Economic impact of remote patient monitoring: an integrated economic model derived from a meta-analysis of randomized controlled trials in heart failure

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Aims	To assess the cost-effectiveness and the cost utility of remote patient monitoring (RPM) when compared with the usual care approach based upon differences in the number of hospitalizations, estimated from a meta-analysis of randomized clinical trials (RCTs).
Methods and results	We reviewed the literature published between January 2000 and September 2009 on multidisciplinary heart failure (HF) management, either by usual care or RPM to retrieve the number of hospitalizations and length of stay (LOS) for HF and for any cause. We performed a meta-analysis of 21 RCTs (5715 patients). Remote patient monitoring was associated with a significantly lower number of hospitalizations for HF [incidence rate ratio (IRR): 0.77, 95% CI 0.65–0.91, $P < 0.001$] and for any cause (IRR: 0.87, 95% CI: 0.79–0.96, $P = 0.003$), while LOS was not different. Direct costs for hospitalization for HF were approximated by diagnosis-related group (DRG) tariffs in Europe and North America and were used to populate an economic model. The difference in costs between RPM and usual care ranged from €300 to €1000, favouring RPM. These cost savings combined with a quality-adjusted life years (QALYs) gain of 0.06 suggest that RPM is a 'dominant' technology over existing standard care. In a budget impact analysis, the adoption of an RPM strategy entailed a progressive and linear increase in costs saved.
Conclusions	The novel cost-effectiveness data coupled with the demonstrated clinical efficacy of RPM should encourage its acceptance amongst clinicians and its consideration by third-party payers. At the same time, the scientific community should acknowledge the lack of prospectively and uniformly collected economic data and should request that future studies incorporate economic analyses.
Keywords	Heart failure • Hospitalization • Direct costs • Meta-analysis

Introduction

Hospital discharges for chronic heart failure (CHF) in the USA increased from 877 000 in 1996 to ~1 million in 2006, and data from outpatient clinic Medical Care Utilization Estimates for 2007 showed >3 million visits for CHF.[1] In Europe, CHF represents 1–2% of all hospitalizations, making it the leading cause of hospitalization in the elderly.[2,3] The total estimated direct and indirect cost of CHF in the USA for 2010 is $39.2 billion, this is likely an underestimate because only data for CHF as the primary diagnosis or underlying cause of death is considered. Although no solid European data are available for 2010, US

numbers may apply equally to other Western countries.[3] Almost 70% of direct HF costs have been shown to be due to hospitalizations.[3,4] In a previous meta-analysis, we and others[5–7] were able to show that remote patient monitoring (RPM) strategies may delay or prevent hospitalization or even death due to worsening of heart failure by recognizing early changes in haemodynamic and clinical status.

However, very little is known about costs associated with implementation of such patient management strategies,[8] and most data are related to device management rather than to disease management.[9–11] However in the context of disease management, effectiveness (rather than efficacy) should be evaluated, thus including health resource use and health state utilities together with clinical outcomes measures.[12] Given the demonstrated intriguing beneficial effects of RPM on heart failure hospitalization, cost reduction in the management of CHF patients may be anticipated, possibly due to a reduction in the number of hospitalizations.

The purpose of our study was to assess both the cost effectiveness and the cost utility of RPM when compared with the usual care approach, over a period of 1 year, based upon differences in the number of hospitalizations estimated from a meta-analysis of controlled clinical trials.

Methods

Retrieval of information on the burden of hospitalization

Our previous search[5] was extended to randomized clinical trials (RCTs) published up to 15 September 2009 using the same extensive bibliographic search (National Guidelines Clearing House, Pubmed, Embase, Cinhail, and the Cochrane Library databases). From each RCT, we retrieved the total number of hospitalizations, the total number of hospitalizations for HF and the mean length of stay (LOS) per patient in order to measure hospitalization costs. Actual costs had been reported in very few articles and assessed very heterogeneously, therefore hampering their use in this meta-analysis.

