Consensus Statement

Remote Monitoring of Patients With Heart Failure: A White Paper From the Heart Failure Society of America Scientific Statements Committee

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ABSTRACT

Background: After several neutral telehealth trials, the positive findings and subsequent Food and Drug Administration approval of an implantable pulmonary arterial pressure monitor (PAPM) led to renewed interest in remote patient monitoring (RPM). Here we seek to provide contemporary guidance on the appropriate use of RPM technology.

Results: Although early trials of external RPM devices suggested benefit, subsequent multicenter trials failed to demonstrate improved outcomes. Monitoring features of cardiac implantable electronic devices (CIEDs) also did not deliver improved HF outcomes, newer, multisensor algorithms may be better. Earlier technologies using direct pressure measurement via implanted devices failed to show benefit owing to complications or failure. Recently, 1 PAPM showed benefit in a randomized controlled trial. Although not showing cost reduction, cost-benefit analysis of that device suggests that it may meet acceptable standards. Additional research is warranted and is in progress. Consumer-owned electronic devices are becoming more pervasive and hold hope for future benefit in HF management. Practical aspects around RPM technology include targeting of risk populations, having mechanisms to ensure patient adherence to monitoring, and health care team structures that act on the data.

Conclusions: Based on available evidence, routine use of external RPM devices is not recommended. Implanted devices that monitor pulmonary arterial pressure and/or other parameters may be beneficial in selected patients or when used in structured programs, but the value of these devices in routine care requires further study. Future research is also warranted to better understand the cost-effectiveness of these devices. (*J Cardiac Fail 2018;24:682–694*)

Key Words: Telehealth, CardioMEMS, heart failure, remote patient monitoring.

Remote patient monitoring (RPM) seeks to use electronic means to optimally manage health conditions outside of health care facilities. RPM first gained popularity in the heart failure (HF) community after several studies, including the 1995 study by Rich et al, demonstrated reductions in HF readmissions with telephone and clinic follow-up.[1] However, subsequent large randomized trials have brought into question the efficacy of various forms of RPM. At the same time, the Food and Drug Administration (FDA) approval of an implantable device that provides direct real-time measurements of pulmonary arterial pressure (CardioMEMS HF system, St Jude Medical [now Abbott], Atlanta, Georgia) has renewed interest and raised additional questions, such as: What is the place for RPM in the management of patients with HF? Why the conflicting results in the trials? What types of RPM are most useful, and what complementary systems of care are required for RPM to be effective in the real world? Are the data around implantable hemodynamic monitoring (IHM) strong enough to justify its widespread use? Is the new

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technology cost-effective? Will emerging personal health technologies (eg, Fitbit, iHealth, etc.) have a role in the care of populations of patients with HF?

The present white paper seeks to provide as meaningful guidance as possible for answering these and other questions that may arise regarding the use of RPM. The goal is to provide clarity to the community managing HF, especially regarding patient selection, optimal setting and appropriate use of RPM technology. This paper also intends to present a blueprint for future goals of RPM technology.

Past and Present Technologies

RPM via External Electronic Devices

In 1995, Rich et al published on the benefit of telephonic monitoring in the treatment of patients with HF and created great enthusiasm for the idea of RPM.[1] Since that time, many studies have been conducted, looking at the benefits of using either scheduled/automatic telephonic interventions or electronic monitoring systems to improve outcomes of patients with HF. Several trials showed value of RPM in reducing clinical events such as mortality and hospitalization rates.[2−6] But several subsequent randomized trials however have been unable to replicate those earlier findings.[7−9] Nevertheless, industry and payers continue to show interest. In 2011, the Veterans Administration invested $1.38 billion in RPM, estimating a 25%−30% reduction in hospitalizations among patients with HF and hypertension.[10] In 2013, Medtronic invested in RPM with the purchase of Cardiocomm Solutions and, more recently, with the rollout of multiple RPM platforms, such as the Beacon HF Management Service.[11] How can we resolve this conflict between ongoing commercial enthusiasm for RPM and research that does not show benefit?

The literature is filled with references to RPM via external electronic devices that were the subject of a Cochrane review.[12] That data synthesis concluded that noninvasive home monitoring reduced all-cause mortality and the rate of HF hospitalizations but did not reduce all-cause hospitalization. However, those positive findings run contrary to more recent contemporary large randomized trials (not part of the Cochrane review) that did not show benefit. A closer look into those neutral trials, as presented in Table 1, suggests that the targeted population (ill enough to gain benefit from monitoring), how the technology is implemented, and how nonadherence is handled may influence whether there is benefit to using RPM via external devices.

The United Kingdom's Whole System Demonstrator (WSD) program represented a wide scale implementation of RPM. It was a large program (n = 3154) carried out in routine clinical practices, but it was not purely an HF trial (it included diabetes and chronic obstructive pulmonary disease as well).[13] WSD demonstrated a significant reduction in emergency hospital admissions and mortality.[14] However, the decline in hospital admissions was confined mostly to the first 3 months of the study when there was an increase in admissions in the control group, raising questions about the clinical relevance of these changes. Furthermore, the WSD program was not judged to be cost-effective, with an average cost of £92,000 per quality-adjusted life-year (QALY).[15] Researchers noted that having "clinical champions" led to increased engagement of the clinical staff and better use of the RPM data.[13]

Which patients should be targeted? Patients who are clinically stable are less likely to appreciate benefit. The WSD investigators speculate that the program's effect could have been stronger if patients were better targeted. They acknowledge however that there are no clear guidelines to identify the most appropriate individuals. Patients with higher New York Heart Association (NYHA) functional class (FC) or a recent hospitalization seem more likely to benefit.[16,17] Common sense would suggest that patients with a history of poor attention to their health might benefit, and clearly, adherence to monitoring is essential.

A recognized limitation of the trials is that many patients chose not to participate (as high as 80% in some). The reasons behind this are varied, but many center on a fear of giving up "in-person" or so-called "warm" care to electronic or "cold" care.[18,19] Staff enthusiasm in recommending and implementing the therapy can be an important factor in overcoming these barriers as well as enhancing adherence.[13]

How the RPM is implemented may also be important. A meta-analysis suggests that the 2 strongest determinants of benefit are the frequency of monitoring (daily monitoring versus less than daily) and whether monitoring is linked to medication adjustments.[20] A common barrier in the large neutral trials was poor adherence. Implementation should therefore focus on daily monitoring, with mechanisms to monitor and improve adherence and with specific measures to ensure that findings from the monitoring drive medication adjustments.

Finally, another novel solution involves the use of a remote dielectric sensing (ReDS) system that can estimate lung water content.[21] That system was shown to correlate closely with thoracic fluid content as estimated with the use of thoracic computerized tomographic scans.[22] In a pilot nonrandomized study, there was benefit. This led to the prospective randomized Sensible Medical Innovations Lung fLuid Status Monitor Allows rEducing Readmission Rate of Heart Failure Patients (SMILE^{TM}) study, but that study was terminated by the sponsor reportedly for financial reasons.[23] In the absence of randomized prospective data, no definite conclusions about the effectiveness or cost-effectiveness of the ReDS system can be made.

Conclusions

1. Multiple small-scale and single-center trials demonstrated the benefit of RPM via external devices on the outcomes of mortality and hospitalization.
2. However, 5 large prospective randomized trials failed to show benefit.

