Safety and efficiency of a common and simplified protocol for pacemaker and defibrillator surveillance based on remote monitoring only: a long-term randomized trial (RM-ALONE)

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Aims	This trial aimed to evaluate the safety and efficiency of a common and simplified protocol for the surveillance of cardiac implantable electronic devices based on remote monitoring (RM) in patients with pacemakers (PMs) and implantable cardiac defibrillators (ICDs) for at least 24 months.
Methods and results	The RM-ALONE is a multicentre prospective trial that randomly assigned 445 patients in two groups, both followed by RM: the home monitoring-only (HMo) based on RM + remote interrogations (RIs) every 6 months and the HM + IO that adds in-office evaluations every 6 months to RM. Four hundred and forty-five patients were enrolled in the study, 294 PMs and 151 ICDs recipients. In the HMo group, 20% of patients experienced ≥1 major adverse cardiac event (MACE) vs. 19.5% in HM + IO group ($P = 0.006$ for non-inferiority). The proportion of patients with a PM/ICD who experienced ≥1 MACE was 15.2/29.3% in HMo group and 16.1/26.3% in HM + IO group (hazard ratio 0.95/1.15, 95% confidence interval 0.53–1.70/0.62–2.10). There were 789 in-office evaluations (136 in the HMo and 653 in the HM + IO; $P < 0.001$). There was a 79.2% reduction of in-office evaluations with no significant differences in unscheduled visits between groups: 122 (54.5%) in HMo and 101 (45.3%) in HM + IO; $P = 0.15$. The time a physician/nurse spent per patient/follow-up was significantly reduced in the HMo group: 4/5 min (0–30)/(1–30) vs. 10/10 min (0–40)/(1–40) in HM + IO ($P < 0.0001$).
Conclusion	The RM-ALONE protocol common for ICD and PM surveillance, consisting of RM + RI every 6 months has proven safe and efficient in reducing hospital visits and staff workload.
Keywords	Remote monitoring • Remote interrogation • Pacemaker • Implantable cardiac defibrillator • Telemedicine

Introduction

The surveillance of patients carrying cardiac implantable electronic devices (CIEDs) is crucial for the early detection of clinical and technical problems that may arise but places a significant workload on the staff of the institutions that manage them. A Heart Rhythm Society (HRS) survey on physician workforce trends showed that the follow-up of CIEDs was the most frequent activity reported by cardiac electrophysiologists.[1]

Different trials have shown, besides their reliability, the multiple advantages of remote monitoring (RM: Automated transmission of data based on prespecified alerts; provides rapid detection of arrhythmias or device malfunction) in the management of CIEDs by studying pacemakers (PMs) and implantable cardiac defibrillators (ICDs), mainly separately.[2,3]

In terms of safety, RM is non-inferior to conventional follow-up in ICDs[4,5] and PMs,[6] reduces the time to clinical decision, and can therefore prevent many worsening conditions in ICDs[4,7,8] and even in PMs using only remote interrogation (RI: Routine, scheduled remote device interrogation structured to mirror in-office follow-ups).[9] Moreover, RM reduces inappropriate shocks and spares ICD's batteries[5] and, unlike RI, has shown improvement in survival.[10–13]

Regarding efficiency, RM and RI reduce the face-to-face visits in PMs and ICDs,[4,6,14] and RM has proven to be a cost-effective approach in ICDs,[15,16] resulting in a high degree of patient satisfaction.[7,11]

Despite the wide range of data supporting this technology, the adoption of RM yet remains suboptimal.[11] The current expert consensus[17,18] recommends after the first visit 2–12 weeks post-implantation, an annual in-person evaluation in addition to continuous RM + RI every 3–12 months for PMs and every 3–6 months for ICDs.[19]

The main objective of this study is to demonstrate, assuming that RM is the standard follow-up method, that it is possible to completely and safely dispense with face-to-face visits by maintaining the same RI structure every 6 months for both PM- and ICD-bearing patients.

Methods

Study design

RM-ALONE was a prospective, randomized, multicentre clinical trial conducted at 16 Spanish institutions (Supplementary material online, *Appendix SA*) comparing the safety and efficiency of a RM-only approach (HMo group) vs. RM plus standard in-office follow-up (HM + IO group) in single- or dual-chamber PM and ICD recipients.

The study was designed by a steering committee, composed of physicians who also conducted the study, in collaboration with the sponsor, Biotronik that also participated to the study design and data monitoring (Supplementary material online, *Appendixes SB* and *SC*).

The trial was carried out in compliance with Good Clinical Practice and the Declaration of Helsinki and was approved by the Independent ethics committees of each centre. Patient enrolment started on May 2010 and finished on December 2013.

Patients were enrolled after 3–6 months of device implantation (single- or dual-chamber PM or ICD) (Supplementary material online, *Appendix D*) and setup of device parameters.

Patients were eligible for inclusion in the RM-ALONE trial if: they were ≥18 years, had an implanted CIED equipped with Home Monitoring®,
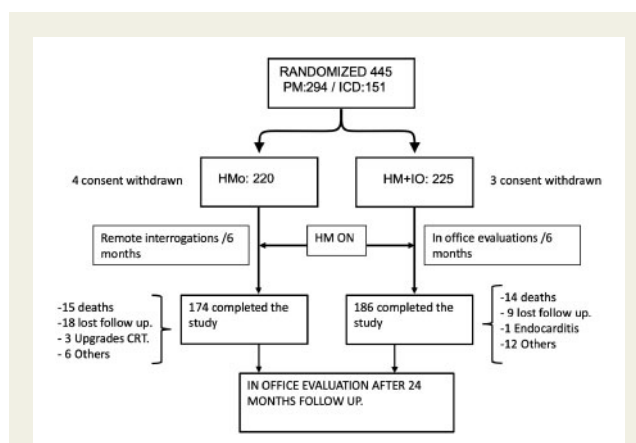

Figure 1 A flowchart of patients between enrolment and end of follow-up. CRT, cardiac resynchronization therapy; HM + IO, home monitoring plus in-office evaluations; HMo, home monitoring only; ICD, implantable cardiac defibrillator; PM, pacemaker.

had medical/psychic status controlled, provided written informed consent and had stable Global System for Mobile communications (GSM) network coverage. Patients were excluded if had a replaced implant or upgraded to cardiac resynchronization therapy (CRT). Cardiac resynchronization therapies were excluded in the absence of reliable tools to automatically optimize QRS narrowing at the time of study design requiring an electrocardiogram (ECG) in the follow-ups for this.