Randomized controlled trials reporting the following approaches of care were considered: (i) a usual care approach considered as a patient visit to a clinic (doctor's office, multidisciplinary outpatient clinic, or emergency department) without additional phone calls from and to the patient; (ii) a telephone monitoring approach including regular structured telephone contact between patients and healthcare providers (with or without home visit), and referral of symptoms and/or physiological data; (iii) a technology assisted monitoring approach relying on information communication technology, with transfer of physiological data collected via remote external monitors or from cardiovascular implantable electronic devices. The latter two approaches were collectively identified as RPM.

This information was included in a meta-analysis to compare the incidence rate (IR) of hospitalization for HF between usual care and RPM. Incidence rates were computed as the ratio of the total number of hospitalizations per patient over 1 year, and reported as hospitalizations per 100 person-year, together with their 95% confidence intervals (95% CI). Other endpoints were the comparison of IR of hospitalization for all causes and the comparison of the mean LOS per patient for both any cause and HF only.

A series of sensitivity analyses were performed for the main endpoint: the IR of hospitalizations for HF in the usual care arm was separately compared with the telephone monitoring and the technology-assisted monitoring arms. Moreover, the IR of hospitalizations for HF in the usual care arm was compared with the RPM arm according to duration of follow-up (≤6 and >6 months), study quality (<8 and ≥8 on a visual analogue scale), and country origin of the first author (USA/Canada or Europe).

The incidence rate ratio (IRR) and its 95% CI for each outcome, within each study, were calculated. Similarly the standardized mean difference (SMD) in LOS between arms was computed for each study [from the reported mean LOS and standard deviation (SD)]. The SD was missing in seven articles analysing hospitalizations for HF and in seven others analysing all-cause hospitalizations; in these cases it was imputed as SD = 1.5*mean LOS (to reflect its distribution over studies). Incidence rate ratios or SMDs from each study were then pooled according to the DerSimonian and Laird random effects method (given the high heterogeneity observed). Heterogeneity was evaluated by the Cochran Q test and measured by the I-squared statistic. The meta-analytic approach followed PRISMA guidelines.[13]

Stata 11 (StataCorp, College Station, TX, USA) was used for computation.

Decision analytic model and analysis of costs (payer perspective)

The cost-effectiveness of RPM was assessed through a linear decision model, implemented on an Excel platform. Because the follow-up time in most RCTs ranged between 6 and 12 months, a time horizon of 1 year was considered. A decision tree and related cost simulation model was constructed comparing the two competing strategies (usual care vs. RPM). The decision tree in both usual care and RPM patients considers two options: (i) the patient is hospitalized for HF (event); or (ii) the patient is not hospitalized for HF (event free) during follow-up (Figure 1).

Costs were assessed from the perspective of a third-party payer and only direct healthcare costs for hospitalization were taken into account. In the absence of more detailed information, healthcare resource consumption was valorised using the diagnosis-related group (DRG) reimbursement tariff (in €) for HF hospitalizations in some European countries and in the USA, as a proxy for real-life costs.

The IR of hospitalization for HF (per person-year) was calculated within the meta-analysis and was used to populate the model. The economic burden per patient per year was computed as the product of the IR per patient year and the DRG tariff (Figure 1). Nine different scenarios were constructed by considering the lowest, the highest, and the median DRG reimbursement from Table 1; each of them was multiplied by the pooled IR from the meta-analysis or by its 95% upper or lower confidence limits.