Table 1. Exploration of Neutral Trials of External-Device Remote Patient Monitoring (RPM)

Study	Size	What the Study Involved	Potential Explanation for Lack of Benefit
TIM-HF[8]	n = 710 (355 on RPM)	Randomized trial of a Bluetooth-enabled device designed to follow 3-lead electrocardiography, blood pressure, and weight	Participants had stable HF, so it may be that remote monitoring is not as effective in lower-risk patients.
Tele-HF[7]	n = 1653 (826 on RPM)	Telephone-based interactive voice response system with a higher-risk population than in the TIM-HF study.	Patient adherence was poor, with <55% of the study subjects using the device 3 days per week by the end of the study. Interestingly, a smaller previous trial had shown benefit; this difference in results implies that how a technology is implemented might determine benefit.
BEAT-HF[9]	n = 1437 (715 on RPM)	Health-coaching telephone calls with monitoring of weight, blood pressure, heart rate, and symptoms in a high-risk population with a 50% rehospitalization rate	Nonadherence was the primary limitation, with only 61% of patients more than half-adherent in the first 30 days.
Mayo Clinic study[24]	n = 205 (102 on RPM)	Telemonitoring in a primary care (PC) panel (various health conditions and not only HF) in the top 10% of Elder Risk Assessment Index managed with biometrics (BP, HR, weight, pulse oximetry, etc) plus daily symptom assessment. Video conference capability was present.	Abnormal telehealth data were directed to PC providers. It is unclear what action this drove. It might have caused the PC provider to direct the patient to an emergency department or a hospital. Could increased symptom surveillance actually increase health care utilization?
TEHAF[25]	n = 382 (197 on RPM)	Electronic device to assess symptoms and educate patients on HF. Abnormal symptoms directed to a monitoring nurse. Device tailored itself to patient's knowledge.	Excellent adherence with use of the device. Planned and unplanned face-to-face HF nurse visits were higher in the control group. Event rates for both groups were lower than expected. Primary limitation appeared to be the excellent outcomes in the control group.

3. The WSD program showed improved clinical outcomes but failed to meet cost-benefit expectations.
4. RPM, when applied broadly to patient populations, is unlikely to be beneficial (or at least not in a cost-effective manner.)
5. RPM via external devices is therefore a tool rather than a treatment.
6. If RPM is going to be used, it should be (1) carefully targeted to at-risk patients, (2) implemented/monitored in a way that ensures high utilization and adherence to care or prespecifies time-limited usage, and (3) used to direct and improve patient care (tangible clear actions able to be taken.)
7. The ReDS system is commercially available but does not have results from testing in a randomized controlled trial.

Data Contained Within Cardiac Implantable Electronic Devices

Thoracic Impedance Data

In addition to the development and study of external devices, there has been an increased interest in cardiac implantable electronic devices (CIEDs) that contain remote monitoring data.[26–29] Among the earliest and most thoroughly evaluated examples involves the monitoring of thoracic impedance with the use of implantable cardioverter-defibrillators (ICDs). Impedance is the measure of resistance to flow of an electrical current between 2 points. When measured across the chest by means of either a band electrode or an implanted device, impedance has been shown to reflect thoracic fluid content.[30] An analytical algorithm can be applied to serial thoracic impedance measurements over a set time period to derive the clinically meaningful "fluid index" (FI) impedance threshold risk for a population or individual patient.[27]

In the clinical studies to date, a variety of diagnostic algorithms and definitions of FI risk thresholds have been used. Many, such as the 2007 study by Maines et al[31] and the 2011 study by Abraham et al,[26] used the Optivol system in implanted Medtronic devices. These studies revealed that thoracic impedance measures did not affect the prediction of HF-related events and appear to have resulted in more HF hospitalizations (hazard ratio [HR] 1.79; $P = .022$).[28,32] Several large trials were neutral,[32,33] including one that highlighted the logistical problems of acting on FI threshold crossings.[33] The SENSE-HF trial showed the challenges of the technology, with low sensitivity and positive predictive value, especially early after implantation, which also happened to be the highest risk period for HF events.[34,35] Although there are multiple reasons for the limited predictive abilities of these implanted RPM systems, the most important include (1) the lack of standardized FI threshold definitions, (2) the frequent occurrence of unexplained FI threshold−crossing alarms, resulting in unnecessary response and action, and (3) the logistical difficulties of ensuring timely and effective interventions based on FI threshold alerts and alarms.[28,33] Ultimately, owing to the lack of significant results and the existence of alternatives, RPM trials in HF have either (1) incorporated thoracic impedance into the creation of multisensory predictive device algorithms[36] or (2) abandoned thoracic impedance altogether.

Heart Rate Variability

Another potential predictor of prognosis in HF is heart rate variability (HRV), which is a complex integrated response to multiple adaptive/maladaptive signals, such as neural, environmental, and emotive inputs.[37,38] HRV, when assessed by means of a number of linear and nonlinear methods, has been shown to have prognostic value in chronic HF.[39–41] For example, in the UK-Heart study published in 1998, investigators demonstrated that SDNN (the

standard deviation of R-R intervals by Holter monitoring) was the most powerful predictor of death due to progressive HF.[42] Likewise, in the DIAMOND HF study, $DFA_{\alpha 1}$ (an assessment of fractal characteristics of the R-R interval oscillations)[39] <0.9 was an independent predictor of mortality.[43] Limitations of this approach included the presence of atrial fibrillation, frequent atrial/ventricular premature beats, chronic pacing, and high-dose beta-blocker therapy.[41] Moreover, the available studies are small, and data comparing the benefit of this approach with others is limited. Expert opinion, based on available data, is that the incremental prognostic values of HRV determinations are modest at best.[39,40] To date, no prospective clinical trials using HRV to improve clinical outcomes in HF have been published.

Combination Algorithms

Given the limitations of individual parameters, many investigators have now turned toward developing combination diagnostic algorithms, which can use a more diverse array of implanted sensors contained within devices.[44] For example, in the MultiSENSE study, a combination index/alert algorithm called Heartlogic was used to detect HF events (HFEs). It incorporated heart sounds, respiration, thoracic impedance, heart rate, and activity collected by an implanted cardiac resynchronization therapy−defibrillator (CRT-D) device. The algorithm was used in 900 patients with NYHA FC II−IV HF and had 2 primary end points: to maintain a sensitivity of ≥40% to HFEs and to keep unexplained alerts to ≤2.0 per patient per year (as evaluated at the 1-year follow-up).[44] Both primary end points were met. In fact, 89% of subjects had HFE alerts ≥2 weeks before the corresponding event. The overall sensitivity of the algorithm was 70%, with a median alert window of 34 days before the HFE and an unexplained alert rate of 1.47 per patient-year. This algorithm was predictive independently from natriuretic peptide data. Whether this information can lead to improved management strategies has yet to be determined.

Several other device multisensor diagnostic algorithms, however, have not revealed similar performance. For example, in the CLEPSYDRA (Clinical Evaluation of the Physiologic Diagnosis Function in the Paradym CRT device) study, a diagnostic algorithm based on minute ventilation and activity reported a sensitivity of only 34% and a false positive rate of 2.4 alerts per patient-year.[45] Nevertheless, combination algorithms appear to be a potentially beneficial RPM method for the detection of HFEs, as exemplified by the MultiSENSE study as well as other investigations, such as the PARTNERS-HF study.[46]

Conclusions

1. Investigations into the use of RPM to detect clinically relevant shifts in thoracic impedance have had mixed results, owing to the lack of standardized definitions regarding FI thresholds and uncertainty about timing and appropriateness of acting on the information.
2. Sophisticated analyses of HRV have been shown to provide prognostic information in patients with chronic HF, but the use of HRV as a marker to guide treatment is unproven.
3. Some studies suggest that combination algorithms may be a better approach to RPM via CIEDs, but the impact of these devices on clinical outcomes requires further investigation.

Implantable Pressure-Sensing Devices

Monitoring Right Ventricular Pressures

Beyond external devices and the data gleaned from CRT/ICDs, investigators have argued that direct invasive monitoring of intracardiac and pulmonary arterial pressures may predict HF decompensation at an earlier, asymptomatic phase.[26−29] Ambulatory data has shown that symptomatic HF decompensation is preceded by asymptomatic elevations in intracardiac and pulmonary artery pressures for days or even weeks.[26,47−49] The Medtronic Chronicle implantable continuous hemodynamic monitoring system (ICHM) was the first such direct invasive monitoring system.[48] The Chronicle ICHM used a specialized right ventricular lead and sensor to monitor heart rate, body temperature, activity, right ventricular systolic/diastolic pressure, right ventricular preejection and systolic time intervals, and estimated pulmonary arterial diastolic pressure (ePAD).[48]

In the COMPASS-HF (Chronicle Offers Management to Patients With Advanced Signs and Symptoms of Heart Failure) trial, 274 patients with NYHA FC III−IV HF were randomly divided into 2 groups. One group combined optimal medical therapy with data from the Chronicle ICHM, and the other continued with optimal medical therapy alone.[48] The 3 study end points were (1) freedom from system-related complications, (2) freedom from pressure-sensor failure, and (3) efficacy defined as a reduction in the rate of HF-related events, such as emergency visits requiring intravenous HF therapy and hospitalizations. The first 2 end points were met in so far as there were no pressure sensor failures and only 8% of patients experienced system-related complications. The efficacy end point, however, was not met; the Chronicle group had a nonsignificant 21% lower rate of HF-related events compared with the control group. Therefore, study investigators concluded that the Chronicle system did not significantly reduce total HF-related events compared with optimal medical management. However, the low observed versus expected event rate in the control group may have been attributable to the frequent and intensive contact between subjects and HF clinics for the duration of the study.[50] A post hoc analysis using the time to first HF-related event after randomization revealed a 36% reduction in the relative risk of a HF-related hospitalization in the Chronicle group. Another concern raised about COMPASS-HF was the lack of consistency in the investigators' responses to changes in ePAD in asymptomatic patients.

