The Relationship Between Level of Adherence to Automatic Wireless Remote Monitoring and Survival in Pacemaker and Defibrillator Patients

Niraj Varma, MD, PhD,* Jonathan P. Piccini, MD, MHSc,† Jeffery Snell, BA,‡ Avi Fischer, MD,‡ Nirav Dalal, MS,‡ Suneet Mittal, MD§

ABSTRACT

BACKGROUND Remote monitoring (RM) technology embedded within cardiac rhythm devices permits continuous monitoring, which may result in improved patient outcomes.

OBJECTIVES This study used “big data” to assess whether RM is associated with improved survival and whether this is influenced by the type of cardiac device and/or its degree of use.

METHODS We studied 269,471 consecutive U.S. patients implanted between 2008 and 2011 with pacemakers (PMs), implantable cardioverter-defibrillators (ICDs), or cardiac resynchronization therapy (CRT) with pacing capability (CRT-P)/defibrillation capability (CRT-D) with wireless RM. We analyzed weekly use and all-cause survival for each device type by the percentage of time in RM (%TRM) stratified by age. Socioeconomic influences on %TRM were assessed using 8 census variables from 2012.

RESULTS The group had implanted PMs (n = 115,076; 43%), ICDs (n = 85,014; 32%), CRT-D (n = 61,475; 23%), and CRT-P (n = 7,906; 3%). When considered together, 127,706 patients (47%) used RM, of whom 67,920 (53%) had ≥75%TRM (high %TRM) and 59,786 (47%) <75%TRM (low %TRM); 141,765 (53%) never used RM (RM None). RM use was not affected by age or sex, but demonstrated wide geographic and socioeconomic variability. Survival was better in high %TRM versus RM None (hazard ratio [HR]: 2.10; p < 0.001), in high %TRM versus low %TRM (HR: 1.32; p < 0.001), and also in low %TRM versus RM None (HR: 1.58; p < 0.001). The same relationship was observed when assessed by individual device type.

CONCLUSIONS RM is associated with improved survival, irrespective of device type (including PMs), but demonstrates a graded relationship with the level of adherence. The results support the increased application of RM to improve patient outcomes. (J Am Coll Cardiol 2015;65:2601–10) © 2015 by the American College of Cardiology Foundation.

Remote monitoring (RM) of patients with cardiac electronic implantable devices (CIEDs) continues to evolve (1). Although originally devised to facilitate patient access and/or clinic efficiency by replacing the need for in-person follow-up evaluations, RM is now being explored as a method for improving patient outcomes (2–8). Newer technologies embedded in CIEDs permit daily monitoring with automatic early notification of changes in patient’s clinical condition and device (mal)function (9). These notifications enable prompt clinical intervention, irrespective of follow-up...
Abnormalities and Acronyms

CI = confidence interval  
CIED = cardiac electronic implantable device  
CRT = cardiac resynchronization therapy  
CRT-D = cardiac resynchronization therapy with defibrillation capability  
CRT-P = cardiac resynchronization therapy with pacing capability  
HR = hazard ratio  
ICD = implantable cardioverter-defibrillator  
MIR = mortality incidence rate  
MIRR = mortality incidence rate ratio  
PM = pacemaker  
RM = remote monitoring  
RM None = never used remote monitoring  
TRM = time in remote monitoring  
%TRM = percentage of time in remote monitoring

Schedule (4, 6, 10). However, whether these actions have a tangible effect on patient outcome remains an area of active investigation. First reports from studies using high-voltage CIEDs indicated improved survival among patients assigned to remote management in both an observational cohort (ALTI- TUDE) (11) and the randomized IN-TIME (Influence of Home Monitoring on Mortality and Morbidity in Heart Failure Patients with Impaired Left Ventricular Function) trial (5). Mechanisms remain unclear, but facilitation of ventricular arrhythmia/shock management has been proposed as one explanation.

To better understand the influence of RM on outcomes, we hypothesized that survival would be better in patients with greater RM use and should apply to all types of CIEDs: patients with pacemakers (PMs) who have less cardiovascular risk as well as those with implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) with pacing/defibrillation capability (CRT-P/ CRT-D). We tested this in a cohort of CIED patients, all receiving automatic RM devices, by leveraging “big data” from a nationwide RM system-generated proprietary database, which collects comprehensive longitudinal follow-up data in hundreds of thousands of patients.