A cost utility analysis was planned based on quality-adjusted life years (QALYs). Quality-adjusted life years were computed as the product of the survival gain and the utility gain. Mortality was taken from a recent meta-analysis[5] and was 15 and 12 per 100 person-years in the usual care and RPM groups, respectively. Utilities were retrieved from Herbert et al.[14] and were 0.612 and 0.662 for the usual care and RPM groups, respectively. The cost-effectiveness ratio (cost per QALY gain) could then be calculated as the difference in costs between the two arms divided by the gain in QALY. The gain in QALY, in turn, was the sum of the gain related to the lower mortality [0.612*(0.15−0.12)] and the gain related to the higher utilities [(0.662−0.612)*(1−0.12)] in the RPM group. If both the difference in costs and the difference in QALY favoured the RPM arm, RPM would be declared as a 'dominant' approach and the cost-effectiveness ratio would become futile.
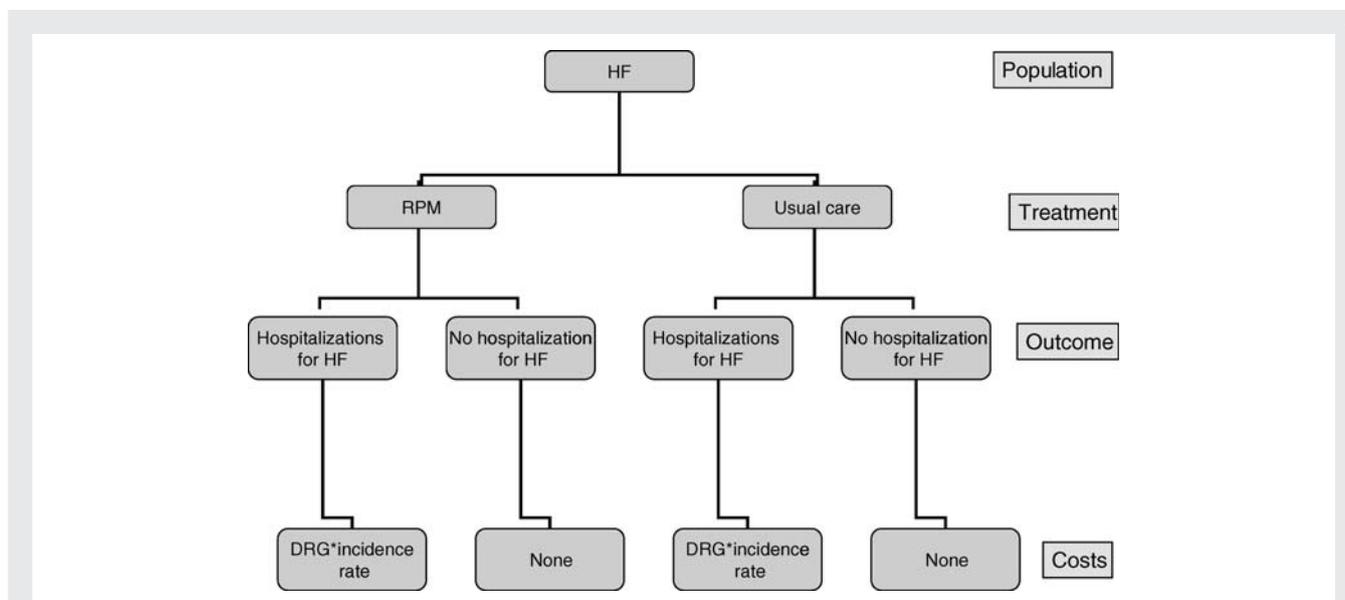
Figure 1 Heart failure and hospitalization costs. Patient pathway in the decision analytic model.

Table 1 Hospitalization and diagnosis-related group reimbursement (€) in Europe and the USA

Country (DRG)	Min (€)	Max (€)
USA[a] (291–293)	2658	5596
Italy[b] (127)	2526	4155
France[b] (05M09x)	2865	7638
Germany[b] (F62A-C)	2360	4202
UK[b] (EB03H-I)	2592	4081

An exchange rate of $1 = €0.667 and of £1 = €1.114 was used (http://www.xe.com/ accessed on 29 October 09). Median reimbursement = €3473, Min = €2360, Max = €7638.
[a]Medicare.
[b]Public health system.

Finally, we performed a budget impact analysis (BIA) by simulating the economic impact (Euro saved, from a third-party payer) of a change in the approach of the care pathway of a theoretical population of HF patients followed-up for 1 year with an RPM implementation rate ranging from 0 to 50%.