Although 2 retrospective studies of the COMPASS-HF trial demonstrated similarly nonsignificant improvements in

clinical outcomes,[49,51] they also revealed an important connection between decompensated HF and increases in ePAD. So too did the REDUCEhf trial,[52] which used the same sensor as the Chronicle device integrated into an implantable defibrillator. The trial randomized 1300 patients with NYHA FC II−III symptoms to medical and disease management with or without the hemodynamic information provided by an ICHM. Trial enrollment was halted prematurely owing to the revelation of lead failures in earlier studies using this lead. As a result, although the end point of 90.5% freedom from system-related complications was met, premature termination of enrollment did not permit adequate assessment of the clinical efficacy end point, which required a greater number of subjects. Nevertheless, study investigators revealed that ePAD pressures were slightly lower in the treatment group versus the control group during the 12-month follow-up, and that subjects with an HF-related event had higher ePADs than those without an event, regardless of treatment group. In addition, patients with at least 1 HF-related event had progressive increases in ePAD in the days preceding hospitalization,[47,52] and baseline ePAD and change from baseline ePAD were found to be strong independent predictors of mortality.[53] Thus, although the trials failed to demonstrate significant benefit, they advanced our understanding of HF pathophysiology through what they revealed about ePAD levels.

Conclusions.

1. The trials of pressure monitoring with the use of a lead in the right ventricular outflow tract were unable to show improved patient outcomes based on the prespecified end points.
2. The lack of efficacy may have been related to trial design and termination of further research due to failures of the pressure-sensing lead.
3. Regardless of the efficacy of the RPM systems, the trials revealed important information regarding the pathophysiology of HF in "free-living" patients, which may prove to be useful in the development of future systems.

Monitoring Left Atrial Pressure

The LAPTOP-HF (Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy) trial used a left atrial pressure−monitoring lead which was placed via transeptal puncture.[54] Data from the lead was fed to a Patient Advisor Module (PAM) that would provide patients specific advice on changes in their HF therapy based on their hemodynamic measurements and physician direction. The trial was designed to enroll 730 patients with NYHA FC III HF regardless of ejection fraction but was terminated after 486 patients were enrolled owing to a cluster of implant-related complications. From the available data presented, the treatment group (feedback instructions based on hemodynamic data) appeared to have a lower rate of HF events than the control group (daily medication reminders without hemodynamic measures input): 0.40 vs 0.70 events per patient-year, HR 0.57; $P = 0.003$.[55] In the absence of peer-reviewed data from a completed trial, however, no conclusions can be made about efficacy.

Conclusions.

1. The LAPTOP-HF trial of a left atrial pressure monitor failed owing to an excess of complications from the implantation procedure.
2. Limited data from the trial suggest that the hemodynamic monitoring and associated management algorithm for patient-directed therapy adjustments could have been effective.

Monitoring Pulmonary Arterial Pressures

The CardioMEMS device is a sealed pressure sensor placed into a distal pulmonary artery branch and anchored with the use of nitinol loops. The device has a coil and capacitor that resonate at a specific frequency when pulsed with radiofrequency waves. External pressure on the device causes a characteristic shift in the resonance frequency that can be detected and serve as a reliable indicator of pressure in the pulmonary artery where the device is placed.[56] A balloon-tipped flow-directed catheter is used to guide the device into a pulmonary artery and calibrate the pulmonary artery pressure measurement. An external antenna placed briefly under the patient provides power to the device and then monitors the resonant frequency of the CardioMEMs sensor. Those resonant frequencies then are used to generate pulmonary artery pressure waveforms. Data are transmitted to a secure website for subsequent analysis.[57] Notification alerts for pressure thresholds can be individualized, and triggered alerts can be communicated via multiple platforms, including through text messages to the care provider. Trends over time can be examined for individual patients.

The CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Functional Class III Heart Failure Patients) trial was a prospective multicenter single-blind trial in 550 patients with NYHA FC III HF and an HF hospitalization within 12 months before enrollment. Patients were followed for a minimum of 6 months. All patients were implanted with a CardioMEMS device and then randomized to allow clinician access to transmitted data (in the treatment group) or usual care (control group).[57] The investigators demonstrated a 28% reduction in the primary end point of HF hospitalizations at 6 months and a 37% reduction in HF hospitalizations over the entirety of the trial. Freedom from death and from first HF-related hospitalization was significantly reduced in the treatment group. In addition, both primary safety end points of the trial were met.

The data were presented to the FDA Circulatory Systems Device panel in 2011, but the device was not approved owing to panel concerns regarding sponsor access to pressure data and recommendations for management in some

treatment group subjects.[58] Consequently, an analysis of long-term ongoing follow-up of patients enrolled in CHAMPION was performed, this time without sponsor communications.[59] In the patients who had previously received usual care, open access to pulmonary arterial pressure data for a mean period of 13 months resulted in a 48% reduction in HF hospitalization rate, and the risk of death or first HF hospitalization was reduced by 47%. Targeted changes in diuretics and vasodilators were shown to be in large part responsible for these benefits.[60] Based on these data, the CardioMEMS device received FDA approval in May 2014. A postmarket registry study was required and is still under way.

Additional analyses of the CHAMPION study have reported reduced HF hospitalizations with PA pressure monitoring in patients with HF and preserved ejection fraction[61] and reductions in both morbidity and mortality on top of optimal medical therapy in patients with HF and reduced ejection fraction.[62]

Thus, in a single trial, wireless IHMs measuring pulmonary arterial pressure appeared to be effective in reducing HF hospitalizations in NYHA FC III patients with a history of HF hospitalization. A postapproval observational study of 1114 patients with the use of Medicare claims data suggested "real-world" effectiveness of the CardioMEMS IHM in reducing HF hospitalizations outside the clinical trial setting,[63] although an accompanying editorial delineated the limitations of that observational report.[64]

Controversy remains around the technology, however, based on its approval after a single trial. Adoption has been limited by variable payer coverage, including the lack of a national coverage decision from the Centers for Medicare and Medicaid Services (CMS) in the United States. This has prompted a second large-scale randomized controlled trial. The GUIDE-HF trial (ClinicalTrials.gov identifier NCT03387813) aims to enroll 3600 patients, will study the technology in a broader population (NYHA FC II, III, and IV rather than just III), and has an estimated completion date of April 2023.[65]

Conclusions.

1. Clinical care with the use of the CardioMEMS device resulted in fewer HF hospitalizations than standard care in NYHA FC III patients with recent HF-related events.
2. Additional data to confirm earlier findings, determine best practices, and define cost-effectiveness are needed.

Cost/Benefit

Ultimately, the successful integration of RPM into the care of patients with HF will depend on the cost-effectiveness and value of such technology. Owing to the large and growing economic burden of HF, even small costs on a per-patient basis can have large financial ramifications. Because most direct HF costs are related to inpatient care, RPM technology, with its goal of reducing hospitalizations, offers the possibility of substantial savings. Moreover, because performance measures and payments are increasingly associated with the quality of chronic disease management, health care providers and systems may see cost benefits from enhanced disease-management strategies.[66]

Value derived from the incremental benefits of a treatment strategy is weighed against its risks, burdens, and distractions, all relative to added costs.[67] Critical to cost-effectiveness appraisals are the costs not only of the device, but also of ongoing monitoring and the follow-up of remotely captured data. Most analyses of RPM assume that the increased cost of the technology and associated monitoring are offset by reduced hospitalization and other resource use. However, determining these various inputs can be difficult, especially in the setting of rapidly evolving technologies and taking heterogeneity into account.

