursement of both RM or in-clinic control to maximum 5 per year. Additionally, an approval by the responsible Association of Statutory Health Insurance Physicians is required.

In all countries, the following aspects were highlighted:

- At least one consultation per year is required (that can be done by phone or video conference in the Netherlands);
- Events must be registered in the patient record;
- RM is not an obligatory service and patients can refuse it;
- The patient's informed consent is required and must contain a.o. information on the fact that patients must contact usual emergency services in case of serious adverse events (RM should not be considered as an emergency service).
- There are also common requirements in terms of respects to the General Data Protection Regulation (GDPR) and in terms of data encryptions to guarantee patient data privacy and confidentiality (see the chapter on legal aspects for more details).

Table 18 – Quality, organizational, and legal aspects

France	Netherlands	Germany

• **For ICD and PM**:
  ○ RM system must be registered in the list of reimbursed services and products (LPP)
  ○ Specification of a minimum list of alerts that must be programmed
  ○ A prescription must be renewed each year; except if the prescribing physician is the physician performing the remote monitoring. In this case, no prescription is required
  ○ At least one annual face to face consultation (more if required by alerts)
  ○ Patient information and agreement on RM activitties (see also the protocol described in Box 6 and the patient informed consent)
• **For ICD:** A protocol between the RM system provider and the responsible physician must be drawn up (see Box 6)
• **For ILR:** Not yet reimbursed but an assessment done by the HAS with recommendations on requirements is already published (see the appendix).
	• At least one consultation per year, either in clinic or remotely
	• Patients data must be registered in the patient file
	• Other specific requirements were not communicated by the contacted health insurers but the following aspects were highlighted in the 2011 expert consensus of the Netherlands Society of Cardiology:
	  ○ RM cannot be an obligatory patient care;
	  ○ It is not a continuous 24 h/d, 7d/w monitoring;
	  ○ Device companies are not responsible for delays or lack of alerts and follow-up due to failing landline or global system for mobile Communications technology;
	  ○ Attention should be given to the patient's informed consent, including information on the expectations and restrictions of RM (not an emergency service, use of the standard way if serious acute events), the contribution and responsibilities of the patient (proper handling of the transmitter, ensuring proper communication with the centre), the timing of unscheduled transmission, analysis of data and feedback to the patient, and if done, an agreement on the use of data for assessing long-term CIED performance;
	  ○ A protocol should formalize the manufacture's interaction with the cardiologist, allied professional and hospital as well as their responsibilities;
	  ○ Security and confidentiality of data must be ensured (encrypted messages, secure websites)
	  ○ Increasing the uniformity of methods of remote CIED monitoring as well as standardized presentation of data would be needed;
	  ○ They also recommended required alerts and thresholds for schedulled and unschedulled monitoring as well as optional alerts.
		• Prior in-office functional analysis
		• Approval of the responsible Association of Statutory Health Insurance Physicians
		• Maximum 5 controls (both in-office and remote) per year

Box 6 – The French protocol between the RM system provider and the responsible physician (for the remote monitoring of ICDs)

The protocol must include:

- **The identification of the treating/responsible physician;**
- **A description of:**
  - **how the remote monitoring is organized, in accordance with good clinical practice and device's requirements;**
  - **how alerts are defined and how data are collected;**
  - **how to obtain the patient consent and who must obtain it (the physician / RM system providers). The patient informed consent must include a.o. the fact it is not an emergency service, that patients have been correctly informed, that they agreed with the transfer of data, that they will take care of the transmitter, and that they will communicate new contact data in case of changes (example of informed consent: https://www.sfcardio.fr/publication/telesurveillance-des-protheses-rythmiques-cardiaques) ;**
  - **the role of both (a) the treating physician and other health professionals implied in the process and (b) the RM system provider at each stage of the procedure;**
  - **how to respond to alerts (both for the treating physician and the RM system provider), i.e. the description of the procedures and response times to be respected;**
  - **the practical procedures for maintaining regular contacts between the treating physician and the RM system provider in the absence of alert and**
  - **the procedures for regularly checking the validity of the patient's contact details and the action to be taken in the event of failure to transmit the information**
  - **the skills, training, and specialisations required for both the patient and the health professionals involved (routinely and in the event of an alert)**
  - **the rules for authorising and securing access rights to the information system supporting the system,**
  - **the rules for the security, traceability and confidentiality of the data transmitted and stored.**
- **A technical appendix specifying the maintenance of the system.**

7.5 Who participates in the process and what are their responsibilities?

In France, a medical specialist in cardiovascular diseases with expertise in rhythmology and cardiac stimulation must be the responsible for RM activities (responsible physician). Other physicians can also participate in the process, such as the patient's GP or another medical specialist in cardiovascular diseases treating the patient. The physician carrying out the remote monitoring must declare the activity to his/her civil liability insurance. Nurses can also be involved in the process but if they perform tasks that are normally performed by physicians (transfer of medical tasks to nurses), a cooperation protocol must be established and agreed by the regional health authorities ('*Autorité Régionale de Santé*'– ARS). Nurses involved in such a cooperation protocol have a duty to be trained, must register his/her activities to the ARS and are responsible of their acts, which require insurance coverage. The potential role for the advanced practice nurse in the future is also currently under discussion.

In the Netherlands, the responsible of the RM should not especially be a medical specialist. It can also be a nurse specialist (similar to the international concept of 'advanced practice nurse'), a clinical technologist or a physician assistant. The condition is that they must be skilled for these activities (in agreement with the health insurers).

In Germany, guidelines on responsibilities have been published for the RM of heart failure patients. RM should be carried out in cooperation between the treating physician ('*primär behandelnde Arzt/Ärztin*' - PBA) and a medical RM centre. The PBA is responsible for the guideline-compliant care of the patient and for the treatment measures resulting from RM. The medical RM centre is responsible for the processes related to the implementation of RM (e.g. data collection, etc.). RM in the medical RM centre may only be provided by medical specialists in internal medicine and cardiology (cardiologist).

Table 19 – Who is part of the process?

France	Netherlands	Germany
• Responsible physician: medical specialist in cardiovascular diseases with expertise in rhythmology and cardiac stimulation • If transfer of medical tasks to nurses: cooperation protocol agreed by regional health authorities • In the future: potential role for the advanced practice nurse	RM can be declared to the health insurer by a medical specialist, a nurse specialist (internationally called 'advanced practice nurses'), a physician assistant, or a clinical technologist if they are skilled for these activities (in agreement with the health insurer).	Shared responsibilities between: • The treating physician: responsible for the treatment resulting from RM. • The medical RM centre: responsible for the process of RM implementation. RM in the medical RM centre may only be provided by medical specialists in internal medicine and cardiology (cardiologist).

7.6 Discussion and limitations

The aim of this chapter was to analyze reimbursement practices and related organizational aspects in a selection of countries to provide insights on possible financing models that could be considered in Belgium.

Based on this analysis, the following financing models can be highlighted for RM activities of **health care professionals**:

- Based on France: a fee-for-service system (FFS) for in-clinic visits (also if brought up by an alert) and a yearly lump sum for RM activities (scheduled remote data interrogations, managements of alerts, etc.). This yearly lump sum of €130, payed in two times, corresponds to around 2 in-clinic controls of CIEDs in France.
- Based on the Netherlands: a yearly lump sum[a] that covers the whole episode of care (i.e. the RM system and related services, RM activities of health care professionals, and in-clinic visits) whatever the type of monitoring (remote or standard monitoring). This yearly lum sum is the same for RM and SM patients but can include potential additionnal costs related to RM if there is a wish to promote RM activities.
- Based on Germany: Same FFS for both in-clinic visits and scheduled remote data interrogations, with a maximum number per year (5 in Germany). No payment for the management of alerts.

[a] To transfer the Dutch model to the Belgian setting, the DBC tariff is seen as a yearly lump sum.

In terms of requirements for health professionals, the importance of having at least one face-to-face consultation per year (teleconsultations autorized in the Netherlands), of registering events in the patient's record, and of ensuring a proper patient's information was highlighted. Good clinical practice guidelines also included minimum thresholds for required alerts, the number of required scheduled remote data interrogations, and the level of required permanence. The role of nurses, and their qualification level, was also important (including the requirement of a cooperation protocol agreed by national authorities in case of substitution of physician tasks by nurses).

For the RM systems' providers, the following financing models can be considered:

- Based on France (for PMs): A financing included in the implant tariffs, but with higher amounts (bonus) if combined with a RM system (If RM is actively performed);
- Based on France for ILR and on Germany: A financing included in the implant tariff (no higher amounts if combined with a RM system);
- Based on France (for ICDs): A separate financing, payed in one-time (for the lifetime of the implant), and covering both the transmitter and related RM infrastructure (such as data transmission and storage);
- Based on the Netherlands: Inclusion in the yearly lump sum covering the whole episode of care (i.e. inclusion in the remuneration of health care providers);
- Based on the request of RM system providers: a daily lump sum.

Requirements for the RM systems' providers mostly concerned the minimum alerts that must be included in the RM system, the respect of the rules on security, traceability and confidentiality of data transmitted and stored, and the provision of a technical assistance.

Concerning the patients, countries highlighted the fact that no contribution can be asked to the patients for RM systems (and data transmission). A focus was also done on patients' rights (patients are free to refuse such service), patients' privacy protection (with the respect to the GDPR) and patients' information (patient informed consent) and education.

The impact of these models for the Belgian context is discussed in the next chapter.