Results

Study population

A total of 102 full text articles were examined; 96 of them were from the original search and 6 additional articles were retrieved with the updated search (*Figure 2*). Eighty-one papers were excluded for different reasons. Thus, 21 RCTs reporting total number of hospitalizations and LOS were included in the meta-analysis.[15–35] These RCTs included a total of 5715 patients. Women were well represented (2071 patients or 36% of the study population). The median age over all of the studies was 70.7 (range: 45–78) years. The NYHA functional class was retrievable in only 18 RCTs involving 5411 patients, with 2601 patients (48.1%) being in NYHA functional class III–IV. The median follow-up duration was 6 months and ~15% of follow-ups were 3 months or less. Half (52.4%) of the RCTs had a high quality scoring (≥8); 16 studies were conducted in North America and 5 in Europe.

Meta-analysis

The IR of hospitalization for HF was computed for 17 studies. Remote patient monitoring was associated with a significantly lower number of hospitalizations for HF (pooled IRR: 0.77, 95% CI 0.65–0.91, $P < 0.001$) when compared with usual care (*Table 2*). The heterogeneity between studies was not negligible (I-squared = 53%), as shown in *Figure 3*.

The IR of hospitalization for all causes was computed over 18 studies. A similar, yet less pronounced beneficial effect of RPM approach was shown (pooled IRR: 0.87, 95% CI: 0.79–0.96, $P = 0.003$), with high heterogeneity between studies (I-squared = 59%, *Figure 3*, lower panel). Of note, one study[35] was not included in the meta-analysis as no hospitalizations were considered in either arm.

In the sensitivity analysis, the telephone and the technology-assisted monitoring approach provided a comparable benefit compared with usual care reducing both HF and all-cause hospitalizations. Moreover, when IRRs were computed separately according to the duration of follow-up (short/long), to the quality-of-study (low/high), and to countries of origin, the strength of the association between RPM and hospitalization reduction for HF and for any cause did not change substantially (Supplementary material online, *Table A*).

Length of stay for HF hospitalization could be retrieved from 12 studies (*Table 2*) and was comparable in both management strategies (SMD 0.01, 95% CI −0.12–0.13, $P = 0.88$; *Figure 4*, upper panel). Similarly, the LOS for all-cause hospitalizations did not
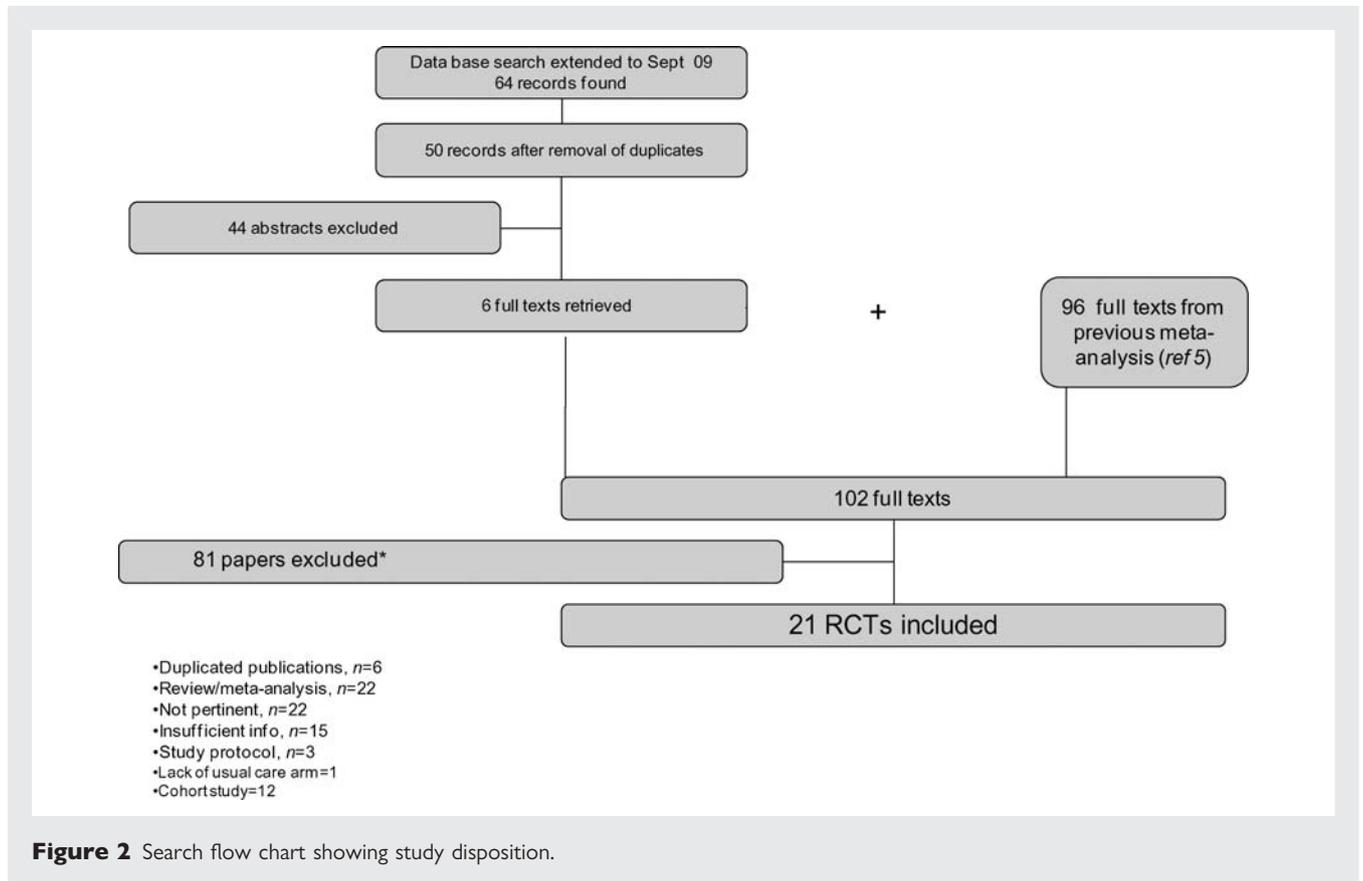
Figure 2 Search flow chart showing study disposition.