Unlike previous studies, no patient was excluded because of PM dependency or ICD indication for secondary prevention.[4,6,8,14]

Home monitoring[20] is a RM system that transmits automatically and daily the data stored in the CIED to the Biotronik HM-Service centre. The staff responsible for the patient's care can check this information on a secure website, where the patients are automatically classified and flagged for attention. Additionally, physicians are notified on prespecified alerts (Supplementary material online, *Appendix online*).

After a 12-week post-implant face-to-face visit to reprogramme the CIED and check the wound, patients were randomly assigned to the HMo group or to the HM + IO group in a 1:1 ratio (*Figure 1*). To prevent bias, the randomizations blocks and schedule were generated before the study implantation by an external consultant. Randomization was stratified by site and by device, so two randomization schemes (one for ICDs and one for PM) were produced for each site according to these specifications: two groups (HMo and HM + IO groups), allocation ratio (1:1), and block size of 4.

Both groups had HM programmed ON, and all the alert events generated were checked at the discretion of each centre according to their usual practice. Patients in the HMo group were scheduled for a RI every 6 months without any patient intervention. Patients in the HM + IO group were scheduled for in-office-visits for device check only every 6 months.[19]

Patients in both groups attended an in-office evaluation after at least 24 months (end of study visit). All programmed visits with other health providers were unmodified and patients received standard treatment for their underlying diseases. Additional visits could be programmed upon patients and/or physician request or by the occurrence of an alert notified by HM and were considered unscheduled visits.

After every follow-up, patients in both groups received a report summarizing his/her health and device status. While this is a common practice in face-to-face visits, in the remote group this report served to reassure patients.

Study objectives

Primary objective

The primary safety objective was to demonstrate non-inferiority of following up CIEDs with a single remote protocol for PMs and ICDs with RI every 6 months in addition to RM (HMo group) compared to the monitoring with face-to-face visits every 6 months plus RM follow-up (HM + IO group).

The primary study outcome was the proportion of patients with ≥1 major adverse cardiac event (MACE) over 24 months of follow-up.

The following events were considered MACEs: death of any cause, stroke, hospitalization related to device or cardiac cause, and device-related surgical intervention.

Adverse events were reviewed and classified by the Clinical Events Committee (Supplementary material online, *Appendix D*) composed of an expert cardiologist who was not involved in the trial and was not aware of the treatment allocation groups. The ultimate decision to qualify the events as MACE relied on this committee.

Secondary objectives

The secondary safety objective was to demonstrate that differences in terms of MACE occurrence were not statistically significant between the HMo and HM + IO groups in each type of device (PM and ICD).

The secondary efficiency objectives were to measure the decrease in the number of in-office follow-ups in the HMo group, and to compare the workload of healthcare professionals in following up patients of the HMo and HM + IO groups.

The efficiency was evaluated by means of three parameters: number of in-office evaluations, time per patient in each followup, and total workload.

The time dedicated by each healthcare professional per patient in each follow-up resulted from the total time dedicated by clinicians and nurses to the following activities: (a) follow-up of patients through HM, (b) follow-up of patients through in-office-visits, (c) review of HM alerts, (d) follow-up requested by the patient, and (e) follow-up triggered by HM alerts.

The total workload of each healthcare professional per patient and day was calculated as the total time invested by the staff $(a + b + c + d + e)$ on the surveillance of the patients divided by the number of patients and total days they remained within the study. As the fraction obtained from each staff member per patient was multiplied by 100 patients and 22 working days, the workload of each staff is presented in minutes/100 patients/month.

Statistical analyses

The primary study hypothesis was that patient safety was not inferior in the HMo group compared to the HM + IO group. Non-inferiority was established using a 10% non-inferiority margin for the lower limit of the one-sided 97.5% confidence interval (CI) on the difference in the proportion of patients with ≥1 MACE between groups.

The non-inferiority margin was defined considering data from principal trials on RM. A non-inferiority margin of 5% was defined in TRUST (ICD population)[4] and of 7% in COMPAS (PM population).[6] In contrast, RM-ALONE trial combined both PMs and ICDs (ratio of 2:1), increasing the heterogeneity of the sample population. Consequently, and given the random nature of the onset of arrhythmic events, the non-inferiority margin was set at 10%, so this had an effect of reducing the total population sample size. Furthermore, the ICD population was further reduced as the event rate in this subgroup of patients was expected to be higher than in those having a PM. That was the reason we had a proportion of 2:1 of PMs vs. ICDs.

According to published studies, the frequency of MACE is 14.9% and, based on these data, 201 patients per arm were required to demonstrate non-inferiority between groups with 80% power. Assuming a drop-out rate of 5%, 424 patients were required (212 per arm). The study was powered only for the primary analysis; secondary endpoints were considered as supportive analysis with an exploratory purpose.

Statistical analyses were performed in the intention-to-treat population comprised by all randomized patients.