Methods

Study Design and Patient Selection. This retrospective, national, observational cohort study evaluated 371,217 consecutive patients receiving new implants of market-released PMs, ICDs, CRT-Ps, and CRT-Ds (St. Jude Medical, Inc., Sylmar, California). To assess the impact of RM use on outcome, patients whose implanted device did not support automatic daily monitoring were excluded (deemed not automatic RM capable) (Figure 1). The remaining patients with ICD/CRT-D devices implanted between October 2008 and December 2011 and PM/CRT-P devices implanted between October 2009 and December 2011 comprised the study cohort (automatic RM capable). Patients enrolled in another clinical trial or with follow-up time <90 days also were excluded. Included patients were followed until death or device replacement/removal through November 2013.

Study data were obtained from 4 sources: device implant registration, device RM, postal (ZIP) code sociodemographic data, and the U.S. Social Security Death Master File. Age, sex, device type, and follow-up duration were ascertained using manufacturer device tracking data. Remote monitoring status was determined from the Merlin patient care network (St. Jude Medical) and date of death from the U.S. Social Security Death Master File, with all death records through November 30, 2013. We added death reports through this date made directly to the device manufacturer’s U.S. tracking system by health care providers or family members (this accounted for <1% of deaths). Socioeconomic data were gathered from the 2012 U.S. Census Bureau American Community Survey, 2008 to 2012, by individual ZIP code tabulation area, specifically, 4-year college degree, median income, below poverty level, telephone or cell phone service, employment status, health care insurance, and total urban/rural classification of population counts (12). The urban percentage for a region was computed as the ratio of urban to total population counts. We obtained data without patient identifiers from implant registration records of devices manufactured by St. Jude Medical, Inc. Data included date of implantation, age at implantation, sex, patient ZIP code, site ZIP code, and device model numbers. For patients enrolled in the Merlin patient care network remote monitoring, we obtained data without patient identifiers consisting of maintenance transmission dates linked to implant registration data.

Among RM-capable patients, RM service use was computed using weekly status data sent from each user of Merlin to the central server. A multiple-retry algorithm ensured the status data were communicated when an attempt to send data to the server failed. Those patients having had at least 1 transmission ever were classed as RM Any. RM adherence per patient was defined as the proportion of total follow-up weeks having at least 1 status transmission or percentage of time in RM (%TRM). To determine whether %TRM affected outcome, RM-capable patients were assigned to 1 of 3 groups based on extent of their RM use. Those with 0%TRM were designated as RM None. RM Any patients were further divided into high %TRM or low %TRM groups by a cut point of 75% use (this value approximated median %TRM) Thus, low %TRM patients were those sending weekly maintenance records to the server <75% (but >0%) of their follow-up time in this study, whereas high %TRM patients were those who sent weekly maintenances record to the server ≥75% of their follow-up time.

Statistical Analysis. The primary endpoint of this study was all-cause mortality, which was determined using unadjusted mortality incidence rates (MIRs) and adjusted survival via Cox proportional hazards survival models. The MIR ratio (MIRR), RM
Any/RM None, and 95% confidence intervals (CIs) were determined from the patient deaths, and the follow-up duration determined for patients in each group. All-cause survival was compared for each device type among patients with high %TRM, low %TRM, and RM None using multivariable Cox proportional hazards modeling with stratification based on age and covariates of sex plus the RM predictor census variables. The Cox proportional hazard ratio (HR) and 95% CI were determined. Length of follow-up was calculated for each patient as the time from device implantation until device explantation, replacement, death, or end of study surveillance. To assess socioeconomic influences on %TRM, the 8 census variables were evaluated between high %TRM and low %TRM using logistic regression and stepwise backward elimination for \( p < 0.2 \). These variables were then used for adjustment in the Cox survival regression.

All statistical analyses were performed with Revolution R Enterprise 7.1.0 (Revolution Analytics, Mountain View, California). Patient demographics were assessed as mean ± SD, median (interquartile range), or n (%). The Student \( t \) test was used to determine the \( p \) value for mean comparison and the chi-square test for the \( p \) value for count.

To assess the geographic distribution of RM use across the United States, a 2-dimensional clustering of RM Any patients was performed based on latitude and longitude from the 3-digit ZIP code. For low-density regions, additional aggregation was performed using a nearest-neighbor method to combine adjacent ZIP codes until a minimum of 100 patients per geographic grouping was obtained. The groups were then merged, and the center of the combined group was determined as the weighted average of the latitude and longitude for the combined group. All resulting geographic groups were divided into tertiles based on the mean %TRM in each group.