Because the CHAMPION trial provides some of the only positive efficacy data for RPM, assessment of RPM value is most straightforward for CardioMEMS[68] and sets the stage for how value may be determined for other RPM technologies. Two detailed cost-effectiveness analyses have been published. The first was by the California Technology Assessment Forum (CTAF).[69] For that, a Markov model was constructed of the natural history of chronic HF using event rates from recent literature. The cost of the CardioMEMS device was estimated from the Medicare price ($17,750) plus additional costs, such as implantation, complications, and routine monitoring. As outlined in Table 2, the CardioMEMS arm showed an increased life expectancy of 0.44 years and 0.30 quality-adjusted life-years (QALYs) per patient at an increased cost of $17,274, resulting in a cost per QALY of $57,933. The second analysis was from a US payer perspective. Over a 5-year horizon assuming consistent benefits over time, patients in the CHAMPION treatment group had an average of 2.56 QALYs, whereas patients in the control group had 2.16 QALYs. Total costs were $212,004 in the treatment group and $200,360 in the control group, leading to an incremental cost-effectiveness ratio (ICER) of $29,593 per QALY. When confined to costs of HF-related events, the ICER at 5 years improved to $12,262. Thus, both analyses concluded that use of CardioMEMS, according to conditions matching the CHAMPION trial, falls below the accepted willingness to pay thresholds of $50,000−150,000 per QALY. It should be noted that these cost-effectiveness projections are derived from the CHAMPION trial, which was single-blind and followed some patients for less than a year and has not yet been

Table 2. California Technology Assessment Forum Assessment Results

Result	CardioMEMS Arm	Routine Care Arm
Hospitalizations per patient	2.19	3.18
Life-years per patient	5.72	5.28
QALYs per Patient	2.74	2.44
Total cost per patient	$174,037	$156,764

QALY, quality-adjusted life-year.

replicated in another controlled trial. This leaves questions about whether benefit is sustained and what the degree of benefit would be outside of the bounds of a structured clinical trial.

Assessment of the value of other RPM technologies is limited, owing to a relative lack of high-quality evidence on effectiveness or a lack of effectiveness in rigorous assessments. Notably, without benefit, questions of risk, burden, and cost become moot. With questionable benefit—as in the case for most RPM technologies—there may be a willingness to try approaches that have relatively low risks, burdens, and costs, but not to try anything too disruptive or costly.[70]

A few other key assumptions may help guide future cost effectiveness evaluations: (1) although replacing in-person visits with RPM is cost-saving in general,[71] because most RPMs represent an add-on to usual care, an RPM may actually increase in-person visits at first; (2) decrements in patient adherence are likely to reduce benefit[72]; and (3) the perspective from which cost-effectiveness is assessed can significantly alter the assessment of value. In particular, it is important to understand patient perspectives as well as the society or payer view. Ultimately, merging health policy and payments to create favorable value perceptions is likely to accelerate the development, testing, and implementation of useful RPM technologies for HF. In fact, one area in which this has proven especially true is in reimbursement for data retrieval.

It is important to note that although CardioMEMS appears to meet acceptable cost-effective thresholds, it is not cost saving. At present, no technology has been able to demonstrate that degree of benefit for the costs involved. In the UK WSD program, it was estimated that with wide-scale implementation of RPM costs might be reduced 80%. Even with this reduction, the technology would just meet criteria for cost-effectiveness but would still not be cost saving.[15]

A further barrier of implementation, as previously stated, is willingness to pay. In the US, CMS coverage for CardioMEMs has been regulated by local coverage decisions rather than a national coverage decision.[73] To date, this has resulted in nonpayment by Medicare in at least 11 states.[74] This has in part prompted further research that is currently in progress.[65]

Conclusions

1. RPM technology may result in cost-effectiveness, particularly if reductions in hospitalization are realized.
2. Future cost-effectiveness evaluations need to consider multiple factors, including patient adherence, when assessing the value of RPM technology.
3. To further the development and implementation of RPM technologies, there needs to be a strong effort to merge health policy with payment strategies.

Practical Application

Beyond the issue of cost, there are many other practical patient-centric and health care provider−specific questions regarding RPM that should be addressed. For example: Should transmissions and data be sent to health care providers or simply entered into an electronic health record? Who should be responsible for reviewing the data and making clinical decisions? How often should data be reviewed? Should support tools or algorithms be used when data are abnormal, or should each case be treated individually?

These considerations ensure that data use is balanced with both health care resources and costs. Toward these goals, Table 3 provides an overview and suggestions for handling questions that may arise while implementing, managing, and evaluating RPM systems and data. It is important that health care team members are knowledgeable about who is responsible for what data, how to interpret values accurately, and how to incorporate data into an assessment and plan of care. It is also important for electrophysiology and HF teams to collaborate to ensure that data are communicated in a timely and direct manner that supports optimal care. Furthermore, because reimbursement is available for medically necessary data retrieval every 30 days, billing services should be coordinated between electrophysiology and HF services. It may be important to develop a nurse-directed program whereby 1 nurse is responsible for reviewing all routine and unscheduled remote interrogations to assess trends in data so that treatment changes can be made in a time-sensitive manner.

Specific recommendations for use of an implantable hemodynamic monitor (IHM) can be taken from the clinical trial design upon which device approval was based.[57]

- Who (which patients): Patients with a hospitalization for HF in the previous 12 months and persistent significant symptoms despite best efforts at optimal management (NYHA FC III).
- Who not:
  - Too late: Is the patient headed to transplant or ventricular assist device?
  - Too late: Is the patient so advanced that goals-of-care discussions are more appropriate?
  - Renal insufficiency (limiting ability to provide benefit): estimated creatinine clearance <25 mL/min.
  - Recurrent pulmonary embolism.
  - Body mass index >35 kg/m^2 and chest >52 inches may not be suitable (pulmonary angiogram will be necessary for further measurement.)
  - Inability to tolerate antiplatelet or anticoagulation therapy.
- Where: Within the context of an HF disease management program capable of frequent monitoring and intervention (weekly or greater telephone contact with patients).
- How:
  - Goal is pulmonary arterial pressure 15−35/8−20, mean 10−25 mm Hg.
    - In this range: window of opportunity to titrate/optimize HF medications.
    - Above this range: increase diuretics or vasodilators.
    - Below this range: reduce diuretics (or vasodilators if systemic hypotension)

Table 3. Practical Use of Remote Patient Monitoring Data

Area of Concern	External Electronic Devices	ICD-Based Data	IHM
Developing the systems and structures	• Identify clinical "champions" who can create enthusiasm in patients and staff for robust use (high % daily monitoring). • Develop criteria that accurately target the at-risk patients (recently hospitalized, prone to fluid overload, struggles with medication adherence, etc) • Train key clinical staff to identify and deploy the technology for these patients.	• Implement an efficient notification system. • Decrease the number of clicks needed to retrieve data. • Develop a reporting system for technical issues. • Determine the best support staff and system of HF team billing.	• Develop inclusion and exclusion criteria for use that may trigger identification of patients who will be most likely to benefit. • Train clinical staff to identify optimal patients. • Determine which staff members are responsible for obtaining payer approval, scheduling the implantation, and teaching patients and families.
Clinical practice	• The technology is not a treatment. It is a tool to make your clinical care better. It will only have benefit if you use the tool to direct your care. • It may not be as useful in stable patients with HF.	• Use physician-approved algorithms to understand EP and HF cardiologist perspectives on making changes to a plan of care based on data. • Also talk to the patient about the process and offer impartial medical counseling.	• Determine the correlation between PA wedge pressure and PA diastolic pressure. • Establish practice protocols for the efficient management of trended data.
Ensuring patient understanding	• Communicate clearly and regularly with patients to ensure high utilization. • Check that patients understand how to properly use the technology.	• Communicate data findings regularly with patients to maintain or improve engagement. • Review data with the patients during clinic visits.	• Train patients and family members in the steps of obtaining and submitting data and have patients carry out the steps at least once independently.
Handling patient nonadherence	• Reassert to patients the usefulness of telephonic monitoring in improving their care. • Assure them that it will not completely replace face-to-face interactions. • Convey the impression that the technology (cold) is actually an extension of the clinical team's touch (warm).	• Create a system that flags patients who have not submitted data and then sends them messages. • Collaborate with patients to learn rationale for nonadherence. • Reassure patients that RPM results are shared and that an office appointment can be made at any time.	• Set a notification threshold for the number of days without transmitted pressures. • Contact patients directly when data are not submitted and encourage them to provide data as requested. • Review the data with the patients during clinic visits to emphasize the value.
Dealing with abnormalities	• Develop a system for dealing with abnormalities either on a case-by-case basis or more broadly.	• Develop performance metrics surrounding actions taken after the discovery of abnormal data and clinical outcomes.	• Health care providers should determine if each abnormal case will be individually managed or if an algorithm will be used.