Table 2 Hospitalization incidence rates and length of stay according to approach of care

	Incidence rate[a]			
	n = 17[c]	(95% CI)	n = 12	LOS (days)[b] [median (25–75th)]
Hospitalizations for heart failure				
RPM	2746	29.5 (27.4–31.7)	2073	3.9 (1.1–6.0)
Usual care	2089	42.1 (39.2–45.2)	1406	3.6 (2.1–7.5)
	n = 18		n = 12	
Hospitalizations for all causes				
RPM	2980	89.4 (85.9–93.0)	2028	6.2 (4.7–10.9)
Usual care	2332	105.1 (100.7–109.7)	1370	6.1 (4.7–14.5)

RPM, remote patient monitoring.
[a]Number of hospitalizations per 100 person-year.
[b]Per patient (median over studies of the reported mean LOS).
[c]n, number of studies/patients.

differ between RPM and usual care (SMD -0.08 95% CI -0.18–0.02, $P = 0.83$; Figure 4, lower panel).

## Decision analytic model, analysis of costs and utility analysis

The economic model presented in Figure 1 was applied to hospitalizations for HF; computations accounted for repeated hospitalizations. The average cost per patient for a time horizon of 1 year for the nine considered scenarios and for each approach of care is shown in Table 3. The difference in costs between RPM and usual care ranged from about €300 to €1000, RPM always being less costly than usual care.