### RESULTS

From the initial 371,217 patients, 101,746 whose devices were not RM capable were excluded (Figure 1). The study cohort consisted of 269,471 automatic RM capable patients (age, 71.0 ± 13.5 years; 64.8% male) with a mean follow-up of 2.9 ± 1.0 years (Table 1). Missing ZIP code data accounted for <0.1% (1,694) of patients for whom missing values were imputed from the median value for the state of residence.

Overall, 141,765 (53%) patients with automatic RM-capable devices never used RM (RM None). Among those patients using RM (RM Any; \( n = 127,706 \)), distribution of use was skewed (Central Illustration, top), but 90,087 patients (70.6%) used RM \( \geq 50\% \) of the time. Dichotomization by a 75% use value (close to the median) divided RM Any into relatively balanced patient populations of high %TRM (\( n = 67,920 \) [53.1%]) and low %TRM (\( n = 59,786 \) [46.9%]). Thus, high %TRM comprised 25.2% (67,920 of 269,471) of all automatic RM capable patients. The median (interquartile range) time to initiation of RM from device implantation was 12 (4 to 33) weeks for RM Any, 33 (11 to 74) weeks for low %TRM, and 6 (3 to 15) weeks for high %TRM.

### MORTALITY AND SURVIVAL RESULTS

Overall, survival was greater in those patients with some %TRM
TABLE 1  Patient Demographic Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All (N = 269,471)</th>
<th>RM None* (n = 141,765)</th>
<th>RM Any* (n = 127,706)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, yrs</td>
<td>2.9 ± 1.0</td>
<td>2.8 ± 1.1</td>
<td>3.0 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>71.0 ± 13.5</td>
<td>70.8 ± 14.0</td>
<td>71.1 ± 12.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>174,553 (64.8)</td>
<td>92,103 (65.0)</td>
<td>82,450 (64.6)</td>
<td>0.028</td>
</tr>
<tr>
<td>Device type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD</td>
<td>85,014 (31.6)</td>
<td>45,232 (31.9)</td>
<td>39,782 (31.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PM</td>
<td>115,076 (42.7)</td>
<td>60,494 (42.7)</td>
<td>54,582 (42.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRT†</td>
<td>69,381 (25.8)</td>
<td>36,039 (25.4)</td>
<td>33,342 (26.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Remote monitoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RM use, %</td>
<td>NA</td>
<td>NA</td>
<td>78.1 (41.6-92.9)</td>
<td></td>
</tr>
<tr>
<td>First RM transmission, weeks</td>
<td>NA</td>
<td>NA</td>
<td>12 (4-33)</td>
<td></td>
</tr>
<tr>
<td>Last RM transmission, weeks</td>
<td>NA</td>
<td>NA</td>
<td>1 (1-10)</td>
<td></td>
</tr>
<tr>
<td>ZIP code-linked data†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bachelor's degree</td>
<td>26.2 ± 15.1</td>
<td>26.1 ± 15.1</td>
<td>26.3 ± 15.1</td>
<td>0.023</td>
</tr>
<tr>
<td>Median income</td>
<td>54.6 ± 21.8</td>
<td>54.2 ± 21.1</td>
<td>54.9 ± 21.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Below poverty line</td>
<td>14.1 ± 8.4</td>
<td>14.6 ± 8.8</td>
<td>13.4 ± 7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Have telephone</td>
<td>97.5 ± 2.3</td>
<td>97.4 ± 2.5</td>
<td>97.6 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Receive SNAP</td>
<td>1.1 ± 1.1</td>
<td>1.2 ± 1.1</td>
<td>1.1 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Uninsured</td>
<td>14.6 ± 7.5</td>
<td>15.2 ± 7.9</td>
<td>13.9 ± 6.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residence: urban</td>
<td>76.3 ± 33.4</td>
<td>79.4 ± 21.5</td>
<td>72.4 ± 35.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Not in labor force</td>
<td>37.4 ± 8.9</td>
<td>37.5 ± 8.9</td>
<td>37.4 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unemployed</td>
<td>9.7 ± 4.4</td>
<td>10.1 ± 4.5</td>
<td>9.3 ± 4.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, n (%), or median (interquartile range). *For some parameters, comparison between RM Any and RM None yields differences that are very small in magnitude but statistically significant. This is due to the large number of patients in each group, for whom even a small difference between largely similar populations becomes significant statistically. †CRT included CRT-D (n = 61,471; 23% total) and CRT-P (n = 79,906; 3% total) devices. **All parameters in this section were measured as % in ZIP code except median income, which was thousands of dollars in ZIP code.