Continuous variables were described by the number of available and missing data, mean, 95% CI, median, standard deviation (SD), extremes (min–max); and categorical variables were described by n (%).

The distribution of variables was assessed using the Kolmogorov–Smirnov test, and equality of variances was verified by the Levene's test. Comparisons between groups for the number of patients with ≥1 MACE were performed using the non-inferiority test and Cox-Regression (hazard ratio [HR] and 95% CI), the log-rank test to evaluate the differences in the time to first MACE, the χ^2 test for the number of patients with MACE, and the Analysis of Variance (ANOVA) test for the mean number of MACEs per patient. Comparisons between groups for workload were performed using the ANOVA test or the Mann–Whitney test if abnormal distribution was met.

The level of statistical significance was set at $P < 0.05$. Statistical analyses were performed using SAS software (SAS Institute, Cary, SC, USA) for Windows, version 9.2. nQuery Advisor 6.2 software was used for sample size calculation.

The statistics work was carried out by an external consultant and a biostatistician contracted by the sponsor.

Results

Study population

Between May 2010 and December 2013, 445 participants were randomized to the HMo group ($n = 220$) or to the HM + IO group ($n = 225$). Of them, 294 had an implanted PM and 151 had an ICD. Eighty-five patients (19.1%) finished the study prematurely (before Month 24): 46 (20.0%) in the HMo group and 39 (17.3%) in the HM + IO group ($P = 0.337$). Most common reasons for early termination were patient's death (32.6% in the HMo vs. 38.5% in the HM +IO groups), lost to follow-up (26.1% vs. 23.1%), and other reasons (19.6% vs. 30.8%) (*Figure 1*).

The overall attrition rate (consent withdrawal, moving, and lost to follow-up) was 11.5% and for each group individually 12.7% (HMo) and 10.2% (HM + IO) ($P = 0.461$).

Baseline characteristics were balanced between both arms. Demographic and clinical characteristics are shown in Supplementary material online, *Table S1*. The mean duration of follow-up was 20.7 ± 7.1 months.

Mean age in the overall population was 68.9 years and 71% were men, with no marked differences between groups. Among all the participants included, 33.9% had an implanted ICD and 66.1% a PM, both showing a similar distribution in clinical and demographic baseline characteristics (*Table 1*).

In PM patients, 79.6% were double chambered, 61.9% indicated by atrioventricular (AV) block, 70.7% diagnosed of primary disease of the conduction system, and 54% were PM dependent (>75% or time paced).

In ICD patients, 72.2% were single-chamber devices, 55.6% indicated in primary prevention, and 58.5% due to ischaemic cardiomyopathy (*Table 1*).

Table 1   Baseline characteristics in pacemaker and implantable cardiac defibrillator patients

PMs	HMo (n: 145)	HM + IO (n: 149)	Total (n: 294)
Sex male/female (male%)	89/56 (61.4)	100/49 (67.1)	189/105 (64.3)
Age (years), mean ± SD (min–max)	72.2 ± 11 (25–89)	73.1 ± 9.9 (19–87)	72.7 ± 10.6 (19–89)
NYHA ≥III	8 (5.5)	4 (2.7)	12 (4)
LVEF (%), mean ± SD	62.2 ± 8	62 ± 9.7	62.2 ± 8.8
Persistent/permanent AF	23 (15.9)	20 (13.4)	43 (14.6)
Paroxysmal AF	15 (10.3)	27 (18.1)	42 (14.28)
Pacing indication			
Sick sinus syndrome	43 (29.7)	58 (39)	101 (34.4)
Slow AF	27 (18.6)	27 (18.1)	54 (18.4)
AV block	94 (64.8)	88 (59.1)	182 (61.9)
Neuromediated syncope	5 (3.4)	6 (4)	11 (3.7)
Others	11 (7.6)	10 (6.7)	21 (7.1)
Underlying heart disease			
Primary conduction system disease	104 (71.7)	104 (69.8)	208 (70.7)
Ischaemic heart disease	17 (11.7)	27 (18.1)	44 (15)
Valvular heart disease	8 (5.51)	12 (8)	20 (6.8)
Single chamber	30 (20.7)	30 (20.13)	60 (20.4)
Dual chamber	115 (79.3)	119 (79.9)	234 (79.6)
ICDs	HMo (n: 75)	HM + IO (n: 76)	Total (n: 151)
Sex male/female (male%)	63/12 (84)	64/12 (84.2)	127/24 (84)
Age (years), mean ± SD (min–max)	62.5 ± 14.8 (18–89)	60.4 ± 13.8 (28–85)	61.5 ± 14.3 (18–89)
NYHA ≥III	2 (2.7)	4 (5.3)	6 (4)
LVEF (%), mean ± SD	38.3 ± 14	36.9 ± 15	37.6 ± 14.9
Persistent/permanent AF	17 (22.6)	13 (17.1)	30 (19.9)
Paroxysmal AF	2 (2.66)	4 (5.26)	6 (3.4)
ICD indication			
Primary prevention	40 (53.3)	44 (58)	84 (55.6)
Secondary prevention	35 (46.6)	32 (42)	67 (44.4)
Underlying heart disease			
Ischaemic cardiomyopathy	40 (56.3)	43 (60.6)	72 (58.5)
Dilated cardiomyopathy	13 (17.3)	16 (21)	29 (19.2)
Hypertrophic cardiomyopathy	13 (17.3)	9 (11.8)	22 (14.6)
Channelopathies	2 (2.7)	1 (1.3)	3 (2)
Single chamber	54 (72)	55 (72.3)	109 (72.2)
Dual chamber	21 (28)	21 (27.6)	42 (27.8)

Results are expressed as n (%).
AF, atrial fibrillation; HM + IO, HM + in-office; HMo, HM-only; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PM, pacemaker.
No statistically significant differences were found for any variable (P < 0.05).