These models were also presented at a **stakeholder meeting** on June 17, 2021. Based on this meeting, the following opinions were raised:

- It will be important to decide if the payment should be done at the level of the centre or at the level of the responsible physician;
- Concerning the responsible physician, it should be noted that the specialiation in electrophysiology is not a recognized title or qualification in Belgium.
- The reimbursement decision could also take into account the recent developments on the creation of loco-regional networks and the allocation of care assignements within each network (see Box 7). For example, one centre could be designated within each network to organize a high quality RM services for all hospitalisals of the network. A number of stakeholders were in favor of such expertise concentration because it would ensure the quality of the RM services, especially in terms of rapidity of interventions in case of alerts and ensured permanence. Such quality would be ensured by the recruitment of a dedicated staff, correctly trained and using well-defined protocols, which are conditions unlikely to be met if the volume of patients is low. Smaller hospitals nevetheless noted they were also able to organise RM activities. It was also specified that the designated hospital should not especially be an implanting centre because not all networks have an ICD implanting centre.
- The combination of a lump sum for remote monitoring activities (management of alerts and remote data interrgations) and of a FFS for in-clinic visits was appreciated, but it was highlighted that such a lump sum must be sufficient enough to cover the burden of alerts management. Some stakeholders also mentioned the possibility of a financing per alert, or a financing of phone contacts with the patients, via fees for teleconsultations. A financing based on the number of alerts was nevertheless judged as complex by some other stakholders, also highlighting the fear of administrative burden if they must prove RM is effectively performed.

- The proposal formulated by the Belgian Heart Rhythm Association (BeHRA) in 2011 was also highlighted. Based on a survey, they calculated that 0.5 ETP were needed to follow 200-250 patients in a given year, and that 0.3 minutes and 0,9 minutes per patient, per opening day were required from cardiologists and paramedical staff respectively. By considering mean annual salaries (€120 000 and €60 000 assumed for cardiologists and paramedicals respectively) they estimated a total cost for RM of €225 per patient per year if RM was only performed during the opening hours. They therefore requested for a yearly lump sum of €225 for the management of alerts and other RM related activities. In their proposal, this lump sum could only be asked one time per year, could be cumulated with the fees for in-clinic visits, and could only be asked by medical specialists in cardiology working for hospitals having a recognized cardiac programme E (see the appendix to this chapter for more details). It should nevertheless be noted that such a proposal was done in 2011 and that processes have been improved since then, which may have implied a reduction in the necessary workload.
- The HRS Expert Consensus Statement on remote interrogation and monitoring for CIEDs, including management and organizational aspects (2015 HSR consensus)[80] as well as the 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy[88] were also mentioned. The 2015 HRS Expert Consensus specifies that "*remote monitoring of CIEDs is useful to reduce the incidence of inappropriate ICD shocks"* (Class of Recommendation / Level of evidence I/B-R)[a] and "*for the early detection of atrial fibrillation"* (Class of Recommendation / Level of evidence I/A), and that "*all patients with CIEDs should be offered remote monitoring as part of the standard follow-up management strategy"* (Class of Recommendation / Level of evidence I/A).[80] The 2021 ESC Guidelines has a more narrow scope and specifies that "*remote device management of pacemakers should be considered in order to provide earlier detection of clinical problems (e.g. arrhytmias) or technical issues (e.g. lead failure or battery depletion)"* (Class of Recommendation / Level of evidence IIa/B)[b], and that "*remote device management is recommended to reduce the number of in-office follow-up in patients with pacemakers who have difficulties to attend in-office visits (e.g. due to reduced mobility or other commitments or according to patient preference*"(Class of Recommendation / Level of evidence I/A).[88] The analysis of the content and validity of these guidelines following KCE methods for good clinical practice guidelines was nevertheless out-of-scope for this report.

Box 7 – The creation of loco-regional hospital networks in Belgium

Since 2016, a number of measures have been implemented in the framework of a hospital landscape reform. From 2020, each general hospital must join one local–regional hospital network, with the aim of a.o. allocating care assignements within network. For this, a distinction is done between general care provided by all hospitals; specialised care not provided in every hospital within the network (implying referral agreements); and supra-regional care provided in a limited number of reference hospitals.[89]

[a] In this guidelines, Class I is considered a strong recommendation, denoting a benefit greatly exceeding risk. Level of evidence A refers to data from multiple randomized controlled trials or from a single randomized clinical and a high-quality registry. Level of evidence B-R is moderate quality evidence from randomized trials.[80]

[b] In this guidelines, Class I refers to a recommendation where there is evidence and/or general agreement that the treatment or procedure is beneficial, useful, effective. Class IIa is considered a recommendation where there is conflicting evidence and/or divergence of opinion on treatment efficacy but the weight of evidence/opinion is in favour of usefulness/efficacy. Level of evidence A refers to data derived from multiple randomized clinical trials or meta-analysis. Level of evidence B refers to data derived from a single randomized clinical trial or large non-randomized studies.[88]

BeMedTech also highlighted they have made a reimbursement proposal based on a consensus between all Belgian RM systems' providers, i.e. a lump sum of €0.80 per day per active patient (that can be paid annually) whatever the devices (i.e. for RM of ICDs, PMs, CRT-Ps, CRT-Ds, ILRs), based on a cost analysis of the different health care providers. By active patient, they mean patients that effectively use RM (i.e. transmissions are done). Ideally, they would also like such lump sum to be directly paied to the RM systems providers rathen than to the follow-up centres. Their full proposal can be found in the appendix to this chapter. Estimations of the total cost of RM activities done by RM systems providers were also sent, and varied between around €890 to €2500 for the whole life expectancy of the implant (personnal communication with RM system providers).

This chapter has also some **limitations**. First the international comparison was limited to 3 countries due to a time constraint, while a stakeholder mentioned that Scandinavian countries would have also been interesting. These three countries nevertheless allowed us to identify three different models of financing (i.e. a FFS, a yearly lump sum for the whole follow-up and a mixed model including a FFS and a lump sum). It is unlikely that the inclusion of additional countries such as UK or Switzerland, often selected in KCE international comparisons, would have allowed the identification of any highly different alternative financing model.

Secondly, we decided to focus on what has happened in other countries rather than analysing the literature on organizational aspects. Nevertheless, as the criteria and requirements determined in France are based both on a litterature research and on experts' consultations, using their 'recent' work allowed us to take aspects identified in the litterature into account.

Finally, stakeholders were consulted to obtain their opinions on the financing models identified but this is only a first step in the decision process. A concertation with experts in the field would be needed to obtain a consensus on Belgian good clinical practice guidelines (a.o. on the minimum type of alerts and their required thresholds, the number of scheduled remote data interrogations required, the level of permanence required, the elements to be included in the patient's informed consent, etc.) to link these guidelines to the reimbursement decision.

8 POTENTIAL FINANCING MODELS FOR BELGIUM AND BUDGET IMPACT

8.1 Introduction

The aim of this chapter was to adapt the different models identified in the previous chapter to the Belgian context and to determine what would be the budget impact of these models for the National Institute for Health and Disability Insurance (NIHDI). First, the current situation in Belgium was described. Then, the cost of RM activities in Belgium was estimated based on the KCE manual for cost studies (to have additional amounts than only those identified in other countries). Finally, the potential impact of each model identified in the previous chapter was discussed.

8.2 Current reimbursement in Belgium

Only in-clinic visits are currently reimbursed in Belgium (see Table 20), with a maximum number per year (except the implantation's year or if clinically justified in the medical record of the patient). For ambulatory patients, the tariff for a consultation with a medical specialist in cardiology (102594 or 102093) can be added on the top of each in-clinic control tariff (475893-475904; 475856-475860; 475871-475882).

RM activities of health professionals (remote data interrogations and management of alerts) are currently not reimbursed. There is also no reimbursement for the RM system and related services (such as data storage) delivered by the RM systems' providers.

This means that currently, if the number of in-clinic visits is reduced for patients under RM (hereafter called RM patients), the financing obtained by health care professionals is lower than with a standard monitoring (hereafter called SM patients). Because there is a limitation in the number of controls

(except if clinically justified), the maximum financing for SM patients (stable[a] and >7 years old) is currently as follows (including official patient co-payment and excluding supplements; see also Table 20):

- For SM patients with ICDs or CRT-Ds: €260.88 + €121.65 (if 3 controls were done by an accredited medical specialist in cardiology on ambulatory patients);
- For SM patients with single chamber PMs €49.70 + €81.10 (if 2 controls were done by an accredited medical specialist in cardiology on ambulatory patients);
- For SM patients with double chamber PMs or CRT-Ps €109.32 + €81.10 (if 2 controls were done by an accredited medical specialist in cardiology on ambulatory patients);

For RM patients, the current financing for health care providers is either equal (if no reduction of in-clinic visits) or inferior (if reduction of in-clinic visits) to that for SM patients.

It should also be noted that for ILRs, there is no specific code. According to NIHDI, only a consultation with a medical specialist can be asked (102594 or 102093) for each in-clinic visit related to ILRs control. ILRs are therefore not further analysed in this chapter because it is not possible to determine their current budget impact (no specific code).

Table 20 – Fee for service (FFS) for in-clinic visits in Belgium in 2021 (including official patient co-payments (*ticket modérateurs-remgeld*))

	NIHDI Codes	Official Fees*	Maximum number per patient per year**	Maximum official fees* per patient per year
Control of ICDs / CRT-Ds	475893-475904	€86.96	3	€260.88
Control of single Chamber PM	475856-475860	€24.85	2	€49.70
Control of double Chamber PM and CRT-P	475871-475882	€54.66	2	€109.32
Consultation with a medical specialist in cardiology (accredited*)**	102594	€40.55	-	-
Consultation with a medical specialist in cardiology (non-accredited)	102093	€33.72	-	-

*Source: Nomensoft, NIHDI 2021. *Including the official patient co-payment (ticket modérateurs-remgeld) and excluding supplements (for non-conventioned physicians). It should also be noted that these fees are higher for children below 7 years old and lower for assistants.**Except the year of implantation or if clinically justified. ***An accreditation is the recognition of participation in a range of continuing education activities and peer review sessions. CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

Table 21 shows the number of patients monitored (i.e. having at least one in-clinic visit) as well as the NIHDI expenditures for in-clinic visits in 2019 (latest full year available). Because for in-clinic visits, a consultation can be added on the top of the tariff for the control, total expenditures including consultations were also mentioned (based on mean expenditures for consultations with a medical specialist in cardiology and the percentage of ambulatory patients mentioned in Table 22).