CRT = cardiac resynchronization therapy; CRT-D = cardiac resynchronization therapy with defibrillation capability; CRT-P = cardiac resynchronization therapy with pacing capability; ICD = implantable cardioverter-defibrillator; NA = not available; PM = pacemaker; RM = remote monitoring; RM Any = remote monitoring used at least once; RM None = no remote monitoring use; SNAP = Supplemental Nutrition Assistance Program.

compared with those who failed to use RM at all (Table 2). This relationship existed in all CIED categories, including PMs. The MIRR for RM Any versus RM None was ≤0.55 across all CIED devices, demonstrating that patients using RM have substantially decreased mortality. The Central Illustration shows that for all devices, patients with high %TRM had a lower MIR (MIRR: 3,083 of 6,330 deaths per 100,000 patient-years; MIRR: 0.49) and greater survival than RM None (adjusted HR: 2.10; 95% CI: 2.04 to 2.16; p < 0.001). Significantly, patients with low %TRM also had lower mortality (MIRR: 3,865 of 6,330; MIRR: 0.61) and greater survival than patients with RM None (adjusted HR: 1.58; 95% CI: 1.54 to 1.62; p < 0.001). Patients with high %TRM had lower mortality than those with low %TRM (adjusted HR: 1.32; 95% CI: 1.27 to 1.36; p < 0.001). (These differences remained unchanged whether 75% use or median [78.1%] was used as a cut point to split RM Any into high %TRM and low %TRM groups.) These observations indicate a gradient between the relationship of RM use and outcome.

These relationships were explored further according to individual device types. Results are depicted in

Figure 2 with HR and p value. Overall, outcomes were superior in high %TRM and low %TRM compared with RM None for all device types including PMs. Outcomes were also better in high %TRM compared to low %TRM, except for CRT-P, likely due to the much smaller number of patients studied. Because the trend was directionally consistent with CRT-D (and other groups) (Table 2), we anticipate that a larger study population and/or longer follow-up may reveal a significant difference between these 2 categories for CRT-P.

SOCIOECONOMIC ANALYSIS. All 8 socioeconomic variables linked by ZIP code to the patients in this study were found to be statistically significant in predicting degree of RM use (high %TRM or low %TRM), but the magnitude of the associations was insubstantial. A landline phone or cell phone in the home and completion of at least 4 years of college were positive predictors of RM use. Living below the poverty line, lacking health insurance, unemployed, not in the work force, lower median income, and living in an urban neighborhood predicted less RM use (all p < 0.001). Neither age nor sex affected RM use substantially (RM None vs. RM Any: 70.8 vs. 71.1 years; 65.0% female vs. 64.6% male). (Note that the economic status and education of the specific patients were not known: this was simply an analysis of ZIP code-associated data).

The geographic distribution of %TRM is shown in tertiles of use (Figure 3). The apparent scarcity of patients in the High Plains and Intermountain West is due to aggregation of data to maintain patient privacy. There are fewer patients in that region, but they are more dispersed than suggested by this projection. There is widespread geographic and socioeconomic variability in the degree of RM use nationally, with a small but statistically significant bias toward rural residence for high %TRM patients.

DISCUSSION

In this nationwide comparative effectiveness study of RM use in more than 269,000 patients with implanted CIEDs, there are 3 main findings. First, RM use was associated with improved survival. Second, the degree of adherence to remote management correlated strikingly with the magnitude of survival gain, suggesting a gradient of effect. Thus, patients with high %TRM (≥75%) exhibited the best survival, but those with low %TRM still had markedly better survival compared with patients not using RM at all. For all devices, the MIR (per 100,000 patient-years) was 3,083 for high %TRM, 3,865 for low %TRM, and 6,330 for RM None (p < 0.001). Finally, the association
Remote monitoring (RM) technology embedded in cardiac rhythm devices enables continuous monitoring, but the degree of automaticity (i.e., requirement for active patient participation in using this service) varies. In this study, RM was not used in 53% of patients (RM None) (top). Among those patients using RM at least once (RM Any), median RM use was 78.1% (range, 41.6 to 92.9). In this group, the number of patients according to adherence level (%) was >0% to <25%, 20,796; ≥25% to <50%, 16,823; ≥50% to <75%, 22,167; and ≥75% to ≤100%, 67,920. RM use was divided by a 75% cut point into high %TRM (≥75% use) and low %TRM (<75% use). Greater RM use demonstrably improved patient survival for all devices (bottom). In summary, patients who never used RM (RM None) and low %TRM accounted for 74.7% of all patients; hence, only one-fourth of the U.S. population receiving an automatic RM-capable device maximize its usefulness.
between RM and use persisted across the spectrum of patients receiving CIEDs, including CRT-D, ICD, and, importantly, PMs. These associations were not altered substantively by age, sex, or socioeconomic variations. Remarkably, only one-fourth of all patients receiving automatic RM-capable CIEDs in this nationwide analysis were in the high %TRM category, indicating that the vast majority of recipients do not use the full capabilities of their implantable devices.