Safety assessments

Overall population

No significant differences in safety were observed between the HMo and the HM + IO groups either in the total population or in the PM and ICD subgroups.

By the end of the trial, 88 patients (19.8%) showed ≥1 MACE; 44 (20%) in the HMo group and 44 (19.5%) in the HM + IO group, confirming the non-inferiority for the primary endpoint (P = 0.006; HR 1.04, 95% CI 0.68–1.58, P = 0.838 χ^2 test) (Table 2). The mean ± SD number of MACEs experienced per patient was statistically

comparable between groups: 0.34 ± 0.79 and 0.36 ± 0.87 for patients followed by HMo and HM + IO, respectively (P = 0.894).

Time to first MACE did not significantly differ between both groups in the overall population and neither in PM- nor in ICD-implanted patients (Figures 2 and 3, Take home figure).

In an additional analysis, we found no significant differences between the two groups for each independent component of the composite MACE.

Fifteen patients (6.8%) died in the HMo group and 15 (6.6%) in the HM + IO group (P = 0.942; HR 0.97, 95% CI 0.47–1.99). Among

Table 2 Rate of major adverse cardiac events in the population

Overall population (*n*: 445)	HMo (*n*: 220)	HM + IO (*n*: 225)	*P*-value; HR (95% CI)
Number of patients ≥1 MACE (*n*: 88)	44 (20)	44 (19.5)	0.838; 1.04 (0.68–1.58)[a]
Deaths: CV/non-CV/unknown	15 (6.8): 7/8	15 (6.7): 8/6/1	0.942; 0.97 (0.47–1.99)
Stroke	5 (2.2)	4 (1.8)	0.644
Device-related surgery	2 (0.9)	7 (3.1)	0.110
Hospitalizations due to CIED or CV reasons	53	55	0.708
Total number of MACEs (mean ± SD)	75 (0.34 ± 0.79)	81 (0.36 ± 0.87)	0.894
Number of patients AF detected	44 (20)	47 (20.8)	0.816
PM-bearing patients (*n*: 294)	HMo (*n*: 145)	HM + IO (*n*: 149)	
Number of patients ≥1 MACE (*n*: 46)	22 (15.2)	24 (16.1)	0.876; 0.95 (0.53–1.70)
Deaths CV/non-CV/unknown	8 (5.5): 4/4	12 (8): 6/5/1	0.402; 1.46 (0.59–3.57)
Stroke	5 (3.4)	1 (0.7)	0.055
Device-related surgery	0 (0)	2 (1.3)	0.188
Hospitalizations due to CIED or CV reasons	25	30	0.933
Total number of MACEs (mean ± SD)	38 (0.26 ± 0.70)	45 (0.3 ± 0.86)	0.925
Number of patients AF detected	37 (25.5)	40 (26.8)	0.795
ICD-bearing patients (*n*: 151)	HMo (*n*: 75)	HM + IO (*n*: 76)	
Number of patients ≥1 MACE	22 (29.3)	20 (26.3)	0.649; 1.15 (0.62–2.10)
Deaths CV/non-CV/unknown	7 (9.3): 3/4	3 (3.9): 2/1	0.173; 0.40 (0.1–1.56)
Stroke	0 (0)	3 (3.9)	0.073
Device-related surgery	2 (2.6)	5 (6.6)	0.218
Hospitalizations due to CIED or CV reasons	28	25	0.551
Total number of MACEs (mean ± SD)	37 (0.49 ± 0.93)	36 (0.47 ± 0.90)	0.793
Number of patients AF detected	7 (9.3)	7 (9.2)	0.979
ICD therapies delivered			
Patients receiving ≥1 appropriate therapy delivery	26 (34.6)	21 (27.6)	0.350
Patients receiving ≥1 inappropriate therapy delivery	7 (9.3)	7 (9.2)	0.979
Number of appropriate shocks delivered (mean ± SD)	32 (0.43 ± 1.45)[b]	11 (0.14 ± 0.53)	0.268
Number of patients ≥1 appropriate shock delivered	11 (14.6)	7 (9.2)	0.300
Number of inappropriate shocks delivered (mean ± SD)	9 (0.12 ± 0.63)	3 (0.04 ± 0.25)	0.394
Number of patients ≥1 inappropriate shock delivered	4 (5.3)	2 (2.6)	0.395

Results are expressed as *n* (%).
AF, atrial fibrillation; CIED, cardiac implantable electronic device; CV, cardiovascular; HM, home monitoring.
[a]Non-inferiority *P* = 0.006.
[b]In this group, three patients suffered an electrical storm (≥3 shocks within 24 h) and were delivered 10, 5, and 4 appropriate shocks, and other patient was delivered four shocks within the 24 months, so four patients received 72% of the total shocks in the HMo group.

them, three were due to heart failure (HF), three to strokes, one to sudden unexplained death (SCD) (one PM-bearing patient), and eight to non-cardiac causes in the HMo group, whereas in the HM + IO four patients died from HF, one from an acute myocardial infarction, two from a SCD (one PM-and one ICD-bearing patients), one from stroke, six from non-cardiac causes, and one from unknown cause. The number of MACEs is listed in *Table 2*.

Pacemaker-implanted patients
By the end of the trial, 46 patients (15.6%) showed ≥1 MACE; 22 (15.2%) in the HMo group and 24 (16.1%) in the HM + IO group, confirming no statistically significant differences between groups (*P* = 0.876; HR 0.95, 95% CI 0.53–1.70).

The mean ± SD number of MACEs experienced per patient was statistically comparable between groups: 0.26 ± 0.70 and 0.3 ± 0.86 for patients followed by HMo and HM + IO, respectively; *P* = 0.925.