In the RPM management strategy, the QALY gain due to reduction in mortality was 0.02, whereas the QALY gain due to reduced hospitalizations in surviving patients was 0.04, resulting in a total QALY gain of 0.06.
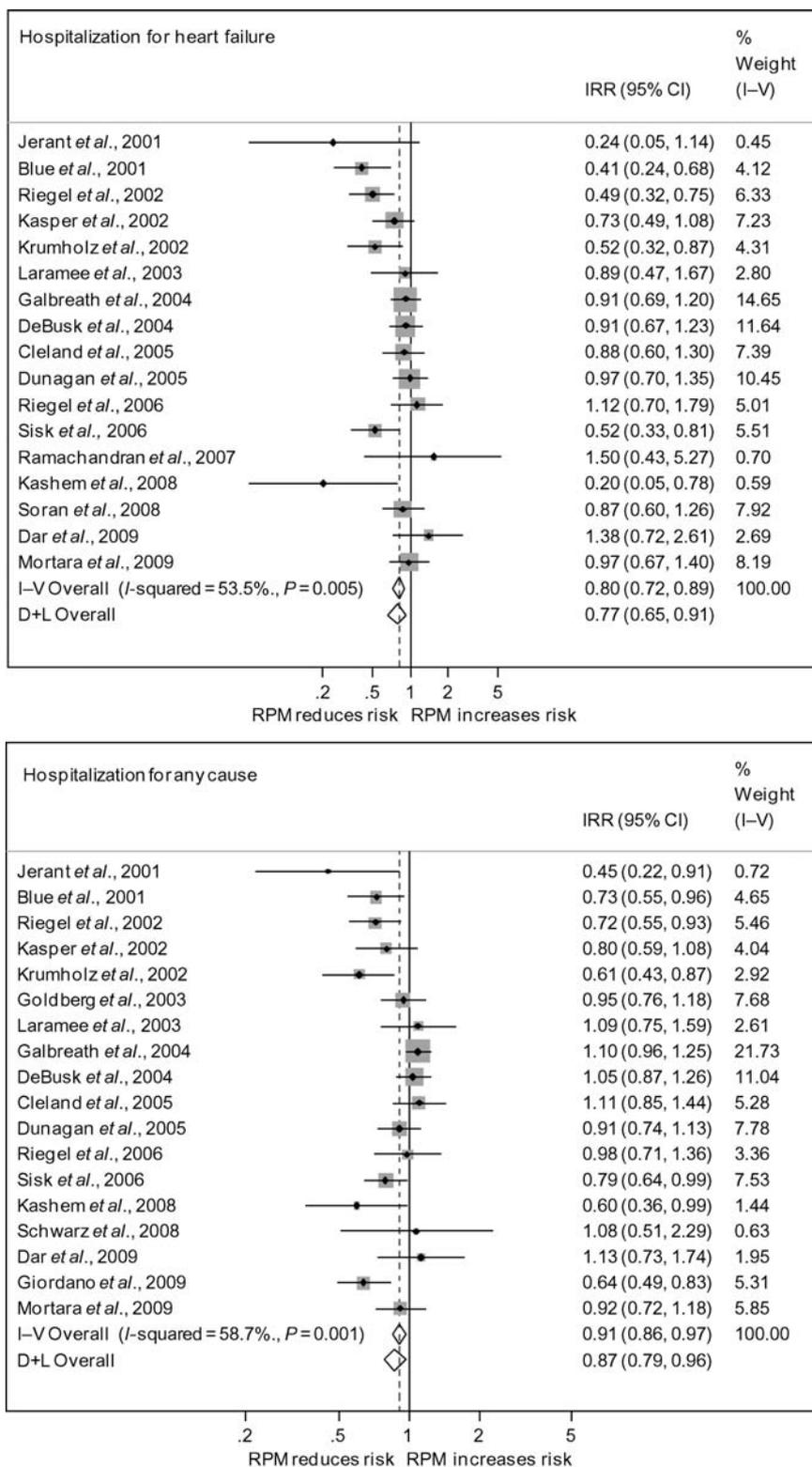
Figure 3 Forrest plots for the analysis of the primary and secondary endpoints. Association of remote patient monitoring and number of hospitalizations for heart failure (upper panel); association of remote patient monitoring and number of hospitalizations for all causes (lower panel). The vertical line corresponds to an incidence rate ratio of 1 (no effect); incidence rate ratios to the left indicate that remote patient monitoring reduces risk; incidence rate ratios to the right indicate that remote patient