[a] Meaning that no control beyond that authorized maximum is clinically justified

These figures, especially concerning the number of patients monitored per CIED, must be used with caution (codes for different implants used for the same patient, see also section 3.4) but show that the maximum number of in-clinic visits allowed was on average not reached. Such observation was also done in the survey reported in section 3.6, except for CRT-P. To confirm such a result, the sample of the IMA – AIM database ('*échantillon permanent – permanente steekproef*' – EPS, see also section 3.4) was analysed, and only patients with a single type of device control were selected (no mix of ICDs, CRT-Ps or PM codes). Based on this analysis, the average number of controls was 2.16 for ICDs, 1.61 for single chamber PMs and 1.79 for double chamber PMs and CRT-Ps, confirming that the maximum was not reached on average. It should nevertheless be noted that these data concerned both RM and SM patients. It is therefore possible that if data were available per type of follow-up, the mean number of in-clinic visits for SM patients would reach the maximum (but no data are available).

Table 21 – Number of patients and NIHDI expenditures in 2019 (latest year fully available)

	NIHDI Codes	Number of Patients	Mean number of in-clinic visits	NIHDI expenditures	Mean expenditures per patient	NIHDI expenditures	Mean expenditures per patient
				Excluding consultations*		Including consultations*	
Control of ICDs / CRT-D	475893-475904	16 347	2.09	€ 2 698 512.00	€ 165.08	€ 3 625 626.49	€ 221.79
Control of single Chamber PM	475856-475860	14 634	1.54	€ 490 319.00	€ 33.51	€ 1 076 365.33	€ 73.55
Control of double Chamber PM and CRT-P	475871-475882	63 291	1.75	€ 5 245 601.00	€ 82.88	€ 8 256 743.92	€ 130.46

*Source: Personal communication of NIHDI, Xavier Van Aubel (N patients) and Doc N provided by NIHDI to KCE (Expenditures). *Because for patients that are not hospitalized (ambulatory patients), a consultation can be added on the top of the tariff for the control, total expenditures including consultations were also mentioned (based on mean expenditures for consultations and the percentage of ambulatory patients mentioned in Table 7). CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

Table 22 – NIHDI expenditures for consultations with a medical specialist in cardiology (102594 or 102093) in 2019

	Mean NIHDI expenditures per consultation*	% ambulatory patients	Mean per in-clinic visit
Control of ICDs / CRT-D	€ 28.94	93.9%	€ 27.17
Control of single Chamber PM	€ 28.94	90.0%	€ 26.06
Control of double Chamber PM and CRT-P	€ 28.94	93.8%	€ 27.15

*Sources: Doc N provided by NIHDI to KCE. *Mean for consultations with both accredited and non-accredited medical specialist in cardiology. We are below the tariffs mentioned in Table 20 because it is 2019 tariffs, patients co-payments are excluded, and fees are lower in some conditions (e.g. if it is an assistant). CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

8.3 Cost of RM activities

In order to have an idea of the cost of RM related activities, own estimations were done based on the time needed per type of health professionals and the cost per minute. Based on the review of the literature on economic evaluations and contacts with stakeholders, a number of recent cost or cost-consequences studies for RM were identified (such as Burri 2013, Heidbuchel 2015, Lapage 2017, Boriani 2017)[9, 40, 90, 91], quoting cost savings or cost neutrality for RM (although subject to the same limitations described in section 5.3.9). Amongst these, we looked for any studies specifying time required for implementing RM and involving Belgian centres. Two studies were identified: the study of Heidbuchel et al 2015[9] and the thesis of Lapage 2017.[91]

Based on the thesis of Lepage 2017, the median time per patient per year for RM of ICDs patients by a specialized nurse was 20.51 min (see Table 23). Additionally, on average, 0.53 transmissions per patient per year required the intervention of a medical specialist (878 interventions[a] for 948 patients in 21 months). By assuming an average time of 8.43 min for such an intervention (maximum time recorded in the study, for events with mixed problems), the physician time for RM activities could be estimated at 4.48 minutes per patient per year.[91] It should nevertheless be noted that such study focuses on the time for nurses and not on the time for physicians.

Based on the multicentre, European RCT of Heidbuchel et al 2015 (the EuroEco study)[9], which included overall 312 patients (159 patients in the RM group) in 6 European countries, including Belgium, the average time per patient per year for RM of ICDs patients (with exclusions of in-clinic visits) can be estimated at 4.90 minutes for medical specialists, 18.95 minutes for nurses, and 5.01 minutes for technicians (see Table 24).[9] These time estimates are therefore far from the time estimated in the study of the BeRHA (mentioned in section 1.1).

By selecting the maximum times from the study of Lepage 2017 [91] and of Heidbuchel et al 2015[9], the following average time per patient per year were assumed:

- Nurses: 20.51 minutes
- Medical specialist in cardiology: 4.90 minutes
- Technologist: 5.01 minutes

The cost per minute was then estimated based on the KCE manual for cost studies (see Box 8).[92] By multiplying the cost per minute by the time per patient per year, we obtained a cost of €42.87 per patient per year (see Table 25). The cost for RM activities can therefore be estimated at around €45 per patient (in centres essentially managed by nurses and with a sufficient number of patients, e.g. at least 159 based on the number of patients in the the study of Heidbuchel 2015 [9]).

The time for medical specialists is nevertheless quite low. An additional scenario (scenario 2) was therefore also calculated, by adding 3x5 minutes[b] to the medical specialist for scheduled remote interrogations. With this additional time, a cost of €118.30 per patient per year is reached (see Table 25), which is very close to the lump sum of €130 in France (see section 7.2) or to the amount calculated based on the survey (also €130, see section 3.6.9).

Based on our own calculations, two estimates were therefore kept: €45 and €130. These estimates correspond to a remote monitoring essentially managed by nurses and with a sufficient number of patients (>159).

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[a] Referring to the discussions with the specialised remote monitoring physicians or electrophysiologists of the hospital

[b] Because guidelines recommend between 2-4 controls per year (with at least one in-clinic visit), we assumed that (maximum) 3 scheduled remote data interrogations will be done. The 5 minutes estimate was based on around the double of the time reported in the study Lapage 2017 for scheduled data interrogations. It is also important to note that a time for scheduled remote interrogations was already included in the amount of €45. This is therefore an additional time of 15 minutes to the time estimated from the two selected studies (i.e. 20 minutes for the medical specialist in cardiology).

Table 23 – Workload and time management of the specialized nurses at the RM department of the University Hospitals of Leuven

	Number of transmissions (948 patients - 21 months)	Average number of transmissions per patient	Average number of transmissions per patient per year	Median time per transmission (in minutes)	Median time per patient per year (in minutes)
Scheduled remote data interrogations	6 289	6.63	3.79	2.62	9.93
Unscheduled transmissions (alerts)	2 856	3.01	1.72	2.69	4.63
Remote monitoring contacts*	1 724	1.82	1.04	5.45	5.66
Total	10 869	11.47	6.55	3.13	20.51

**phone call from a patient with a remote monitoring related question. Source: Lapage 2017[91]*

Table 24 – Workload and time management of nurses, physicians, and technicians in six European countries*

	Average number of services par patient - 2 years	Average number of services per patient per year	Average time needed per service (in minutes)	Average time per patient and per year (in minutes)
Follow-up contacts (other than in-clinic visits)				
Physician	0.22	0.11	5.44	0.60
Nurse	1.53	0.765	5.91	4.52
Technician	0.23	0.115	12.04	1.38
RM services				
Physician	1.86	0.93	2.87	2.67
Nurse	7.74	3.87	3.4	13.16
Technician	1.47	0.735	2.86	2.10
Internal discussion**				
Physician	0.61	0.31	5.31	1.63
Nurse	0.61	0.31	4.14	1.27
Technician	0.61	0.31	4.96	1.52
Total				
Physician	-	-	-	4.90
Nurse	-	-	-	18.95
Technician	-	-	-	5.01

Source: Heidbuchel 2015[9]. Belgium (3 centres), Finland (1 centre), Germany (4 centres), UK (3 centres), Spain (4 centres), The Netherlands (1 centre). ** No repartition given. Assumed similar between physicians, nurses and technicians. RM = Remote Monitoring*

Box 8 – Cost per minute based on the KCE manual for cost studies[92]

Cost per minute for medical specialists in cardiology

A yearly gross cost for medical specialists was calculated by the KCE manual for cost studies.[92] This gross cost was calculated per medical specialty, based on the average yearly remuneration of medical specialists for all activities that are billable to the NIHDI before deductions and subtraction of other costs at charge of the medical specialist, and with exclusion of supplements. In the manual, the average yearly gross cost was €426 045 for medical specialists in cardiology. For more data on this topic, we refer the reader to chapter 2 and appendix 18 of KCE manual for cost studies. The yearly gross costs of the KCE manual for cost studies were based on the year 2010. The indexation to 2019 (latest full year available for NIHDI data) was done as follows:

Stage 1: Determination of activity-mix of medical specialists in cardiology in 2010: with the 2010 expenditures based on the sum of NIHDI reimbursement of all codes for consultations and controls with a medical specialists in cardiology in 2010, and the 2010 volume, i.e. the number of interventions in 2010.

Stage 2: Determination of 2019 expenditures calibrated on 2010 volume: with a 2019 tariff per intervention assessed by dividing the total 2019 expenditures for each code identified in stage 1 and billed in 2019 by the 2019 volume (i.e. the number of interventions in 2019), 2019 expenditures calibrated on 2010 volume were then assessed by multiplying the 2019 calculated tariff per intervention by the 2010 volume.