EP, electrophysiology; HF, heart failure; ICD, implantable cardioverter-defibrillator; IHM, implantable hemodynamic monitoring; PA, pulmonary arterial.

- Patient submits data daily.
- Clinical team monitors and acts on the data daily until the patient is stable and medications are optimized and then sets parameters for alerts.
- Action should be taken whenever pressures fall outside of the alert ranges.

Conclusions

1. The practical side of implementing RPM technology into clinical settings is complex, and issues such as the division of responsibilities and the handling of abnormalities ought to be addressed by health care providers.
2. It is important for electrophysiology teams, HF teams, and nurses to all work together to ensure that data is used well and patients receive the best care possible.
3. IHM should be used in a manner similar to that in the clinical trials (see detailed description above).
4. Further specific recommendations around RPM are provided in Fig. 1.

Consumer Devices and Wearable Technology

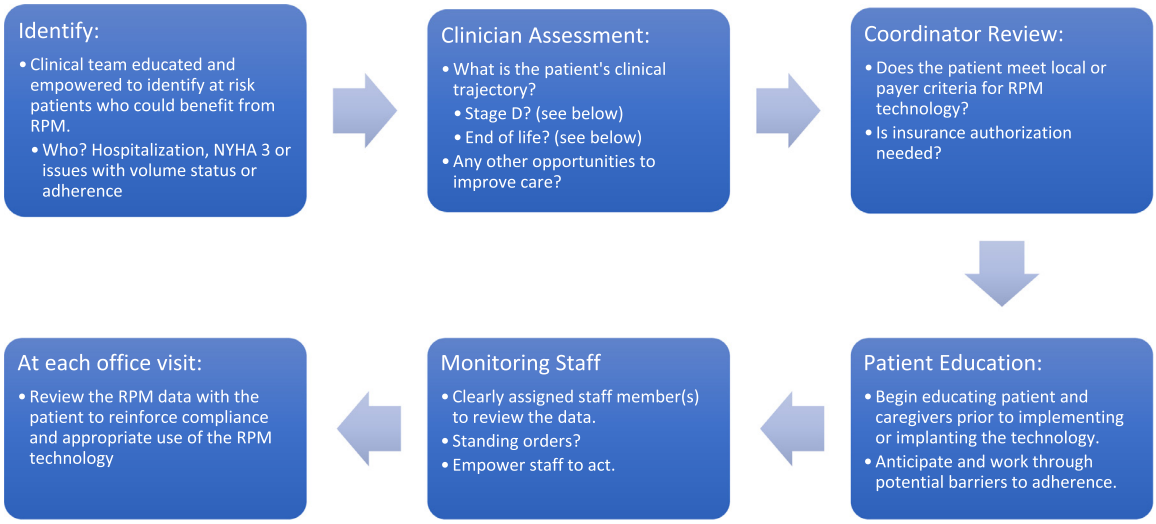
Consumer Device Types

There has been an increased interest among patients and companies in consumer devices, which aim to enhance health and wellness and can collect a wide range of data, from heart rate to sleep quality to medication intake. Importantly, the data recorded by these devices has the potential to empower patients and caregivers, allowing them to work effectively to achieve optimal HF management. However, there are some concerns that these devices may increase the data burden of medical care, threaten patient privacy, or incur additional patient expenses. Therefore, it is essential that health care providers understand the benefits as well as the limitations of incorporating consumer devices into remote monitoring, to best guide patients and technology companies in the further development of this field.

mHealth is the general term for the use of mobile telephones and other communication technologies to collect and access health services and information. These devices may be smartphones, tablets, personal computers (PCs), health-specific wearable technology, or biosensors, with smartphones being the most popular option. Most mHealth approaches use applications ("apps") to collect data, and as of May 2013 there were 710 apps on the market related to cardiology and heart disease, although some were purely educational and medical calculator apps.[77] Given the high prevalence of smart devices across socioeconomic lines, apps hold real potential for patient monitoring.[78] The related apps collect data either automatically, via manual entry, or through a wearable transmitter. The data may then remain locally within the patient's device or be uploaded to cloud-based storage under the control of the app creator. Some consumers may choose to share their personal health and wellness data on social media forums such as Facebook or Twitter, with their health care providers, or with clinical research data repositories. These data collection, storage, and dissemination relationships are outlined in Fig. 2.

RPM technologies are a tool and not a treatment.

They are only effective to the extent that you use them to improve your clinical care of the patient.



- If Advanced (Stage D HF): See HFSA Guideline Committee statement on Stage D. (75)
- If patient facing possible end of life: See HFSA Guideline Committee statement on End of Life in HF. (76)

Fig. 1. Practical implementation of remote patient monitoring (RPM) technology. RPM technologies are a tool and not a treatment. They are only effective to the extent that you use them to improve your clinical care of the patient: if advanced (stage D HF), see HFSA Guideline Committee statement on stage D[75]; if patient facing possible end of life, see HFSA Guideline Committee statement on end of life in HF.[76]

Collectable Health Data

The data elements that can be collected by consumer devices are wide and varied, ranging from HF symptoms to mood to sleep duration and quality. The most advanced data collection devices enable third-party integration into another company's health/fitness app, with popular choices including MyFitnessPal and Microsoft HealthVault. Table 4 outlines the categories of wearable devices that can be used in HF monitoring and includes some of the currently marketed devices. In fact, consumer-directed heart rhythm monitoring is an area in which smartphone technology has clearly surpassed the previous generation of home telehealth devices. For example, one device, called Kardia Mobile, uses 2 electrodes that attach to a smartphone and convert electrical signals from the fingertips into ultrasound that is transmitted to the smartphone's microphone, to produce an electrocardiography (ECG) tracing corresponding to a standard lead I. The ECG tracing can then be downloaded wirelessly for immediate remote interpretation.[79] Such devices also hold potential for unobtrusive physiologic monitoring for participants in HF clinical trials.

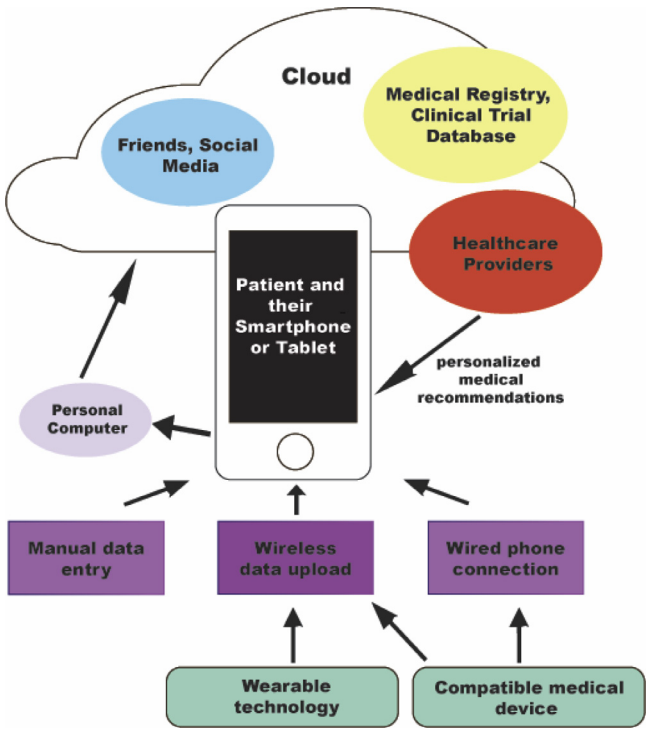


Fig. 2. Collection, storage, and dissemination of personal health and wellness data on social media.