Eight (5.4%) deaths were registered in the HMo group and 12 (8%) in the HM + IO group (*Table 2*).

Implantable cardiac defibrillator-implanted patients
In patients with an implanted ICD, ≥1 MACE occurred in 22 patients (29.3%) in the HMo group and in 20 patients (26.3%) in the HM + IO group (*P* = 0.649; HR 1.15, 95% CI 0.62–2.10).

On average 0.49 ± 0.93 and 0.47 ± 0.90 MACEs were observed per patient in the HMo and HM + IO groups, respectively (*P* = 0.793).
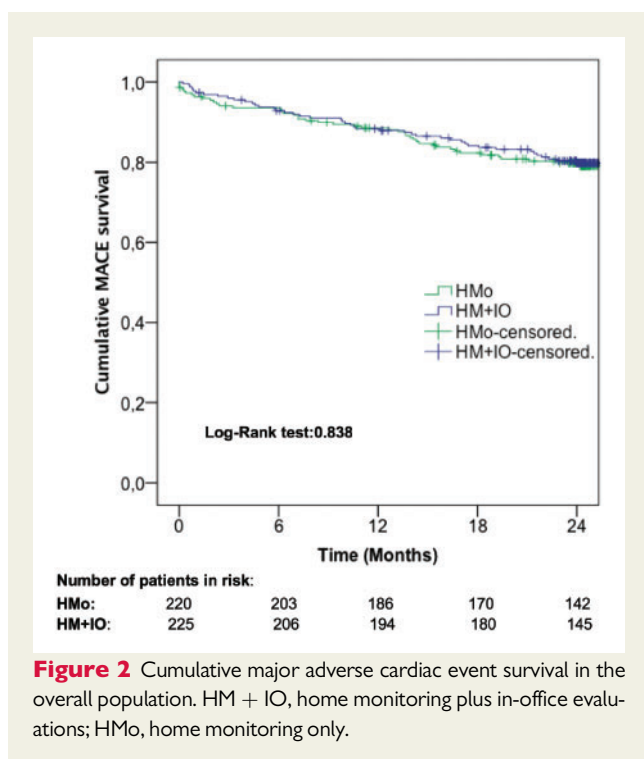
Figure 2 Cumulative major adverse cardiac event survival in the overall population. HM + IO, home monitoring plus in-office evaluations; HMo, home monitoring only.

The number of deaths were 7 (9.3%) in the HMo group and 3 (3.9%) in the HM + IO group (*Table 2* and Supplementary material online, *Table S2*).

Efficiency assessment

Overall population

Excluding the start and closing visits, the overall population attended 136 face-to-face visits in the HMo group and 653 in the HM + IO group, representing a 79.2% reduction in in-office visits. If start and closing visits were not excluded the reduction would be 47.8%.

The proportion of unscheduled visits was statistically comparable between groups, with 122 visits in the HMo group and 101 visits in the HM + IO group ($P = 0.160$). Unscheduled visits were triggered by device alert (28.7% in the HMo group and 23.8% in the HM + IO group), patient request (15.6% in the HMo group and 8.9% in the HM + IO group) and other reasons, mainly by scheduling mistakes (55.7% in the HMo group and 67.3% in the HM + IO group). Differences in the proportions of reasons for unscheduled visits did not reach statistical significance ($P = 0.159$).

We observed a significant reduction in the rate of scheduled and total in-office visits per patient in the HMo group at 24-month follow-up, without this leading to a significant increase in unscheduled visits ($P = 0.15$) (*Figure 4A, Take home figure*).

Pacemaker-bearing patients

The PM-recipient population underwent 74 in-office evaluations in the HMo group and 431 in the HM + IO group, representing an 82.8% reduction in face-to-face visits. Of the total number of visits, the proportion of unscheduled visits was 86.5% in the HMo group and 12.3% in the HM + IO group.

We observed a significant reduction in the number of scheduled and total in-office visits that did not result in a significant increase in unscheduled visits ($P = 0.309$) (*Figure 5A*).

Implantable cardiac defibrillator-bearing patients

The ICD population underwent 62 in-office evaluations in the HMo group and 222 in the HM + IO group, with a 72% reduction in face-to-face visits. Unscheduled visits represented a 93.5% of the total number of visits in the HMo group and a 21.6% in the HM + IO group.

We observed a significant reduction in the number of scheduled and total in-office visits and no significant increase in unscheduled visits in the HMo group ($P = 0.33$) (*Figure 5C*).

Staff workload

The mean time required by the clinician per patient on the total amount of follow-ups (remote + in-office) was significantly shorter in the HMo group than in the HM + IO group; 5.9 ± 6.7 min/follow-up vs. 10.2 ± 8.1 min/follow-up, respectively ($P < 0.0001$). Similarly, the mean time spent by nurses for the monitoring of patients with HMo was significantly lower (6.3 ± 5.7 min/follow-up) than for HM + IO (11.1 ± 7.2 min/follow-up) ($P < 0.0001$) (*Figure 4B*). These differences are maintained in both PM or ICD devices (*Figure 5B* and *D*, respectively).

The median time (min) spent by nurses to review 100 patients/month was 92.86 (3.99–1172) in the HMo group and 140.3 (3.65–1764.7) in the HM + IO group ($P = 0.002$), and by the physician was 67.10 (3.9–610.4) in the HMo group and 96.9 (8.05–1666.6) in the HM + IO group ($P = 0.018$). The median workload of the staff was statistically lower in the HMo group than in the HM + IO group [92.86 (3.99–1172) vs. 140.36 (3.65–1764.70); $P = 0.002$] (*Figure 6*).

Discussion

Main findings

The large number and complexity of CIEDs makes the work overload unmanageable in many cases. Here, we provide a simplified, safe, and efficient approach for the management of PM- and ICD-implanted patients.