Stage 3: Determination of the indexation rate from 2010 to 2019, assessed by dividing 2019 expenditures calibrated on 2010 volume (stage 2) by 2010 expenditures (stage 1), resulting in an index of 1.14.

The 2019 yearly gross cost (€487 191.46) was then converted in a cost per hour based on guidelines in the KCE manual for cost studies.[92] The activity level of a full-time-equivalent (FTE) physician was estimated at 11 half-days per week (maximum of half-days that can be reported for the election of the Medical Board (for these elections a vote is assigned to each physician, weighted by its level of activity in the hospital in terms of half days). By taking into account holidays, attendance at congresses, illnesses, etc., it has been estimated that a FTE worked 482 half days per year. The number of billable hours per half day was then estimated at 3.35 hours (using data of the KCE study 251)[93], given a cost per hour of € 301.72 and a cost per minute of €5.03.

Cost per minute for nurses

The KCE manual for cost studies also estimated the cost per hour of a nurse in a consultation unit to € 40.16.[92] As such estimate was from March 2012, results have been indexed by a factor of 1.08244 (wage index March 2012= 1.5769, wage index March 2019= 1.7069), i.e. €43.47 per hour and €0.72 per minute.

Cost per minute for technicians

The KCE manual for cost studies also estimated the cost per hour of a technician (medico-technical services) to € 37.25.[92] As such estimate was from March 2012, results have been indexed by a factor of 1.08244 (wage index March 2012= 1.5769, wage index March 2019= 1.7069), i.e. €40.32 per hour and €0.67 per minute.

Table 25 – Cost of RM activities per patient per year

	Time	Cost per minute	Total	Time	Cost per minute	Total
			Scenario 1			Scenario 2
Nurse	20.51	€ 0.72	€ 14.86	20.51	€ 0.72	€ 14.86
Medical specialist in cardiology	4.90	€ 5.03	€ 24.64	19.9	€ 5.03	€ 100.07
Technician	5.01	€ 0.67	€ 3.37	5.01	€ 0.67	€ 3.37
Total			€ 42.87			€ 118.30

8.4 Budget impact of the financing models identified abroad

8.4.1 Financing of health care providers based on the model in France: A yearly lump sum for RM activities and a FFS for in-clinic visits

Based on the French model, 5 scenarios were estimated concerning the yearly lump-sum:

- Scenario 1: a lump sum of €45, based on the cost calculated in section 1.1 (scenario 1);
- Scenario 2: a lump sum of €130, i.e. the amount provided in France (and close to the cost calculated in section 1.1 scenario 2 and in section 3.6.9);
- Scenario 3: a lump sum equivalent to 1 in-clinic visit, excluding patient's co-payments (i.e. €21.80 for single chamber PMs, €47.29 for double chamber PMs and CRT-Ps, and €79.08 for ICDs and CRT-Ds). This scenario was calculated because for PMs, the maximum number of controls is currently set at 2 and at least one control should be performed in-clinic;
- Scenario 4: a lump sum equivalent to 2 in-clinic visits (i.e. €43.60 for single chamber PMs, €94.58 for double chamber PMs and CRT-Ps, and €158.16 for ICDs and CRT-Ds), because the lump sum in France corresponds to around 2 in-clinic controls;
- Scenario 5: a lump sum equivalent to the amount proposed by the BeHRA, i.e. €225 (see section 1.1 and the appendix to this chapter)

Additionally, the mean number of in-clinic visits in 2019 corresponds to both patients under remote monitoring (RM patients) and patient with a standard monitoring (SM patients). Because we have no data on the number of in-clinic visits for each patient category (RM or SM patients), additional scenarios were added:

- For SM patients: a number of in-clinic visits either equal to the 2019 mean (2019 mean) or to the current maximum (maximum).
- For RM patients : a number of in-clinic visits either equal to 1 (minimum), to the 2019 mean (2019 mean), or to the current maximum (maximum).

Finally, because the impact of the financing of RM activitites on the number of RM patients was unknown, two scenarios on the percentage of RM patients were tested: a same percentage than current estimates and all patients under RM (scenario maximum[a]). It should also be noted that the budget impact is based on the 2019 situation (2019 tariffs and 2019 number of patients), i.e. the latest year with full data available.

As shown in Table 26, based on the French model, the financing of health care providers per RM patient is always higher than the current situation (that also corresponds to the financing per SM patient if their mean number of in-clinic visits correspond to the 2019 mean, in grey in the table), except in the following cases (in red in the table):

[a] Such scenario is not expected in practice because not all patients / physicians will accept RM (upper estimation).

- If no more than 1 in-clinic visit are performed for the control of RM patients and if the yearly lump-sum corresponds to 1 in-clinic visit (scenario 3) for every CIED;
- If no more than 1 in-clinic visit are performed for the control of RM patients and if the yearly lump-sum corresponds to €45 as estimated in section 1.1 (scenario1) for ICDs, CRT-Ds, double chamber PMs and CRT-Ps but not for single chamber PMs

Table 27 (in-clinic visits for SM patients assumed equal to the 2019 mean) and Table 28 (in-clinic visits for SM patients assumed equal to the maximum authorized) show the high variations around the budget impact according to the scenarios.

If we assume 1 in-clinic visit for RM patients and a number of in-clinic visits equal to the 2019 mean for SM patients, the financing of RM patients would be neutral with the following lump sums:

- €115.54 for ICDs / CRT-Ds;
- €25.70 for single chamber PMs;
- €56.02 for double chamber PMs and CRT-Ps.

Table 26 – Annual mean expenditures per patient based on the model in France

	SM		RM		
	2019 Mean	Maximum	Minimum: If limited to 1 in-clinic visit	Mean: If no reduction of in-clinic visits (2019 mean)	Maximum: If based on the current authorized maximum
ICDs / CRT-D	€ 221.79	€ 318.75	Scenario 1: €45 + €79.08 + €27.17 = €151.25	Scenario 1: €45 + €221.79 = €266.79	Scenario 1: €45 + €318.75 = €363.75
			Scenario 2: €130 + €79.08 + €27.17 = €236.25	Scenario 2: €130 + €221.79 = €351.79	Scenario 2: €130 + €318.75 = €448.75
			Scenario 3: €79.08 + €79.08 + €27.17 = €185.33	Scenario 3: €79.08 + €221.79 = €300.87	Scenario 3: €79.08 + €318.75 = €397.83
			Scenario 4: €158.16 + €79.08 + €27.17 = €264.41	Scenario 4: €158.16 + €221.79 = €379.95	Scenario 4: €158.16 + €318.75 = €476.9
			Scenario 5: €225 + €79.08 + €27.17 = €331.25	Scenario 5: €225 + €221.79 = €446.79	Scenario 5: €225 + €318.75 = €543.75
Single Chamber PM	€ 73.55	€ 95.71	Scenario 1: €45 + €21.8 + €26.06 = €92.86	Scenario 1: €45 + €73.55 = €118.55	Scenario 1: €45 + €95.71 = €140.71
			Scenario 2: €130 + €21.8 + €26.06 = €177.86	Scenario 2: €130 + €73.55 = €203.55	Scenario 2: €130 + €95.71 = €225.71
			Scenario 3: €21.8 + €21.8 + €26.06 = €69.66	Scenario 3: €21.8 + €73.55 = €95.35	Scenario 3: €21.8 + €95.71 = €117.51
			Scenario 4: €43.6 + €21.8 + €26.06 = €91.45	Scenario 4: €43.6 + €73.55 = €117.15	Scenario 4: €43.6 + €95.71 = €139.31
			Scenario 5: €225 + €21.8 + €26.06 = €272.86	Scenario 5: €225 + €73.55 = €298.55	Scenario 5: €225 + €95.71 = €320.71
Double Chamber PM and CRT-P	€ 130.46	€ 148.87	Scenario 1: €45 + €47.29 + €27.15 = €119.43	Scenario 1: €45 + €130.46 = €175.46	Scenario 1: €45 + €148.87 = €193.87
			Scenario 2: €130 + €47.29 + €27.15 = €204.43	Scenario 2: €130 + €130.46 = €260.46	Scenario 2: €130 + €148.87 = €278.87
			Scenario 3: €47.29 + €47.29 + €27.15 = €121.72	Scenario 3: €47.29 + €130.46 = €177.75	Scenario 3: €47.29 + €148.87 = €196.16
			Scenario 4: €94.58 + €47.29 + €27.15 = €169.01	Scenario 4: €94.58 + €130.46 = €225.03	Scenario 4: €94.58 + €148.87 = €243.44
			Scenario 5: €225 + €47.29 + €27.15 = €299.43	Scenario 5: €225 + €130.46 = €355.46	Scenario 5: €225 + €148.87 = €373.87

CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker; RM = remote monitoring; SM = standard monitoring (in-clinic visits)

Table 27 – Yearly budget impact* of RM financing based on the French model compared to no financing (2019 situation – to be used with caution), with in-clinic visits for SM patients equal to the 2019 mean

Implant	Scenarios on RM patients %	Number SM patients	Number RM patients	Scenario 1: Lump sum of 45€		Scenario 2: Lump sum of 130 €	
				Max 1 in-clinic visits for RM patients	No reduction of in-clinic visits for RM patients	Max 1 in-clinic visits for RM patients	No reduction of in-clinic visits for RM patients
ICD, including CRT-D	Current % of RM patients	6 798	9 549	-€ 673 614.85	€ 429 705.00	€ 138 050.15	€ 1 241 370.00
	All patients under RM	0	16 347	-€ 1 153 165.98	€ 735 615.00	€ 236 329.02	€ 2 125 110.00
Single Chamber PM	Current % of RM patients	14 120.38	513.62	€ 9 914.50	€ 23 112.99	€ 53 572.37	€ 66 770.85
	All patients under RM	0	14 634	€ 282 481.68	€ 658 530.00	€ 1 526 371.68	€ 1 902 420.00
Double Chamber PM or CRT-P	Current % of RM patients	61 069.62	2 221.38	-€ 24 487.32	€ 99 962.01	€ 164 329.82	€ 288 779.15
	All patients under RM	0	63 291	-€ 697 687.04	€ 2 848 095.00	€ 4 682 047.96	€ 8 227 830.00