Practical Applications of Consumer Devices

Devices alone are unlikely to make a significant impact on patient outcomes; rather, it is the framework in which the patient and health care provider interact with the use of data from consumer devices that will determine their

Table 4. Examples of Wearable Technology With HF Monitoring

Type of Wearable Technology	Example Devices/Companies:
Smart clothing	Hexoskin, Athos
Activity trackers	Fitbit, Jawbone Up, Nike Fuelband
Sleep sensors	Beddit Sleep Tracker
Smart glasses	Google Glass
Smart watch	Apple iWatch, Fitbit Charge, Kardia Band
Biosensors and patches	Heart rate monitoring belts, Scanadu Vitals device that measures vital signs from left side of the forehead
Ingestibles, tattoos, and smart implants	Proteus Helius smart sensor pills, skin implants monitoring circulating lactate or glucose levels[16]

Brands listed are examples only; other companies are available, and the Heart Failure Society of America does not endorse any specific brands.

success. This point was reaffirmed by a systematic review of 9 mHealth studies, which found that consumer devices had mixed results regarding the improvement of HF outcomes and noted the need for actionable mHealth monitoring strategies.[80] Ultimately, to increase the impact of mHealth platforms, developers will need to minimize the pathway between incoming data and outgoing information that directs adjustments in HF therapy, enabling patient empowerment and ownership of their HF disease management. Patient empowerment through technology is already a reality in other disease settings. For example, patients with diabetes can use apps that integrate their blood glucometer readings with software that calculates insulin dosing to promote optimal glycemic control. A similar approach could be envisaged whereby HF apps integrate weight, blood pressure, heart rate, physical activity data, and hemodynamic measurements to automatically calculate diuretic dosing or alert the patient to seek medical attention.

Of course, it is still uncertain how patients with HF, particularly those who are older and less technologically engaged, will feel about adopting mHealth platforms. Because there appears to be a growing acceptance of mHealth platforms overall, the Heart Failure Society of America has stepped into the fray with an app that enables self-directed recording of symptoms, vital signs, and medications.[81] Patients can choose which of these elements they wish to track, building a summary titled "My Storylines." The goal is for patients to share personal health data with their health care provider to build a more complete picture of their health status between clinic visits.

Some investigators have identified research opportunities presented by the vast quantity of health and wellness data being collected. The Health eHeart study, for example, enrolls adults who are either healthy or diagnosed with heart disease with the goal to create a new paradigm for clinical research that does not require enrollment in a specific study at a specific research center. In the future, it is hoped that electronic patient-centered research approaches will reduce the cost and inconvenience of conducting clinical research and provide "big data" to address cardiology research questions that have remained unanswered by traditional studies.

Although there appear to be many benefits to using mHealth platforms, from the empowerment of patients[82] to the possibilities for research, there are also limitations. Data from the Health eHeart study, for example, show that volunteer participation can lead to enrollment bias that may limit generalizability.[83] In addition, there are concerns regarding data privacy and security. Experts have highlighted serious lapses in mHealth apps that may result in accidental or unlawful loss of data, as well as unauthorized access or disclosure.[84] In addition, data quality remains an issue, because there is no centralized oversight or credentialing of medical apps, with only a fraction of platforms requiring evaluation by the FDA.[85] Major mHealth data quality flaws have been described, especially in insulin-dosing apps where inaccurate data processing could be life threatening.[86] Strategies for improving the quality of medical apps have been proposed, from boosting app literacy to enforcing transparency.[87] In addition, more diverse and representative patient samples must be studied before widespread use of mHealth in HF can be fully recommended. However, the potential to integrate IHM into mHealth remote monitoring platforms that also track weight, blood pressure, heart rate/rhythm, and physical activity may represent the future paradigm of HF disease management.

Conclusions

1. mHealth tools present an opportunity for greater patient empowerment and ownership of their HF disease management.
2. The future impact of mHealth platforms in HF care will depend less on the amount of data and more on the integration of quality information sources into clinical algorithms that generate actionable information, such as HF medication dosing.
3. Health care providers and patients with HF must work closely with app developers and device companies and subject mHealth HF management tools to rigorous academic review.
4. The academic HF community has an opportunity to embrace mHealth tools to conduct research on a scale beyond that achievable by standard study designs.

Conclusion

RPM has experienced a resurgence of interest based on industry investment as well as the commercial availability of an implantable PAPM system. Depending on the platform, results in randomized controlled trials have often failed to show benefit. We conclude with the following recommendations:

1. RPM with the use of external devices has had variable efficacy in clinical trials. Clinical teams can not assume that it will provide benefit.
2. If RPM with the use of external devices is used it should be (a) focused on higher-risk populations, (b) with dedicated efforts to ensure patient adherence with monitoring, and (c) in collaboration with a disease management

team capable of monitoring and responding to actionable changes in readings.
3. Optimal target populations for RPM are not well defined. Patients to be considered include those with recent hospitalization, persistent symptoms (NYHA III), or problems with self-monitoring or adherence to treatment. Patients with very advanced disease or with significant renal insufficiency may be too ill to achieve benefit from RPM.
4. Data obtained from CIEDs have not delivered clear improvements in outcomes. Combination algorithms that use multiple risk indicators could prove to be more useful in the future, and multicenter prospective studies are encouraged.
5. IHM via wireless PAPM did appear to be effective in a single trial in reducing hospitalizations and other outcomes regardless of ejection fraction.
6. If used, IHMs should be deployed in a manner similar to that in the CHAMPION trial. This should include well defined (a) mechanisms for monitoring data, (b) ability to make tangible changes in therapy in response to the data, and (c) clinical teams that understand the strategies used in the clinical trial.
7. RPM platforms may be cost-effective but have not yet proven to be cost reducing. Implementation should include monitoring for cost versus benefit.
8. RPM via consumer devices is rapidly growing. Currently, the data are interesting but they have not yet been used in a systematic way to manage HF.

Disclosures

Dickinson an Investigator at the Saint Jude Medical (Investigator in CHAMPION trial and CardioMEMs post-approval study), Speaker/Consultant at Medtronic, Abbott; Allen a Consultant at Novartis, Boston Scientific, Janssen, Amgen, Duke Clinical Research Institute, Grants: PCORI, NIH/NHLBI, American Heart Association; Albert a Consultant at Boston Scientific, Duke Clinical Research Institute; DiSalvo a Consultant at GE Healthcare, GLC; Ewald an Investigator at Saint Jude Medical (CHAMPION trial, CardioMEMs post approval study), Speaker at Abbott; Whellan an Investigator at ResMed, NIH, CVRx, Consultant at Medtronic, Fibrogen, CVR Global, Novartis, CSL Behring, Cytokinetics, ResMed; Zile a Consultant at Abbott, Boston Scientific, Endotronix, Medtronic; Givertz (Research) at St Jude Medical (CHAMPION trial and CardioMEMs post-approval study), Consultant at St Jude Medical.