The RM-ALONE protocol consisting of continuous RM and RI every 6 months, demonstrated non-inferiority in terms of safety with respect to continuous RM associated with on-site visits every 6 months for the overall population of PM and ICD.

In addition, RM reduced 79.2% the number of face-to-face visits, without a significant increase in unscheduled follow-ups, and significantly decreased the workload of the personnel involved.

Attrition rate

In a previous trial,[4] many scheduled visits were missed in the conventional group, and some data suggested that RM increased patient engagement during follow-up.[21] Despite these results, follow-up lengthening was associated with an increase in attrition rate and was one of the main concerns in REFORM reaching 20.7%.[14] In our trial, the low attrition rate observed in the HMo group (12.7%) can be plausibly explained by the frequent contact with the patient, even if remotely, which helps them comply with therapy and not leave the follow-ups.
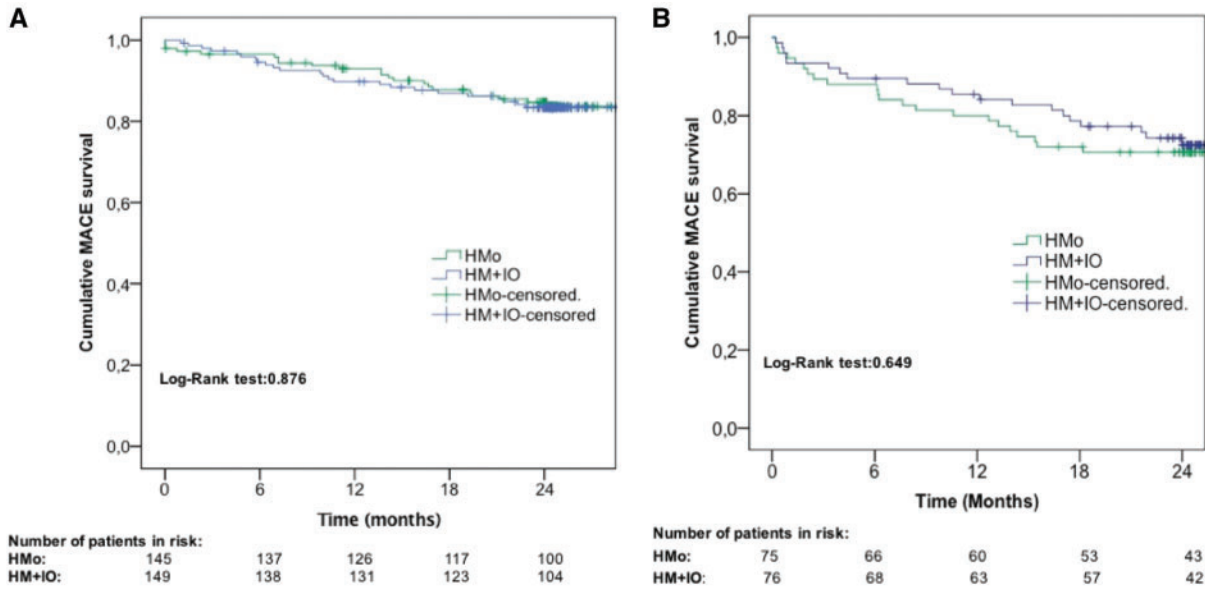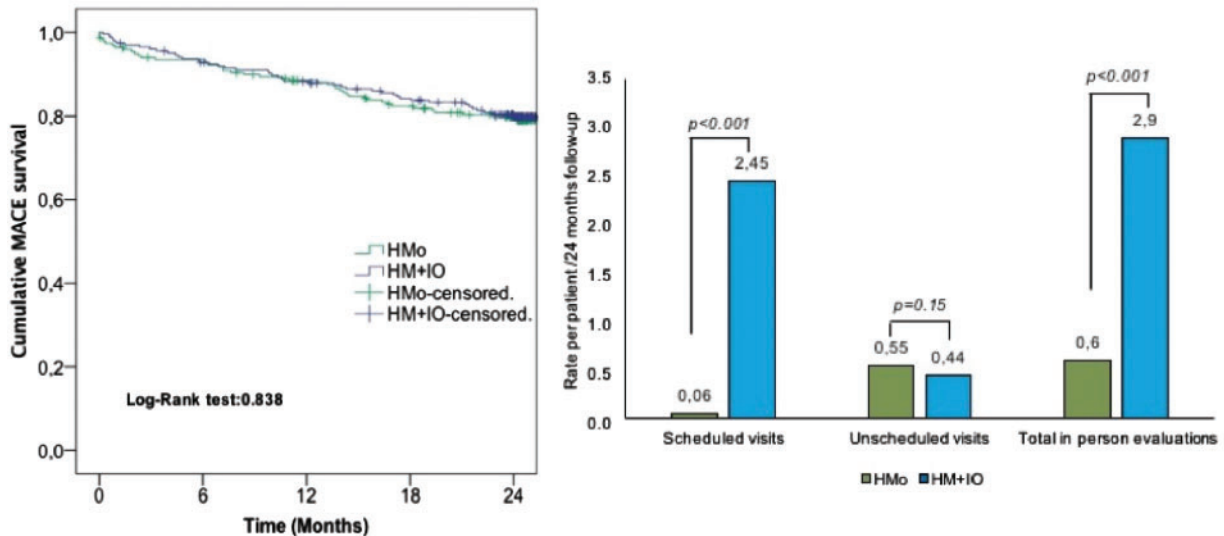
Figure 3 Cumulative major adverse cardiac event survival in the pacemaker (*A*) and implantable cardiac defibrillator (*B*) population. HM + IO, home monitoring plus in-office evaluations; HMo, home monitoring only.