Implant	Scenarios on RM patients %	Number SM patients	Number RM patients	Scenario 3: Lump sum of 1 in-clinic visit		Scenario 4: Lump sum of 2 in-clinic visits		Scenario 5: Lump sum of €225	
				Max 1 in-clinic visits for RM patients	No reduction of in-clinic visits for RM patients	Max 1 in-clinic visits for RM patients	No reduction of in-clinic visits for RM patients	Max 1 in-clinic visits for RM patients	No reduction of in-clinic visits for RM patients
ICD, including CRT-D	Current % of RM patients	6 798	9 549	-€ 348 188.82	€ 755 131.02	€ 406 942.20	€ 1 510 262.05	€ 1 045 205.15	€ 2 148 525.00
	All patients under RM	0	16 347	-€ 596 066.89	€ 1 292 714.09	€ 696 647.21	€ 2 585 428.18	€ 1 789 294.02	€ 3 678 075.00
Single Chamber PM	Current % of RM patients	14 120.38	513.62	-€ 2 001.68	€ 11 196.81	€ 9 195.13	€ 22 393.62	€ 102 366.45	€ 115 564.94
	All patients under RM	0	14 634	-€ 57 031.41	€ 319 016.91	€ 261 985.49	€ 638 033.81	€ 2 916 601.68	€ 3 292 650.00
Double Chamber PM or CRT-P	Current % of RM patients	61 069.62	2 221.38	-€ 19 404.05	€ 105 045.28	€ 85 641.23	€ 210 090.56	€ 375 360.73	€ 499 810.06
	All patients under RM	0	63 291	-€ 552 855.70	€ 2 992 926.34	€ 2 440 070.64	€ 5 985 852.68	€ 10 694 692.96	€ 14 240 475.00

*SM patients = patients with a standard monitoring (in-clinic visits); RM patients = patients with a remote monitoring; *Based on 2019 tariffs. Official patients' co-payments and supplements are excluded.**The total number of patients is based on 2019 data provided by NIHDI. We could expect that a higher number would be monitored now but no data is available. The estimation of the number of patients currently under RM was provided by BeMedTech (based on a survey send to the RM systems' providers). Because no distinction was done between single chamber PM and double Chamber PM/CRT-P, we used the same repartition than in total 2019 NIHDI data. It should also be noted that the scenario with all patients under RM is not expected in practice because not all patients / physicians will accept RM (upper estimation). CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker.*

Table 28 – Yearly budget impact* of RM financing based on the French model compared to no financing (2019 situation – to be used with caution), with in-clinic visits for SM patients equal to the maximum allowed

Implant	Scenarios on RM patients %	Number SM patients	Number RM patients	Scenario 1: Lump sum of 45€			Scenario 2: Lump sum of 130 €		
				In-clinic visits for RM patients = **1**	In-clinic visits for RM patients = **2019 mean**	In-clinic visits for RM patients = **maximum**	In-clinic visits for RM patients = **1**	In-clinic visits for RM patients = **2019 mean**	In-clinic visits for RM patients = **maximum**
ICD, including CRT-D	Current % of RM patients	6 798	9 549	-€ 14 520.31	€ 1 088 799.54	€ 2 014 615.04	€ 797 144.69	€ 1 900 464.54	€ 2 826 280.04
	All patients under RM	0	16 347	-€ 1 153 165.98	€ 735 615.00	€ 2 320 525.04	€ 236 329.02	€ 2 125 110.00	€ 3 710 020.04
Single Chamber PM	Current % of RM patients	14 120.38	513.62	€ 322 802.06	€ 336 000.55	€ 347 381.68	€ 366 459.93	€ 379 658.41	€ 391 039.55
	All patients under RM	0	14 634	€ 282 481.68	€ 658 530.00	€ 982 798.69	€ 1 526 371.68	€ 1 902 420.00	€ 2 226 688.69
Double Chamber PM or CRT-P	Current % of RM patients	61 069.62	2 221.38	€ 1 099 797.22	€ 1 224 246.54	€ 1 265 141.85	€ 1 288 614.35	€ 1 413 063.68	€ 1 453 958.99
	All patients under RM	0	63 291	-€ 697 687.04	€ 2 848 095.00	€ 4 013 274.84	€ 4 682 047.96	€ 8 227 830.00	€ 9 393 009.84

Implant	Scenarios on RM patients %	Number SM patients	Number RM patients	Scenario 3: Lump sum of 1 in-clinic visit			Scenario 4: Lump sum of 2 in-clinic visits			Scenario 5: Lump sum of €225		
				In-clinic visits for RM patients = **1**	In-clinic visits for RM patients = **2019 mean**	In-clinic visits for RM patients = **maximum**	In-clinic visits for RM patients = **1**	In-clinic visits for RM patients = **2019 mean**	In-clinic visits for RM patients = **maximum**	In-clinic visits for RM patients = **1**	In-clinic visits for RM patients = **2019 mean**	In-clinic visits for RM patients = **maximum**
ICD, including CRT-D	Current % of RM patients	6 798	9 549	€ 310 905.72	€ 1 414 225.57	€ 2 340 041.07	€ 1 066 036.74	€ 2 169 356.59	€ 3 095 172.09	€ 1 704 299.69	€ 2 807 619.54	€ 3 733 435.04
	All patients under RM	0	16 347	-€ 596 066.89	€ 1 292 714.09	€ 2 877 624.13	€ 696 647.21	€ 2 585 428.18	€ 4 170 338.23	€ 1 789 294.02	€ 3 678 075.00	€ 5 262 985.04
Single Chamber PM	Current % of RM patients	14 120.38	513.62	€ 310 885.88	€ 324 084.37	€ 335 465.50	€ 322 082.69	€ 335 281.18	€ 346 662.31	€ 415 254.01	€ 428 452.50	€ 439 833.63
	All patients under RM	0	14 634	-€ 57 031.41	€ 319 016.91	€ 643 285.60	€ 261 985.49	€ 638 033.81	€ 962 302.51	€ 2 916 601.68	€ 3 292 650.00	€ 3 616 918.69
Double Chamber PM or CRT-P	Current % of RM patients	61 069.62	2 221.38	€ 1 104 880.49	€ 1 229 329.81	€ 1 270 225.12	€ 1 209 925.77	€ 1 334 375.09	€ 1 375 270.40	€ 1 499 645.27	€ 1 624 094.59	€ 1 664 989.90
	All patients under RM	0	63 291	-€ 552 855.70	€ 2 992 926.34	€ 4 158 106.18	€ 2 440 070.64	€ 5 985 852.68	€ 7 151 032.52	€ 10 694 692.96	€ 14 240 475.00	€ 15 405 654.84

*SM patients = patients with a standard monitoring (in-clinic visits); RM patients = patients with a remote monitoring; *Based on 2019 tariffs. Official patients' co-payments and supplements are excluded.**The total number of patients is based on 2019 data provided by NIHDI. We could expect that a higher number would be monitored now but no data is available. The estimation of the number of patients currently under RM was provided by BeMedTech (based on a survey send to the RM systems' providers). Because no distinction was done between single chamber PM and double Chamber PM/CRT-P, we used the same repartition than in total 2019 NIHDI data. It should also be noted that the scenario with all patients under RM is not expected in practice because not all patients / physicians will accept RM (upper estimation). CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

8.4.2 Financing of health care providers based on the model in the Netherlands: A yearly lump sum

According to the model in the Netherlands, the financing would be the same whatever the place of the monitoring (RM = SM) but instead of a fee-for service system, the financing would be based on a yearly lump-sum per patient. Concerning such yearly lump sum, multiple scenarios were tested:

- Scenario 1: a lump sum equivalent to the current average 2019 expenditures per patient (see Table 29).
- Scenario 2: a lump sum equivalent to the expenditures per patient if the maximum number of controls was done (see Table 29).
- Scenario 3: a higher lump-sum if RM is considered more costly and if there is a wish to promote RM activities, corresponding for example to the amounts obtained in Table 26 based on the French model (with a budget impact as described in Table 27 and Table 28).

Table 29 – yearly budget impact* of RM financing based on the model in the Netherlands compared to no financing (2019 situation)

	Scenarios (based on)	Nb patients	Lump sum per patient per year	Total
ICD, including CRT-D	Scenario 1 (Average 2019)	16 347	€ 221.79	€ 0.00
	Scenario 2 (Maximum)	16 347	€ 318.75	+ € 1 584 910.04
	Scenario 3 (see Table 26)	16 347	Between €236.25 and €543.75	Between + € 236 329.02 and + € 5 262 985.04
Single Chamber PM	Scenario 1 (Average 2019)	14 634	€ 73.55	€ 0.00
	Scenario 2 (Maximum)	14 634	€ 95.71	+ € 324 268.70
	Scenario 3 (see Table 26)	14 634	Between €91.45 and €320.71	Between + € 261 985.49 and + € 3 616 918.69
Double Chamber PM or CRT-P	Scenario 1 (Average 2019)	63 291	€ 130.46	€ 0.00
	Scenario 2 (Maximum)	63 291	€ 148.87	+ € 1 165 179.84
	Scenario 3 (see Table 26)	63 291	Between €169.01 and €373.87	Between + € 2 440 070.64 and + € 15 405 654.84

*SM patients = patients with a standard monitoring (in-clinic visits); RM patients = patients with a remote monitoring; * The total number of patients is based on 2019 data provided by NIHDI. We could expect that a higher number would be monitored now but no data is available.**Official patients' co-payments and supplements are excluded. CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

8.4.3 Financing of health care providers based on the model in Germany: FFS for both in-clinic visits and scheduled RM

In the German model, the fee is the same whatever the place of the monitoring (remote or standard monitoring), with a limitation in the number of controls (maximum number of in-clinic visits + remote data interrogations). Such financing therefore covers scheduled remote data interrogations but not the management of alerts.