References

1. Rich MW, Beckham V, Wittenberg C, Leven CL, Freedland KE, Carney RM. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. N Engl J Med 1995;333:1190–5.
2. Cleland JG, Louis AA, Rigby AS, Janssens U, Balk AH, TEN-HMS I. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: the Trans-European Network−Home-Care Management System (TEN-HMS) study. J Am Coll Cardiol 2005;45:1654–64.
3. Gesica I. Randomised trial of telephone intervention in chronic heart failure: DIAL trial. BMJ 2005;331:425.
4. Goldberg LR, Piette JD, Walsh MN, et al. Randomized trial of a daily electronic home monitoring system in patients with advanced heart failure: the Weight Monitoring in Heart Failure (WHARF) trial. Am Heart J 2003;146:705–12.
5. Kimmelstiel C, Levine D, Perry K, et al. Randomized, controlled evaluation of short- and long-term benefits of heart failure disease management within a diverse provider network: the SPAN-CHF trial. Circulation 2004;110:1450–5.
6. Rich MW, Gray DB, Beckham V, Wittenberg C, Luther P. Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure. Am J Med 1996;101:270–6.
7. Chaudhry SI, Mattera JA, Curtis JP, et al. Telemonitoring in patients with heart failure. N Engl J Med 2010;363:2301–9.
8. Koehler F, Winkler S, Schieber M, et al. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the Telemedical Interventional Monitoring in Heart Failure study. Circulation 2011;123:1873–80.
9. Ong MK, Romano PS, Edgington S, et al. Effectiveness of remote patient monitoring after discharge of hospitalized patients with heart failure: the Better Effectiveness After Transition—Heart Failure (BEAT-HF) randomized clinical trial. JAMA Intern Med 2016;176:310–8.
10. Wasden C. The Department of Veteran Affairs #mHealth Case Study. August 1, 2014. https://www.himss.org/department-veterans-affairs-mhealth-case-study. Accessed October 23, 2018.
11. Weaver C. Medtronic Expands Into Disease Management: Acquisition of Cardiocom Fits with New Law's Push to Reduce Hospital Readmissions. The Wall Street Journal. August 11, 2013. https://www.wsj.com/articles/medtronic-expands-into-disease-management-1376269497.
12. Inglis SC, Clark RA, Dierckx R, Prieto-Merino D, Cleland JG. Structured telephone support or noninvasive telemonitoring for patients with heart failure. Cochrane Database Syst Rev 2015. CD007228.
13. Newman SP, Bardsley M, Barlow J, Beecham J, Beynon M, Billings J, Bower P, Cartwright M, Chrysanthaki T, Dixon J, Doll H, Fernandez JL, Fitzpatrick R, Henderson C, Hendy J, Hirani SP, Knapp M, MacNeill V, Rixon L, Rogers A, Silva LA, Steventon A. The Whole System Demonstrator Programme: Executive Summary of Findings. Accessed 23 October 2018. https://www.city.ac.uk/__data/assets/pdf_file/0003/243066/WSD_Exec_Sum_28th_20Aug.PDF.
14. Steventon A, Bardsley M, Billings J, et al. Effect of telehealth on use of secondary care and mortality: findings from the Whole System Demonstrator cluster randomised trial. BMJ 2012;344:e3874.
15. Henderson C, Knapp M, Fernández JL, et al. Cost effectiveness of telehealth for patients with long term conditions (Whole Systems Demonstrator telehealth questionnaire study): nested economic evaluation in a pragmatic, cluster randomised controlled trial. BMJ 2013;346:f1035.
16. Xiang R, Li L, Liu SX. Meta-analysis and meta-regression of telehealth programmes for patients with chronic heart failure. J Telemed Telecare 2013;19:249–59.
17. Kitsiou S, Paré G, Jaana M. Effects of home telemonitoring interventions on patients with chronic heart failure: an overview of systematic reviews. J Med Internet Res 2015;17:e63.
18. Greenhalgh T, A'Court C, Shaw S. Understanding heart failure, explaining telehealth—a hermeneutic systematic review. BMC Cardiovasc Disord 2017;17:156.

19. Sanders C, Rogers A, Bowen R, et al. Exploring barriers to participation and adoption of telehealth and telecare within the Whole System Demonstrator trial: a qualitative study. BMC Health Serv Res 2012;12:220.
20. Nakamura N, Koga T, Iseki H. A meta-analysis of remote patient monitoring for chronic heart failure patients. J Telemed Telecare 2014;20:11–7.
21. Amir O, Rappaport D, Zafrir B, Abraham WT. A novel approach to monitoring pulmonary congestion in heart failure: initial animal and clinical experiences using remote dielectric sensing technology. Congest Heart Fail 2013;19:149–55.
22. Amir O, Azzam ZS, Gaspar T, et al. Validation of remote dielectric sensing (ReDS) technology for quantification of lung fluid status: comparison to high resolution chest computed tomography in patients with and without acute heart failure. Int J Cardiol 2016;221:841–6.
23. Amir O, Ben-Gal T, Weinstein JM, et al. Evaluation of remote dielectric sensing (ReDS) technology-guided therapy for decreasing heart failure re-hospitalizations. Int J Cardiol 2017;240:279–84.
24. Takahashi PY, Pecina JL, Upatising B, et al. A randomized controlled trial of telemonitoring in older adults with multiple health issues to prevent hospitalizations and emergency department visits. Arch Intern Med 2012;172:773–9.
25. Boyne JJ, Vrijhoef HJ, Crijns HJ, et al. Tailored telemonitoring in patients with heart failure: results of a multicentre randomized controlled trial. Eur J Heart Fail 2012;14:791–801.
26. Abraham WT. The role of implantable hemodynamic monitors to manage heart failure. Heart Fail Clin 2015;11:183–9.
27. Hawkins NM, Virani SA, Sperrin M, Buchan IE, McMurray JJ, Krahn AD. Predicting heart failure decompensation using cardiac implantable electronic devices: a review of practices and challenges. Eur J Heart Fail 2016;18:977–86.
28. Mooney DM, Fung E, Doshi RN, Shavelle DM. Evolution from electrophysiologic to hemodynamic monitoring: the story of left atrial and pulmonary artery pressure monitors. Front Physiol 2015;6:271.
29. von Lueder TG, Krum H. Current modalities for invasive and noninvasive monitoring of volume status in heart failure. Heart 2012;98:967–73.
30. Tang WH, Tong W. Measuring impedance in congestive heart failure: current options and clinical applications. Am Heart J 2009;157:402–11.
31. Maines M, Catanzariti D, Cemin C, Vaccarini C, Vergara G. Usefulness of intrathoracic fluids accumulation monitoring with an implantable biventricular defibrillator in reducing hospitalizations in patients with heart failure: a case-control study. J Interv Card Electrophysiol 2007;19:201–7.
32. van Veldhuisen DJ, Braunschweig F, Conraads V, et al. Intrathoracic impedance monitoring, audible patient alerts, and outcome in patients with heart failure. Circulation 2011;124:1719–26.
33. Böhm M, Drexler H, Oswald H, et al. Fluid status telemedicine alerts for heart failure: a randomized controlled trial. Eur Heart J 2016;37:3154–63.
34. Conraads VM, Tavazzi L, Santini M, et al. Sensitivity and positive predictive value of implantable intrathoracic impedance monitoring as a predictor of heart failure hospitalizations: the SENSE-HF trial. Eur Heart J 2011;32:2266–73.
35. Cowie MR, Conraads V, Tavazzi L, Yu CM, SENSE-HF I. Rationale and design of a prospective trial to assess the sensitivity and positive predictive value of implantable intrathoracic impedance monitoring in the prediction of heart failure hospitalizations: the SENSE-HF study. J Card Fail 2009;15:394–400.
36. Boehmer JP, Hariharan R, Devecchi FG, et al. A multisensor algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. JACC Heart Fail 2017;5:216–25.
37. Bilchick KC, Berger RD. Heart rate variability. J Cardiovasc Electrophysiol 2006;17:691–4.
38. Valentini M, Parati G. Variables influencing heart rate. Prog Cardiovasc Dis 2009;52:11–9.
39. Huikuri HV, Stein PK. Heart rate variability in risk stratification of cardiac patients. Prog Cardiovasc Dis 2013;56:153–9.
40. Sassi R, Cerutti S, Lombardi F, et al. Advances in heart rate variability signal analysis: joint position statement by the e-Cardiology ESC Working Group and the European Heart Rhythm Association co-endorsed by the Asia Pacific Heart Rhythm Society. Europace 2015;17:1341–53.
41. Lorvidhaya P, Addo K, Chodosh A, Iyer V, Lum J, Buxton AE. Sudden cardiac death risk stratification in patients with heart failure. Heart Fail Clin 2011;7:157–74. vii.
42. Nolan J, Batin PD, Andrews R, et al. Prospective study of heart rate variability and mortality in chronic heart failure: results of the United Kingdom Heart Failure Evaluation and Assessment of Risk Trial (UK-Heart). Circulation 1998;98:1510–6.
43. Mäkikallio TH, Huikuri HV, Hintze U, et al. Fractal analysis and time- and frequency-domain measures of heart rate variability as predictors of mortality in patients with heart failure. Am J Cardiol 2001;87:178–82.
44. Boehmer JP. Nonhemodynamic parameters from implantable devices for heart failure risk stratification. Heart Fail Clin 2015;11:191–201.
45. Auricchio A, Gold MR, Brugada J, et al. Long-term effectiveness of the combined minute ventilation and patient activity sensors as predictor of heart failure events in patients treated with cardiac resynchronization therapy: results of the Clinical Evaluation of the Physiological Diagnosis Function in the Paradym CRT Device Trial (CLEPSYDRA) study. Eur J Heart Fail 2014;16:663–70.
46. Whellan DJ, Ousdigian KT, Al-Khatib SM, et al. Combined heart failure device diagnostics identify patients at higher risk of subsequent heart failure hospitalizations: results from PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) study. J Am Coll Cardiol 2010;55:1803–10.
47. Adamson PB, Gold MR, Bennett T, et al. Continuous hemodynamic monitoring in patients with mild to moderate heart failure: results of The Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure (REDUCEhf) trial. Congest Heart Fail 2011;17:248–54.
48. Bourge RC, Abraham WT, Adamson PB, et al. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. J Am Coll Cardiol 2008;51:1073–9.
49. Zile MR, Bennett TD, St John Sutton M, et al. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. Circulation 2008;118:1433–41.
50. Teerlink JR. Learning the points of COMPASS-HF: assessing implantable hemodynamic monitoring in heart failure patients. J Am Coll Cardiol 2008;51:1080–2.
51. Zile MR, Bourge RC, Bennett TD, et al. Application of implantable hemodynamic monitoring in the management of patients with diastolic heart failure: a subgroup analysis of the COMPASS-HF trial. J Card Fail 2008;14:816–23.
52. Reiter MJ, Stromberg KD, Whitman TA, Adamson PB, Benditt DG, Gold MR. Influence of intracardiac pressure on spontaneous ventricular arrhythmias in patients with systolic heart failure: insights from the REDUCEhf trial. Circ Arrhythm Electrophysiol 2013;6:272–8.
53. Zile MR, Bennett TD, El Hajj S, et al. Intracardiac Pressures Measured Using an Implantable Hemodynamic Monitor:

Relationship to Mortality in Patients With Chronic Heart Failure. Circ Heart Fail 2017;10.
54. Maurer MS, Adamson PB, Costanzo MR, et al. Rationale and design of the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy Study (LAPTOP-HF). J Card Fail 2015;21:479–88.
55. Lou N. HFSA: Did LAP Monitoring Cut HF Rehospitalizations - LAPTOP-HF investigators tried to make sense of terminated study. Medpage Today Sept 19, 2016. http://www.medpagetoday.com/meetingcoverage/hfsa/60327. Accessed October 23, 2018.
56. Verdejo HE, Castro PF, Concepción R, et al. Comparison of a radiofrequency-based wireless pressure sensor to Swan-Ganz catheter and echocardiography for ambulatory assessment of pulmonary artery pressure in heart failure. J Am Coll Cardiol 2007;50:2375–82.
57. Adamson PB, Abraham WT, Aaron M, et al. CHAMPION trial rationale and design: the long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. J Card Fail 2011;17:3–10.
58. Loh JP, Barbash IM, Waksman R. Overview of the 2011 Food and Drug Administration Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting on the CardioMEMS Champion heart failure monitoring system. J Am Coll Cardiol 2013;61:1571–6.
59. Abraham WT, Stevenson LW, Bourge RC, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet 2016;387:453–61.
60. Costanzo MR, Stevenson LW, Adamson PB, et al. Interventions Linked to decreased heart failure hospitalizations during ambulatory pulmonary artery pressure monitoring. JACC Heart Fail 2016;4:333–44.
61. Adamson PB, Abraham WT, Bourge RC, et al. Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. Circ Heart Fail 2014;7:935–44.
62. Givertz MM, Stevenson LW, Costanzo MR, et al. Pulmonary artery pressure−guided management of patients with heart failure and reduced ejection fraction. J Am Coll Cardiol 2017;70:1875–86.
63. Desai AS, Bhimaraj A, Bharmi R, et al. Ambulatory hemodynamic monitoring reduces heart failure hospitalizations in "real-world" clinical practice. J Am Coll Cardiol 2017;69:2357–65.
64. Krumholz HM, Dhruva SS. Real-world data on heart failure readmission reduction: real or real uncertain. J Am Coll Cardiol 2017;69:2366–8.
65. Sood P. Hemodynamic-Guided Management of Heart Failure (GUIDE-HF) NCT03387813. https://clinicaltrials.gov/ct2/show/NCT03387813?term=Hemodynamic-GUIDEd+Management+of+Heart+Failure&rank=1; 2018.
66. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013;6:606–19.
67. Porter ME. What is value in health care? N Engl J Med 2010;363:2477–81.
68. Martinson M, Bharmi R, Dalal N, Abraham WT, Adamson PB. Pulmonary artery pressure-guided heart failure management: US cost-effectiveness analyses using the results of the CHAMPION clinical trial. Eur J Heart Fail 2017;19:652–60.
69. Ollendorf DA, Sandhu AT, Chapman R, et al. CardioMEMS™ HF System (St. Jude Medical) and Sacubitril/Valsartan (Entresto™, Novartis) for Management of Congestive Heart Failure: Effectiveness, Value, and Value-Based Price Benchmarks. Institute for Clinical and Economic Review 2015 http://ctaf.org/sites/default/files/u148/CHF_Revised_Draft_Report_100915.pdf. Accessed October 10, 2015.
70. Malbaski N, Balazs T, Dozsa C, Zima E. Cost-effectiveness analysis of continuous remote monitoring of heart failure patients with cardiac electronic implantable device. Value Health 2015;18:A355.
71. Ricci RP, Vicentini A, d'Onofrio A, et al. Economic analysis of remote monitoring of cardiac implantable electronic devices: results of the Health Economics Evaluation Registry for Remote Follow-Up (TARIFF) study. Heart Rhythm 2017;14:50–7.
72. Hameed AS, Sauermann S, Schreier G. The impact of adherence on costs and effectiveness of telemedical patient management in heart failure: a systematic review. Appl Clin Inform 2014;5:612–20.
73. 2018 Abbott Reimbursement Guide and FAQ. CardioMEMS ™ HF System. Effective January 1, 2018. Accessed 23 October 2018. https://www.sjm.com/~/media/galaxy/hcp/resources-reimbursement/reimbursement-support/hf/cardiomems-reimbursement-faq-2018.pdf?la=en.
74. St. Jude's CardioMEMS heart failure monitor denied coverage in 11 states. MedTech. FierceBiotech. Feb 22, 2016. Accessed 23 October 2018. https://www.fiercebiotech.com/medical-devices/st-jude-s-cardiomems-heart-failure-monitor-denied-medicare-coverage-11-states.
75. Fang JC, Ewald GA, Allen LA, et al. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. J Card Fail 2015;21:519–34.
76. Whellan DJ, Goodlin SJ, Dickinson MG, et al. End-of-life care in patients with heart failure. J Card Fail 2014;20:121–34.
77. Martínez-Pérez B, de la Torre-Díez I, López-Coronado M, Herreros-González J. Mobile apps in cardiology: review. JMIR Mhealth Uhealth 2013;1:e15.
78. Neubeck L, Lowres N, Benjamin EJ, Freedman SB, Coorey G, Redfern J. The mobile revolution—using smartphone apps to prevent cardiovascular disease. Nat Rev Cardiol 2015;12:350–60.
79. Tarakji KG, Wazni OM, Callahan T, et al. Using a novel wireless system for monitoring patients after the atrial fibrillation ablation procedure: the iTransmit study. Heart Rhythm 2015;12:554–9.
80. Cajita MI, Gleason KT, Han HR. A systematic review of mHealth-based heart failure interventions. J Cardiovasc Nurs 2016;31:E10–22.
81. Heart Failure Society of America. Heart Failure Society of America Mobile & Web App: Keeping Track of Your Health Just Got Easier!. Accessed 23 October 2018. https://www.hfsa.org/patient/patient-tools/patient-app/.
82. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. Circulation 2015;132:1157–213.
83. Guo X, Vittinghoff E, Olgin JE, Marcus GM, Pletcher MJ. Volunteer participation in the Health eHeart study: a comparison with the US population. Sci Rep 2017;7:1956.
84. Martínez-Pérez B, de la Torre-Díez I, López-Coronado M. Privacy and security in mobile health apps: a review and recommendations. J Med Syst 2015;39:181.
85. Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff February 9, 2015. https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf.
86. Huckvale K, Adomaviciute S, Prieto JT, Leow MK, Car J. Smartphone apps for calculating insulin dose: a systematic assessment. BMC Med 2015;13:106.
87. Wicks P, Chiauzzi E. Trust but verify"—five approaches to ensure safe medical apps. BMC Med 2015;13:205.