Take home figure

Safety aspects

The main concern about extending the time between in-office visits is that safety may be compromised. In this regard, we have proven non-inferiority in terms of safety in the overall population. Previous randomized trials have shown that RM is non-inferior to conventional follow-ups in terms of safety, but studying independently patients with ICDs and PMs with different follow-up schemes.[4–7] To the best of our knowledge, RM-ALONE is the first randomized trial surveilling

PMs and ICDs with the same follow-up pattern and using RM as a gold standard in both groups.

RM-ALONE is distinct from prior studies in that patients that were dependent on pacing[4,6] or had an ICD for secondary prevention[14] were not excluded; therefore, these study attributes are more reflective of a 'real world' population.

In RM-ALONE, the number of cardiovascular deaths in ICD patients predominantly followed by RM are slightly higher than
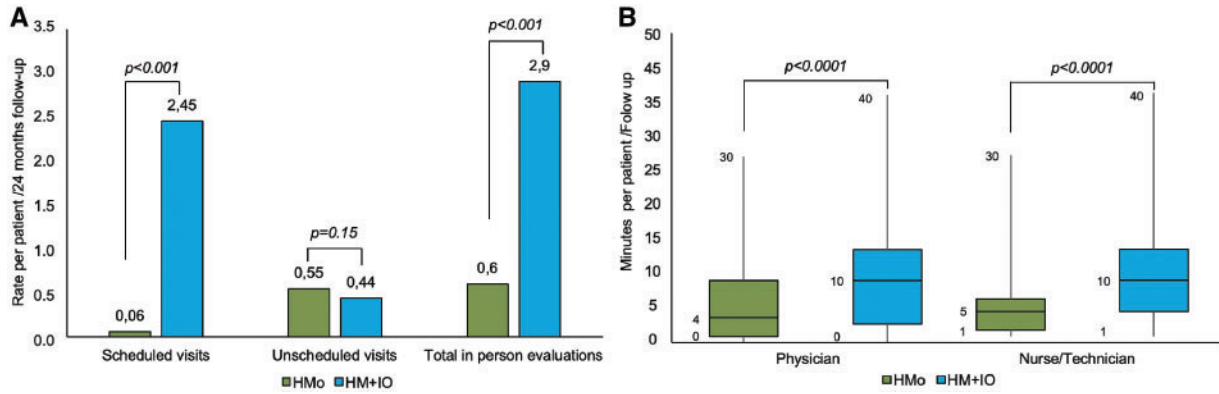
Figure 4 Efficiency in the overall population. (*A*) Difference between groups in the rate of in-person evaluations per patient for the whole follow-up. (*B*) Difference between groups in the mean time spent by physicians and nurses per patient and follow-up.
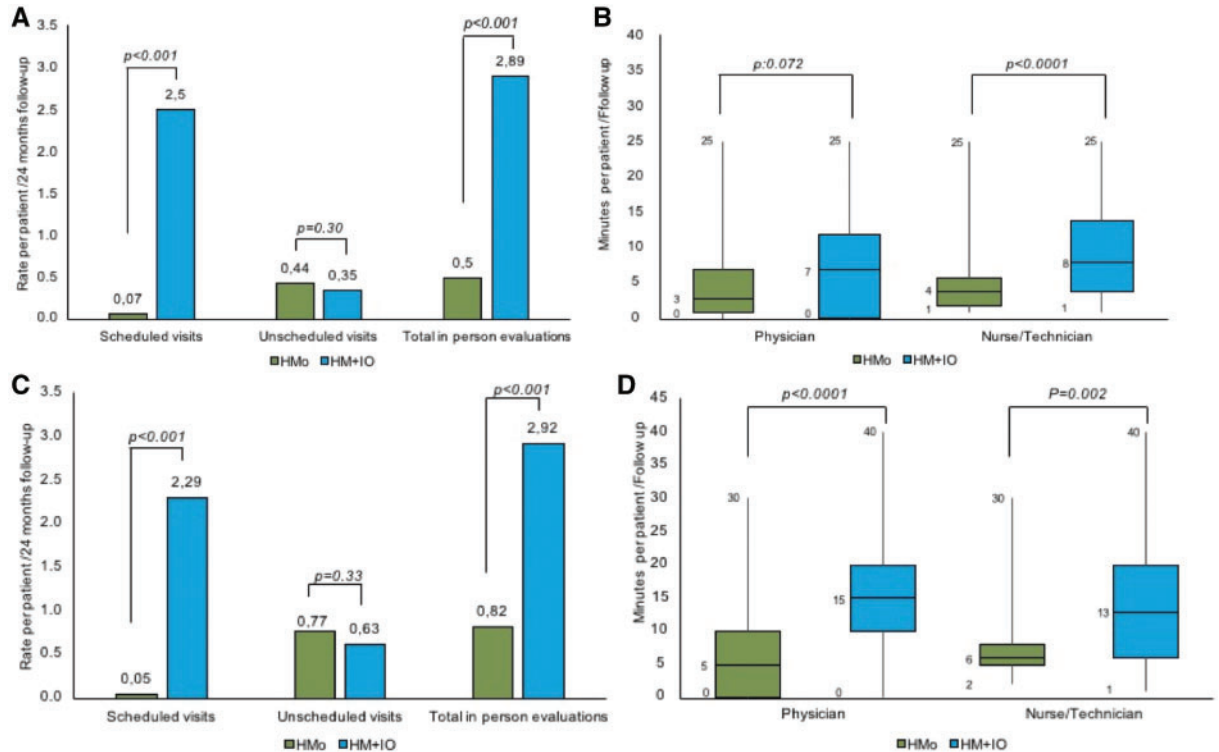

Figure 5 Efficiency in the pacemaker (*A*, *B*) and implantable cardiac defibrillator (*C*, *D*) population. (*A* and *C*) Difference between groups in the rate of in-person evaluations per patient for the whole follow-up. (*B* and *D*) Difference between groups per patient and follow-up measuring the mean time (min) spent by staff members on each patient in any of the follow-up activities.

those in TRUST[4] (2% vs. 1%), even considering that in TRUST only 25% were secondary prevention indications while in RM-ALONE this reached a 46%. However, in the ECOST trial, the percentage of secondary prevention was similar to that in RM-ALONE, so was the total number of cardiovascular deaths in the RM group.[5]

The proportion of patients with ≥1 appropriate therapy was 34.6% in the HMo group and 27.6% in the HM + IO group (*P* = 0.350); 58% of the total amount were in secondary prevention ICD-recipients.