From the Belgian context nevertheless, the situation is quite different because of the consultation fee with the medical specialist in cardiology that can be added on the top of the fee for the control of CIEDs for in-clinic-visits (see below). The total fees for in-clinic visits (fee for the control and fee for the consultation) will therefore be higher than the fee for remote data interrogations (fee for the control).

Because the number of in-clinic visits and the total number of controls in both groups is unknown, different scenario were tested (see Table 30 and Table 31). Concerning those scenarios, it should be noted that if the mean number of in-clinic visits for RM patients is superior to 1, the total number of follow-up controls for RM patients (in-clinic visits or remote data interrogations) is expected higher than the current 2019 average. The scenario on a number of controls equal to the 2019 mean for RM patients in Table 31 is therefore presented in italic in the table (not expected in practice).

As shown in Table 30 and Table 31, the budget impact of the financing of RM compared to the no financing is highly uncertain, i.e. varying from - € 482 983.07 and + € 1 348 168.35 for ICD and CRT-D, from - € 204 746.22 and + € 318 072.03 for single chamber PM, and from - € 1 293 107.38 to + € 1 150 265.77 for double chambers PM or CRT-P, depending of the number of controls in each group. The analysis also showed that if more than one in-clinic visits were performed for RM patients, the financing of RM would increase NIHDI expenditure.

Table 30 – Yearly budget impact of RM financing based on the model in Germany compared to no financing if only 1 in-clinic visit is performed for RM patients (2019 situation – to be used with caution)

Implants	Scenarios on the number of controls (in-clinic visits or remote data interrogations)	Number of SM patients	Number of RM patients	Annual mean expenditure per SM patient	Annual mean expenditure per RM patient	Budget impact*
If only 1 in-clinic visit for RM patients (minimum)						
ICD, including CRT-D	2019 mean for both SM and RM patients					
	Current % of RM patients	6 798	9 549	€ 221.79	€ 192.25	-€ 282 131.60
	All patients under RM	0	16 347	€ 221.79	€ 192.25	-€ 482 983.07
	2019 mean for SM patients and maximum for RM patients**					
	Current % of RM patients	6 798	9 549	€ 221.79	€ 264.41	€ 406 942.20
	All patients under RM	0	16 347	€ 221.79	€ 264.41	€ 696 647.21
	Maximum for both SM and RM patients**					
	Current % of RM patients	6 798	9 549	€ 318.75	€ 264.41	€ 1 066 036.74
	All patients under RM	0	16 347	€ 318.75	€ 264.41	€ 696 647.21
Single Chamber PM	2019 mean for both SM and RM patients					
	Current % of RM patients	14 120	514	€ 73.55	€ 59.56	-€ 7 186.15
	All patients under RM	0	14 634	€ 73.55	€ 59.56	-€ 204 746.22
	2019 mean for SM patients and maximum for RM patients**					
	Current % of RM patients	14 120	514	€ 73.55	€ 69.66	-€ 2 001.68
	All patients under RM	0	14 634	€ 73.55	€ 69.66	-€ 57 031.41
	Maximum for both SM and RM patients**					
	Current % of RM patients	14 120	514	€ 95.71	€ 69.66	€ 310 885.88
	All patients under RM	0	14 634	€ 95.71	€ 69.66	-€ 57 031.41
Double Chamber PM or CRT-P	2019 mean for both SM and RM patients					
	Current % of RM patients	61 070	2 221	€ 130.46	€ 110.03	-€ 45 385.29
	All patients under RM	0	63 291	€ 130.46	€ 110.03	-€ 1 293 107.38
	2019 mean for SM patients and maximum for RM patients**					
	Current % of RM patients	61 070	2 221	€ 130.46	€ 121.72	-€ 19 404.05
	All patients under RM	0	63 291	€ 130.46	€ 121.72	-€ 552 855.70
	Maximum for both SM and RM patients**					
	Current % of RM patients	61 070	2 221	€ 148.87	€ 121.72	€ 1 104 880.49
	All patients under RM	0	63 291	€ 148.87	€ 121.72	-€ 552 855.70

*SM patients = patients with a standard monitoring (in-clinic visits); RM patients = patients with a remote monitoring; The total number of patients is based on 2019 data provided by NIHDI. We could expect that a higher number would be monitored now but no data is available. The estimation of the number of patients currently under RM was provided by BeMedTech (based on a survey send to the RM systems' providers). Because no distinction was done between single chamber PM and double Chamber PM/CRT-P, we used the same repartition than in total 2019 NIHDI data. It should also be noted that the third scenario with all patients under RM is not expected in practice because not all patients / physicians will accept RM (upper estimation); *Official patients' co-payments and supplements are excluded. **Maximum number of controls for RM patients : 1 in-clinic visit and 2 remote device interrogations for ICDs and 1 in-clinic visit and 1 remote device interrogation for PM and CRT-Ps. CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

Table 31 – Yearly budget impact of RM financing based on the model in Germany compared to no financing if the number of in-clinic visits for RM patients equal to the 2019 mean (2019 situation – to be used with caution)

Implants	Scenarios on the number of controls (in-clinic visits or remote data interrogations)	Number of SM patients	Number of RM patients	Annual mean expenditure per SM patient	Annual mean expenditure per RM patient	Budget impact*
If the number of in-clinic visits for RM patients corresponds to the 2019 mean (2.1 for ICDs, 1.5 for single chamber PM, 1.8 for double chamber PM and CRT-P)						
ICD, including CRT-D	*2019 mean for both SM and RM patients (=> no remote data interrogations, unexpected in practice)*					
	Current % of RM patients	*6 798*	*9 549*	*€ 221.79*	*€ 221.79*	*€ 0.00*
	All patients under RM	*0*	*16 347*	*€ 221.79*	*€ 221.79*	*€ 0.00*
	2019 mean for SM patients and maximum for RM patients					
	Current % of RM patients	6 798	9 549	€ 221.79	€ 293.95	€ 689 073.81
	All patients under RM	0	16 347	€ 221.79	€ 293.95	€ 1 179 630.27
	Maximum for both SM and RM patients					
	Current % of RM patients	6 798	9 549	€ 318.75	€ 293.95	€ 1 348 168.35
	All patients under RM	0	16 347	€ 318.75	€ 293.95	€ 1 179 630.27
Single Chamber PM	*2019 mean for both SM and RM patients (=> no remote data interrogations, unexpected in practice)*					
	Current % of RM patients	*14 120*	*514*	*€ 73.55*	*€ 73.55*	*€ 0.00*
	All patients under RM	*0*	*14 634*	*€ 73.55*	*€ 73.55*	*€ 0.00*
	2019 mean for SM patients and maximum for RM patients					
	Current % of RM patients	14 120	514	€ 73.55	€ 83.65	€ 5 184.47
	All patients under RM	0	14 634	€ 73.55	€ 83.65	€ 147 714.81
	Maximum for both SM and RM patients					
	Current % of RM patients	14 120	514	€ 95.71	€ 83.65	€ 318 072.03
	All patients under RM	0	14 634	€ 95.71	€ 83.65	€ 147 714.81
Double Chamber PM or CRT-P	*2019 mean for both SM and RM patients (=> no remote data interrogations, unexpected in practice)*					
	Current % of RM patients	*61 070*	*2 221*	*€ 130.46*	*€ 130.46*	*€ 0.00*
	All patients under RM	*0*	*63 291*	*€ 130.46*	*€ 130.46*	*€ 0.00*
	2019 mean for SM patients and maximum for RM patients					
	Current % of RM patients	61 070	2 221	€ 130.46	€ 142.15	€ 25 981.24
	All patients under RM	0	63 291	€ 130.46	€ 142.15	€ 740 251.68
	Maximum for both SM and RM patients					
	Current % of RM patients	61 070	2 221	€ 148.87	€ 142.15	€ 1 150 265.77
	All patients under RM	0	63 291	€ 148.87	€ 142.15	€ 740 251.68

*SM patients = patients with a standard monitoring (in-clinic visits); RM patients = patients with a remote monitoring; The total number of patients is based on 2019 data provided by NIHDI. We could expect that a higher number would be monitored now but no data is available. The estimation of the number of patients currently under RM was provided by BeMedTech (based on a survey send to the RM systems' providers). Because no distinction was done between single chamber PM and double Chamber PM/CRT-P, we used the same repartition than in total 2019 NIHDI data. It should also be noted that the third scenario with all patients under RM is not expected in practice because not all patients / physicians will accept RM (upper estimation); *Official patients' co-payments and supplements are excluded. CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker*

8.4.4 Financing of RM systems providers

Only France currently provides a separate one-time payment to RM systems' providers. If we assumed a mean lifetime ranging from 5 to 10 years (see also section 2.3.6) and a same repartition of the one-time amount between these years, the yearly budget impact is showed in Table 32 (Scenario 1, based on French amounts). Two other scenarios were also added, based on what was already asked in the past (i.e. €1300 for the lifetime of the implant allocated to 7 years, scenario 2) and the current request based on a consensus between RM systems' providers (i.e. €0.80/day, scenario 3).