The ALTITUDE observational study in patients with ICDs and CRT-Ds reported improved survival in patients assigned to remote management compared with those without (11). Our results are important for not only confirming this association in a larger patient cohort and with a separate proprietary remote technology, but also for extending this to analysis of PMs and to testing the effect of differing levels of RM use. Furthermore, an ALTITUDE substudy analysis recognized that physician and hospital factors determined a lack of patient enrollment in RM. In these patients, other practice constraints and lower adherence to other recommended treatments possibly may have altered substantively by age, sex, or socioeconomic variations. Remarkably, only one-fourth of all patients receiving automatic RM-capable CIEDs in this nationwide analysis were in the high %TRM category, indicating that the vast majority of recipients do not use the full capabilities of their implantable devices.

The current results illustrate the critical impact of adherence. To benefit from RM, patients (and providers) must use it. Earlier activation and then maintenance of consistent transmissions were associated with the best outcomes. The demonstration of a graded effect of RM use on outcome extends the value of an observational analysis beyond that of previous work that simply compared effects of RM on or off (12,13). In support of a direct RM effect, our results for high %TRM parallel the degree of survival benefit noted among heart failure patients treated with ICDs and CRT randomized to RM with a different proprietary technology (Home Monitoring, Biotronik, Berlin, Germany) when a consistently high (85%) level of connection was ensured (5). Nevertheless, here we demonstrated that patients maintaining some level of connectivity, although gaining less benefit, still derived some survival advantage compared with those not using RM at all. This relationship is analogous to the achievement of therapeutic anticoagulation in patients with atrial fibrillation: %TRM may be as important for device patients as the time in therapeutic range is for patients with atrial fibrillation taking warfarin.

### Table 2: Mortality, MIR, and MIRR

<table>
<thead>
<tr>
<th>Device</th>
<th>n</th>
<th>Deaths</th>
<th>RM Any (%)</th>
<th>MIR (per 100,000 pt-yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>RM None (95% CI)</td>
<td>RM Any (95% CI)</td>
</tr>
<tr>
<td>All</td>
<td>269,471</td>
<td>38,130 (4.9)</td>
<td>47.4</td>
<td>6,329.9 (6,252.0–6,408.8)</td>
</tr>
<tr>
<td>PM</td>
<td>115,076</td>
<td>13,256 (4.2)</td>
<td>49.5</td>
<td>5,364.5 (5,252.8–5,478.6)</td>
</tr>
<tr>
<td>CRT-P</td>
<td>7,906</td>
<td>1,345 (6.6)</td>
<td>45.9</td>
<td>8,612.0 (8,070.1–9,190.9)</td>
</tr>
<tr>
<td>ICD</td>
<td>85,014</td>
<td>11,652 (4.5)</td>
<td>46.8</td>
<td>5,816.9 (5,689.5–5,947.1)</td>
</tr>
<tr>
<td>CRT-D</td>
<td>61,475</td>
<td>11,877 (6.6)</td>
<td>48.3</td>
<td>8,592.8 (8,402.3–8,787.7)</td>
</tr>
</tbody>
</table>

Values are n (% per pt-yr) unless otherwise indicated.

Cl = confidence interval; MIR = mortality incidence rate; MIRR = mortality incidence rate ratio; pt-yr = patient-year; other abbreviations as in Table 1.
RM in isolation is not a treatment but a mechanism for accessing important data regarding device function or incipient clinical conditions. Alerts that drive urgent in-person evaluation carry a high probability of actionability for reprogramming and/or changes in drug therapy, either of which has the potential to improve outcome (4,10). However, physician responses are unavailable given the nature of the current study. Several interdependent cardiovascular factors (e.g., arrhythmias, shifts in right ventricular/biventricular pacing burden, vagal withdrawal, decreased patient activity) may change several days to weeks before clinical deterioration (16,17), permitting provider intervention based on RM data upstream.