The proportion of patients suffering ≥1 appropriate shock in the HMo group (14.6%) was lower than that in the RM group of the
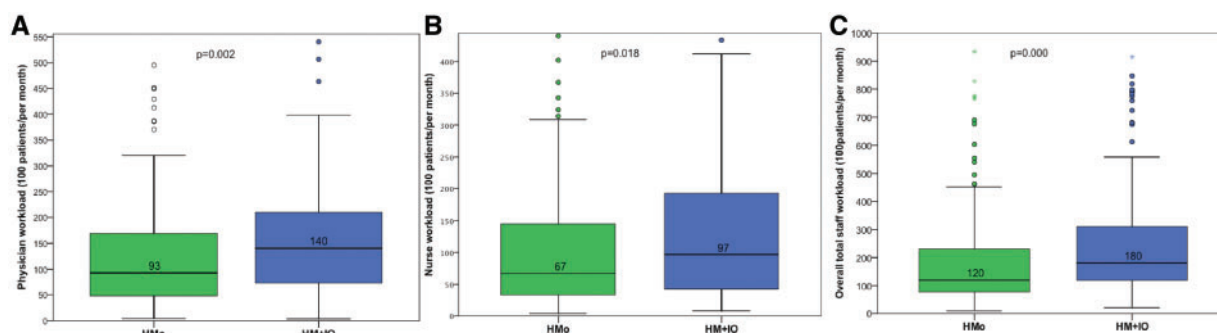
Figure 6 Staff workload. Minutes per 100 patients and month spent by the whole staff (*C*) and separately by each member: nurses (*A*) and physicians (*B*).

ECOST[5] (16.3%), whereas the proportion receiving ≥1 inappropriate shock in the HMo group (5.3%) is nearly identical to that in ECOST (5%), maintaining a substantial reduction with respect to the in-person group of the latter (10%). Therefore, compared to conventional in-office follow-up, RM protects from inappropriate therapies.

However, and though there were very few shocks to come to any conclusion, the proportion of patients with ≥1 inappropriate shock in the HMo group is higher than in the HM + IO group (5.3 vs. 2.7%; $P = 0.395$), and all of them occurred in patients with secondary prevention.

Therefore, we need larger trials to address if dismissing in-office evaluations increases therapies in secondary prevention ICD patients.

Comparing the PM subgroup, we evidenced that RM alone is as safe as adding face-to-face visits. In terms of survival, we found very similar results to COMPASS, and even considering that 54.3% of our patients were PM-dependents, which was a reason for exclusion in the former trial. There were fewer device-related complications in RM-ALONE, which may be due to a later randomization in our trial (3 months vs. 1 month after device implantation).[6] It is noteworthy that we can only compare our results with previous trials that use RM (automatic daily monitoring),[6] the only system with proven clinical improvement, even in the survival of patients,[11] unlike RI that has not shown such improvement in other trial.[9]

RM-ALONE has been performed using a single proprietary system, as most of the RM trials,[4,7,14] but a non-randomized multiproprietary prospective trial has shown that the use of RM is safe in ICD recipients and improves survival in cardiac resynchronization therapy defibrillator (CRTDs).[22]

Reduction of follow-ups and workload of the staff

Scheduled visits, regardless they are face-to-face or remotely driven, are very often futile and frequently result in no action.[6,23] In fact, in RM-ALONE there were 102 significant reprogramming changes, 80% of them due to HM alerts.

We observed a reduction of 79.2% in total interim follow-ups, further more pronounced than in most of the previous trials (ranging from 45% to 56%).[4,6] The single randomized prospective trial using only RM alerts as follow-up of PM lasted 18 months[6] and the remaining studies either had a duration of <1 year or had some face-to-face visits at 12–15 months.[4,8] Therefore, RM-ALONE is, to the best of our knowledge, the trial with the longest surveillance period of CIEDs supported exclusively by RM.

Unlike other trials[4,14] showing an increase in unscheduled visits in the group with fewer face-to-face visits, in RM-ALONE we have not observed this trend. We believe that continuous 'remote' contact with patients, reassuring them by sending clinical reports avoided many unnecessary visits often caused by patient anxiety.

Limitations

RM-ALONE did not include CRT recipients, so the results might be not transferrable to this group. Though we believe that RM is quite useful from the implant, RM-ALONE protocol is only recommended for 'stable' (at least 3 months post-implantation) devices, and lasted 24 months so it could not capture late complications after this period.

RM-ALONE results can be only transferred to platforms capable of continuous RM, and since each proprietary system has its own peculiarities,[24] we advise RM + RI every 6 months or occasionally every 3 months depending on the manufacturer characteristics.

Conclusions

The surveillance protocol common for single- and dual-chamber PMs and ICDs described in 'RM-ALONE', consisting of continuous RM and RI every 6 months, has proven to be safe for at least 2 years of follow-up and very efficient in terms of reducing hospital visits and staff workload (*Take home figure*).

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Funding

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