Table 32 – Yearly budget impact of the financing of RM systems providers

	Type of follow-up	Nb SM patients	Nb RM patients	Yearly financing per SM patient	Yearly financing per RM patient		Total	
Assumptions on life time					5 years	10 years	5 years	10 years
ICDs / CRT-D (€918)	2019 Situation (no financing)	16 347	0	€ 0.00	€ 0.00	€ 0.00	€ 0.00	€ 0.00
	RM financing (current %RM)	6 798	9 549	€ 0.00	€ 183.60	€ 91.80	€ 1 753 196.40	€ 876 598.20
	RM financing (all under RM)	0	16 347	€ 0.00	€ 183.60	€ 91.80	€ 3 001 309.20	€ 1 500 654.60
Single Chamber PM (€500)	2019 Situation (no financing)	14 634	0	€ 0.00	€ 0.00	€ 0.00	€ 0.00	€ 0.00
	RM financing (current %RM)	14 120	514	€ 0.00	€ 100.00	€ 50.00	€ 51 362.19	€ 25 681.10
	RM financing (all under RM)	0	14 634	€ 0.00	€ 100.00	€ 50.00	€ 1 463 400.00	€ 731 700.00
Double Chamber PM and CRT-P (€700)	2019 Situation (no financing)	63 291	0	€ 0.00	€ 0.00	€ 0.00	€ 0.00	€ 0.00
	RM financing (current %RM)	61 070	2 221	€ 0.00	€ 140.00	€ 70.00	€ 310 992.93	€ 155 496.46
	RM financing (all under RM)	0	63 291	€ 0.00	€ 140.00	€ 70.00	€ 8 860 740.00	€ 4 430 370.00
Scenario 1 (total)	2019 Situation (no financing)	94 272	0				€ 0.00	€ 0.00
	RM financing (current %RM)	81 988	12 284				€ 2 115 551.52	€ 1 057 775.76
	RM financing (all under RM)	0	94 272				€ 13 325 449.20	€ 6 662 724.60
Scenario 2 (€1300)	2019 Situation (no financing)	94 272	0	€ 0.00	€ 0.00		€ 0.00	€ 0.00
	RM financing (current %RM)	81 988	12 284	€ 0.00	€ 260.00	€ 130.00	€ 3 193 840.00	€ 1 596 920.00
	RM financing (all under RM)	0	94 272	€ 0.00	€ 260.00	€ 130.00	€ 24 510 720.00	€ 12 255 360.00
Scenario 3 (€0.80 per day)	2019 Situation (no financing)	94 272	0	€ 0.00	€ 0.00		€ 0.00	€ 0.00
	RM financing (current %RM)	81 988	12 284	€ 0.00	€ 292.00	€ 292.00	€ 3 586 928.00	€ 3 586 928.00
	RM financing (all under RM)	0	94 272	€ 0.00	€ 292.00	€ 292.00	€ 27 527 424.00	€ 27 527 424.00

CRT-D= Cardiac resynchronization therapy devices with a defibrillator function; CRT-P= Cardiac resynchronization therapy devices with only pacemaker function; ICD= implantable cardioverter-defibrillator; PM= Pacemaker; RM patients = patients with a remote monitoring; SM patients = patients with a standard monitoring (in-clinic visits). If data are also sent the weekend.

8.5 Discussion and limitations

This chapter showed that the budget impact of RM financing based on the German model (FFS for in-clinic visits and remote data interrogations) would depend on the number of controls in each group but that NIHDI expenditure would increase if the number of in-clinic visits in RM patients was superior to 1. Compared to the lump sum in the Dutch model; the German model has the advantage to be flexible because it allows a higher financing if more in-clinic visits are clinically justified but does not provide a financing for alert management and does not ensure a similar financing between RM and SM patients.

The model in the Netherlands ensures the same financing between RM and SM patients and allows to switch from one type of follow-up to another without impact on the financing but as with every lump sum, it can induce patients selection (only treating patients for which the lump sum is lucrative) if the lump sum is not set per centre according to the risk profile of the patients and underproduction of care (e.g. less follow-up controls performed). This model also modifies the current financing of patients exclusively monitored based on in-clinic visits (financing by a lump sum and not anymore on a FFS basis). It should also be noted that such model would remain budget neutral only if the lump sum was set at the level of 2019 mean expenditure per patients (i.e. when RM activities were not financed).

The French model is the only one that aims to both covers the management of alerts and offers some flexibility (allowing a higher financing if more in-clinic visits are clinically justified, reducing the risk of patient selection). The risk of underproduction for RM care (number of remote data interrogations and management of alerts) nevertheless remain (as it is a lump sum). To maintain a neutral budget impact and to obtain a similar financing of health care providers between RM and SM patients (in the assumption of a number of in-clinic visits for SM patients equal to the 2019 mean), the number of in-clinic visits for RM patients should not exceed 1 per year and the lump sum for the management of alerts and for remote device interrogations should amount to:

- €115.54 for ICDs / CRT-Ds;
- €25.70 for single chamber PMs;
- €56.02 for double chamber PMs and CRT-Ps.

Additionally, the potential introduction of funding for RM system providers, as well as its likely impact on the budget, are factors that should not be neglected.

Nevertheless, it should be noted that the budget impact estimations presented in this chapter do not consider other potential RM benefits than the reduction of in-clinic visits. Despite a general lack of significance in other key clinical outcomes in RCTs, the results based on the mean point estimates could be slighlty numerically superior for RM, as for example concerning heart failure hospitalization for patients with ICDs and CRT-Ds, and we can therefore not exclude that further clinical benefits could be linked to the use of RM. Should these be proven, the budget impact scenarios here presented may be improved.

Beside clinical uncertainties, it is important to note that because of a lack of data, especially on the current number of patients followed-up, on the percentage of RM patients, on the number of in-clinic visits in both groups (SM and RM patients) and on the impact of a reimbursement of RM on current practices, these estimates must be used with caution.

9 GENERAL DISCUSSION

Based on this health technology assessment, the following elements can be highlighted:

RM systems to check the integrity and well-functioning of CIEDs and the patient's condition: a technology choice mainly made by the implanting physician

Chapter 2 overviews health problems (related to hearth rhythm disorders) considered and the available remote monitoring systems. These systems permit to follow both technical parameters on the implant integrity and well-functioning and medical parameters such as the number of arrythmia or the number of shocks delivered. The same RM system can be used whatever the type of CIEDs, i.e. implants with a therapeutic purpose (ICDs and PMs) and implants with a diagnostic purpose (ILRs) but must have the same brand as the implant. There are currently five providers of RM systems in Belgium and the choice for a specific brand is made by the implanting physician based on patient profile. Therefore, many cardiac centres involved in RM allow for the monitoring of different brands.

A higher interest for RM of patients with ICDs and ILRs than with PMs

Chapter 3 of this report analyses the current use of RM systems. While no exact figure is available, our analysis shows that RM is mainly used for ICDs and ILRs. A survey in centres with a NIHDI convention for ICDs implantation reported that RM is used in around 73% of patients with ICDs, 62% with ILRs and 7% with PMs. Data provided by BeMedTech differ a little, reporting that RM is used in 58% of patients with ICDs and 3.5% with PMs. Concerning PMs, the use is higher for double chambers PMs and CRT-Ps than for single chambers PMs (49% versus 3% based on the survey).

A need for additional resources self-reported reported by Belgian centres

Despite high variations in responses between hospitals regarding key factors such as the necessary human resources to carry out RM, a consistent message was found in the survey performed in chapter 3, i.e. additional resources would be required in order to do so.

Due to a lack of time and without the help of well-trained nurses to support the management of RM patients, some physicians also reported limiting the follow-up to the surveillance of alerts for major events.

A reduction of in-clinic visits (protocol based), an earlier detection of events, and a reduced risk of inappropriate shocks (for ICDs) but no significant impact on hospitalizations, quality of life, or mortality and no reduction expected in the total workload

Concerning ICDs and PMs, the review of the clinical literature (based on 19 RCTs for ICDs and 8 for PMs) performed in chapter 4 showed that remote monitoring significantly decreased the time from event onset to data review and medical intervention (for both ICDs and PMs), with a risk of inappropriate shocks lowered by 4% points (95%CI: 1%; 7%; p=0.01) (4 ICD studies) and a lower burden of atrial arrhythmias (2 PM studies). The remote monitoring also resulted in less in-clinic visits (for both ICDs and PMs). Nevertheless, no significant effect of remote monitoring on hard clinical outcomes (all-cause or cardiovascular hospitalizations, stroke, all-cause or cardiovascular mortality) or quality of life indicators could be demonstrated.

The reduction in in-clinic visits was not unexpected as the study protocols imposed that in-clinic visits be scheduled less frequently in the group with remote monitoring. However, it is unclear how this would affect the workload in real-life practice. The number of unscheduled in-clinic visits was higher in the remote monitoring of ICDs in 4 studies over 8, and the total number of follow-up controls (i.e. in-clinic visits plus remote interrogations) in the remote vs. standard monitoring group was not reported in most studies. The monitoring of alerts on top of the scheduled remote interrogations may increase the burden of health professionals, particularly if, as found via our survey to Belgian centres, there is little change in the number of in-clinic visits (as highlighted in the chapter 3 on the current use of remote monitoring). Therefore, the remote monitoring of implanted cardiac devices could result in an increased workload for medical staff in some situations, and strategies to overcome this difficulty might be needed.

Moreover, methods were heterogeneous across studies. It is unclear if remote monitoring could be more efficient for some groups of patients or with specific clinical management protocols. Other limitations included a

plausible publication bias, and relatively old studies not necessarily reflecting current practice.

It should also be noted that the HRS Expert Consensus Statement[80] and the ESC Guidelines[88] consistently reports RM as useful for the prevention of inappropriate shocks and early detection of arrythmias and recommended the use of remote monitoring despite the absence of significant effect on hard outcomes but also on patients' quality of life seen in our systematic review of the literature. The validity and content of these expert consensus were nevertheless not assessed in our HTA. Indeed, the aim of HTA reports is to made recommendations based on strong evidence related to among others the clinical efficacy of a technology via systematic reviews of the literature (RCTs) rather than using expert consensus.