High %TRM patients (orange line) consistently have higher survival curves compared with low %TRM (green line) and RM None patients (blue line) for pacemakers (A), ICDs (B), CRT-P devices (C), and CRT-D devices (D). HR = hazard ratio; other abbreviations as in Figure 1.
of clinical symptoms. Optimized management of clinical conditions and/or device function may underlie the survival advantage among remotely managed patients (5,16,17).

Our observational study cannot confirm a direct cause-and-effect relationship between RM and survival, although alignment of the described mortality effect with that in a smaller numbers of patients managed remotely in randomized trials may point to such an effect (5). Association may be attributed to a “healthy-user effect,” that is, patients who use RM more are less sick and more compliant in general and/or have physicians who are more up to date with recommended treatment. An ALTITUDE subanalysis indicated that both implantation of an RM-capable device and patient activation were diminished in patients with disadvantaged socioeconomic status and/or greater comorbidities (13). However, accounting for 17 such factors generated a modest area under the curve of only 0.62, meaning this “risk-treatment paradox” was an incomplete explanation of the RM effect.

In this regard, our observations in low-voltage CIED categories are salient: a similar increment in survival gained by high adherence in both PM and CRT-D patients supports an effect of RM use that is independent of the gravity of underlying cardiac disease and associated comorbidities. The similar gain among different CIED categories also indicates that the RM effect is independent of the degree of programming versatility or therapeutic potential of the CIED itself (greatest in CRT-D, least in PMs). Notably, the TRUST (Lumos-T Safely RedUceS Routine Office Device Follow-up) trial demonstrated that use of RM itself facilitated patient compliance because randomization to RM promoted patient engagement with follow-up services (18). A similar effect was observed in follow-up clinics: randomization to RM improved patient retention to long-term follow-up (18,19). Collectively, these actions (to “induce” a positive behavioral change) may improve initiation and maintenance of recommended treatments (e.g., medications), extending effects beyond device management. These actions may account for
the graded relationship between RM use and survival noted here. Clearly, the benefit of RM is multifactorial. This may explain why no single intervention leading to a clear-cut mortality benefit was isolated in the IN-TIME trial. In this regard, our nationwide “big data” analysis is more likely to discover and confirm the total result of interconnected factors than a randomized trial with a narrow field of view (20,21).

STUDY LIMITATIONS. Our results apply to implantable units enabled with automatic remote transmission technology and cannot be extended to other remote management systems. In particular, non-implantable RM systems (characterized by modest adherence) have failed to improve patient outcomes (22). Causes of discontinuation or lost transmission in the current study cannot be ascertained. Although socioeconomic factors significantly affected connectivity, the magnitude of this association was slight and insufficient to affect outcomes. Inclusion of earlier versions of RM technology demanding greater patient participation are more vulnerable to transmission loss (23). Change of residence may account for some attrition (19). Our study period commenced after publication of recommendations for CIED follow-up describing the role of RM as an adjunctive mechanism to in-person evaluation, without advocating for continuous monitoring functions (2). This may have contributed to variable connectivity among our patients. Clinical profiles beyond age and sex were unavailable. Demographic characteristics, medications, etiology of heart failure and left ventricular function, comorbidities, heart failure hospitalizations, and, importantly, individual responses to remotely acquired data may all affect mortality. This study was not a randomized clinical trial and therefore cannot comment on efficacy. However, although lacking access to detailed clinical data, this analysis reports outcomes from consecutive patients in a nationwide clinical practice, and, as such, the data are generalizable as opposed to the highly controlled, selected, and relatively small populations studied in clinical trials (20,21).

CONCLUSIONS

RM of patients with cardiovascular disease receiving all types of CIEDs (including PMs) is associated with improved all-cause survival, but maximal gain depends on earlier implementation and consistent adherence. Although our observational study cannot determine a cause-and-effect relationship, the restriction of our analysis to only patients receiving wireless RM, the correlation with survival to the degree of use, and similar gains irrespective of device type among patients with differing gravity of underlying disease provide strong indirect evidence of an independent influence of RM on patient outcome. Our findings endorse recommendations advocating the importance of post-implantation CIED follow-up, but also support extension of function from a periodic remote interrogation mechanism to a daily monitoring system enabling improved outcome (2,7).

This result has a potential impact on millions of individuals with implanted devices worldwide.

ACKNOWLEDGMENT Data were provided by St. Jude Medical.

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KEY WORDS big data, cardiac electronic implantable devices, cardiac resynchronization therapy, device, mortality, survival, time in remote monitoring.