Concerning ILRs, the same benefits as for defibrillators and pacemakers could be expected (i.e. a reduced time between event onset to data review or clinical decision). No RCTs were nevertheless retrieved and such potential benefit is thus not substantiated by direct scientific evidence. The risk of data loss due to memory saturation of the device could also be reduced.

An uncertain cost-effectiveness dependent on multiple assumptions not well backed up by evidence

Overall, economic evaluations (cost-utility or cost-effectiveness) reviewed in chapter 5 indicate that remote cardiac monitoring of ICDs and PMs is cost-effective compared to a monitoring exclusively based on in-clinic visits. No relevant studies were identified for ILRs.

Such cost-effectiveness is nevertheless based on the assumptions that (i) human resources required to carry out remote monitoring would be less than or equal to those required for a standard monitoring exclusively based on in-clinic visits and that (ii) remote monitoring systems (RM devices and related services such as data storage) are either free or equal to a one-time amount that ranged from €864 to €1150 for ICDs (according to the only two high quality CUAs which considered such costs) and was of €450 for PMs (based on the high quality Canadian study by Ontario Health). Transferability of results to the Belgian setting is therefore uncertain, especially because, according to the results from our survey, Belgian hospitals self-reported that remote monitoring would require more resources than with a standard monitoring (see the survey performed in chapter 3).

The cost-effectiveness of remote monitoring for Belgium could not be investigated due to the lack of Belgian-specific data.

Some debates regarding legal aspect remain

The question of physicians' liabilities and the patients' rights were already investigated in the 2010 report and the analysis remains valid now (see the 2010 report for details). Therefore, chapter 6 of this report, focusses on the impact of newly adopted European rules on medical devices and personal data protection and on the national rules regulating the quality of care delivery in Belgium. These new rules are now taking into account the existence of new technologies, but they also bring new debates or challenges for the successful implementation of cardiac remote monitoring legal issues. In particular:

- Like with other medical devices, researchers, health care professionals and patients using CIEDs and their remote monitoring systems have only acces to limited information regarding the possible safety issues. Improvements will be brought when the new version of Eudamed will be functional but this is not be expected before 2025.
- Despite detailed regulatory requirements on cybersecurity, concrete compliance with those requirements remains challenging.
- Under the GDPR the question of who determines the purpose of the personal data processing and which legal ground allows this processing are crucial. Guidelines are needed in that regard to provide the greatest possible clarity for the patient.
- The health care professional implementing remote monitoring of CIEDs must be able to proof his/her competence and experience. To this end, a new Belgian law that will enter into force in the near future, requires health care professionals to maintain a, preferably electronic, portfolio containing evidence to demonstrate that he/she is sufficiently trained in order to be able to provide quality care. Only the actual implementation of this law will show whether this requirement is sufficient or whether a

new specialisation recognised by the law (currently non-existent) should be created to offer this type of care.

Based on international experience, three forms of financing of RM and several quality norms were identified

Based on the three countries investigated in chapter 7 (France, The Netherlands, Germany), three financing models can be highlighted for RM activities performed by health care professionals:

- A mixed system based on a fee-for-service (FFS) for in-clinic visits (scheduled and unscheduled) and a yearly lump sum for RM activities (scheduled remote data interrogations, remote managements of alerts, etc.) (French model).
- A yearly lump sum that covers the whole follow-up whatever the type of monitoring is remote or standard monitoring (Dutch model).
- A FFS for both in-clinic visits and scheduled remote data interrogations (same fee), with a maximum number of controls per year (German model).

Concerning the financing of RM systems' providers (for both the transmitter and the related services), two models were identified, i.e. no additional payments (already included in the implant price or in the financing of health care providers) and a separate one-time payment for the life time of the implant. Based on the request of RM system providers, a third model could be considered, i.e. a daily lump sum.

In terms of quality requirements for health professionals, the importance of having at least one face-to-face in-clinic visit per year (teleconsultations are authorized in the Netherlands), registering events in the patient's record, and ensuring a proper patient information was highlighted. Good clinical practice guidelines also included indications on the minimum thresholds for triggering alerts, the number of required scheduled remote data interrogations per year, and the level of required permanency (at the level of the centre). The role of nurses, including advanced practice nurses, and the required qualifications and cooperation agreements was also a focus point, especially if they performed tasks normally performed by physicians.

Requirements for RM systems' providers mostly concerned the minimum type of alerts that must be included in the RM system, the respect of the rules on security, traceability and confidentiality of data transmitted and stored, and the provision of technical assistance.

The three models were presented to stakeholders and the mixed financing was the most appreciated one, but it was highlighted that the lump sum must be sufficient enough to cover the burden of alerts management. Stakeholders also highlighted the necessity to discuss if the payment should be done at the level of the centre or at the level of the responsible physician (+ at the level of RM systems providers for the RM device and related services), if electrophysiology should be a recognized title or qualification, and if the recent developments on the creation of loco-regional networks and the allocation of care assignments within each network should be applied, with one center designated within each network to organize a high quality RM service for all hospitals of the network.

Which financing model for Belgium?

Given the current lack of reimbursement for RM in Belgium, health care professionals do not receive any additional financing than the fees for in-clinic visits for patients monitored remotely. Chapter 8 highlighted that each financing model identified in chapter 7 has its pros and cons (see below) but that the financing of health care providers for RM activities is expected to increase total NIHDI expenditures (e.g. if more than 1 in-clinic visit is performed on average for RM patients according to the French and the German model). Additionally, the potential introduction of funding for RM system providers (both for the transmitter and the related services), as well as its likely impact on the budget, are factors that should not be neglected.

During the reimbursement decision made by the NIHDI, the following pros and cons of each model should be considered:

- The advantage of a FFS system for both RM and SM patients with a maximum number of controls (German model) is its flexibility compared to the Dutch model, as it allows for higher financing if the patient's condition requires more controls (if clinically justified and reported in the patient record). On the other hand, it only covers scheduled remote data interrogations and in-clinic visits and does not provide a financing for

the workload of the remote management of alerts. Moreover, as with the current system, if the maximum number of controls is exceeded, it will be difficult for the NIHDI monitoring service to determine if it is clinically justified.

- A system based on a yearly lump sum whatever the type of monitoring (RM or SM, Dutch model) guarantees a same financing between SM and RM patients, which allows to switch from one type of follow-up to another without impact on the financing. On the other hand, as with every lump sum, such system could induce underproduction of care (e.g. less follow-up controls performed) and patient selection (only treating patients for which the lump sum is lucrative) if the lump sum is not set per centre according to the risk profile of the patient. This model also modifies the current financing of patients exclusively monitored based on in-clinic visits (financing by a lump sum and not anymore on a FFS basis).
- A mixed system, i.e. a yearly lump sum for remote monitoring activities (remote data interrogation and management of alert) and a FFS for in-clinic visits (French model) is the only one that aims both at covering the management of alerts and offering some flexibility if more in-clinic visits are required (reducing the risk of patient selection). Such model also does not impact the current financing of SM patients. Nevertheless, the risk of underproduction remain for remote care, especially if the lump sum for RM activities is unsufficient. Moreover, it is the system where mean NIHDI expenditure per RM patient are the most likely to exceed mean NIHDI expenditure per SM patient.

Moreover, as for teleconsultations, the question of patients' co-payments is also important when the financing of health care professionals for RM activities is considered. If there is no patient co-payment for remote monitoring, such type of monitoring could become more interesting for patients than standard monitoring, while patients' choice should not be influenced by financial considerations. If remote data interrogations are reimbursed via a FFS, the question is also how to get these patients' co-payments? Reflections on this topic are currently underway within the working groups of NIHDI on telemedicine.

A number of limitations

Because of a lack of data, no economic evaluation in the Belgian setting could be performed. It should also be noted that the budget impact estimations presented in this report do not consider other potential RM benefits than the reduction of in-clinic visits. Despite a general lack of significance in other key clinical outcomes was apparent in RCTs, the results based on the mean point estimates could be slighlty numerically superior for RM, as for example concerning heart failure hospitalization for patients with ICDs and CRT-Ds, and we can therefore not exclude that further clinical benefits could be linked to the use of RM. Should these be proven, the budget impact scenarios presented may be improved. Beside clinical uncertainties, there is also high uncertainties on the percentage of RM patients, on the mean number of in-clinic visits in both groups (SM and RM patients) and on the impact of a reimbursement of RM on current practices. An identification of RM patients in NIHDI data would allow to have a better view of the situation and its evolution.

Ethical issues and social aspects were also not addressed and should be explored in more detail at a later stage. Concerning the impact of remote monitoring on patients, no specific chapter was written, but some aspects were analysed in the following chapters:

- Chapter 4 (on efficacy and safety of remote monitoring) highlighted the following advantages for the patients, i.e. a 'protocol-based' reduction of in-clinic visits, an earlier detection of events, a reduced risk of inappropriate shocks and a lower burden of atrial arrhythmias, but, overall, there was no significant effect of remote monitoring on their health-related quality of life (see sections 4.3.2 and 4.3.3). It should, nevertheless, be noted that in this report, aspects such as patients/physicians' satisfaction and convenience of use were not considered. A summary of these aspects can be found in the HRS experts consensus of 2015[80] but the analysis of the content of this consensus following KCE methods for good clinical practice guidelines was out-of-scope for this report.

- Chapter 6 (on legal aspects) and chapter 7 (on organizational aspects in other countries) highlighted the importance of patients' privacy protection (with respect to the GDPR), of cybersecurity, of the patients' informed consents and of other patients' rights such as the right to refuse RM and to access their data, as well as the need for more transparency a.o. on safety aspects to better inform them. In analysed countries, an attention was also paid to the fact that no financial contribution could be asked to the patients for RM systems and data transmission.

Finally, it is also important to note that no valid data were found on ILRs (no RCT, no economic evaluation, and no Belgian data). Having specific NIHDI codes for the follow-up of patients with ILRs would at least allow to have a better view of the current Belgian situation for these patients.

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