monitoring increases risk. The pooled estimates are indicated by a diamond (fixed effects, above; random effects below). M–H, Mantel and Haenszel fixed effect method; D–L, DerSimoniam and Laird random effect method. Given the high heterogeneity between studies, random effects estimates should be considered.
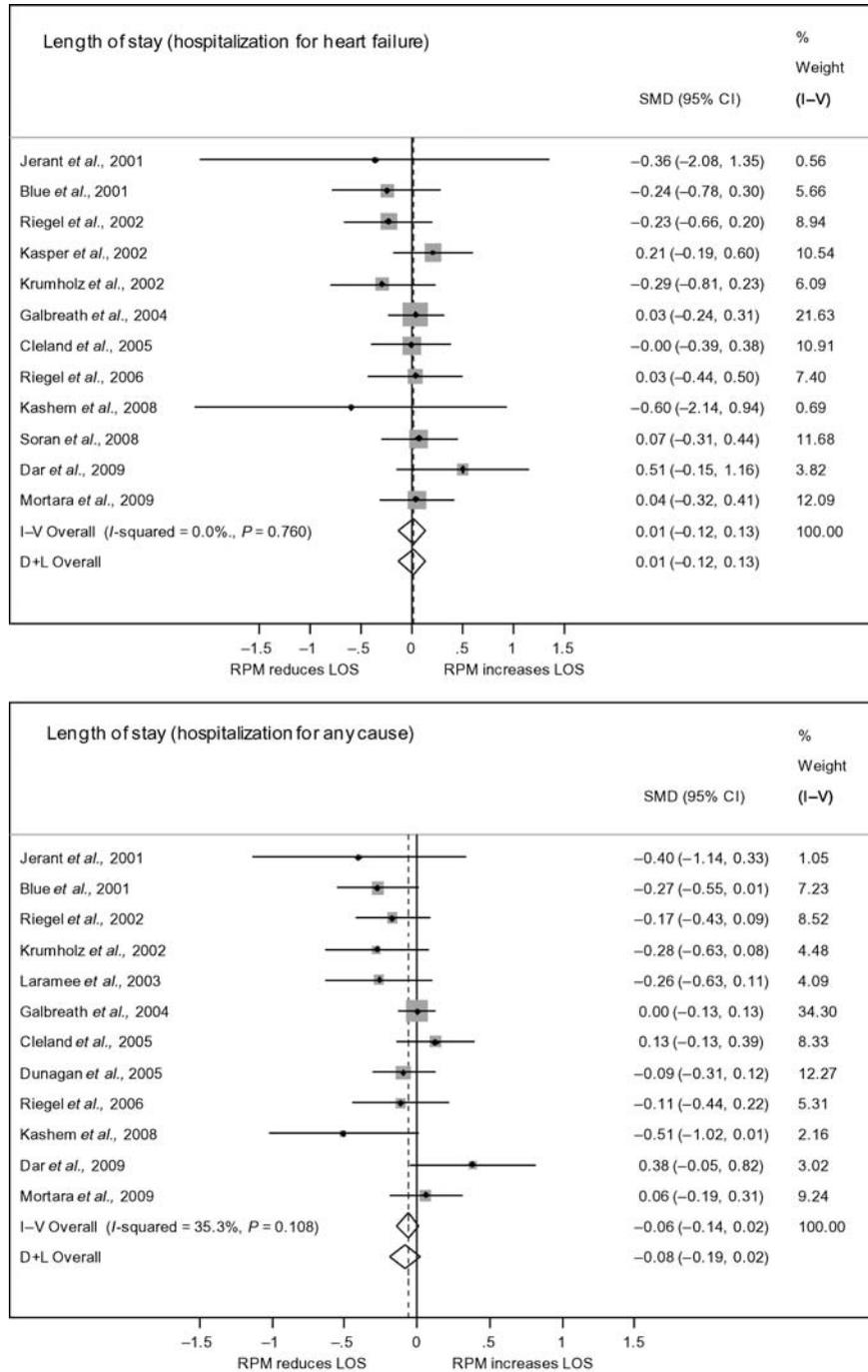
Figure 4 Forrest plots for analysis of mean patients' length of stay for HF hospitalizations (upper panel) and all-cause hospitalizations (lower panel). The vertical line corresponds to a standardized mean difference of 0 (no effect); standardized mean differences to the left indicate that remote patient monitoring reduces risk; standardized mean differences to the right indicate that remote patient monitoring increases risk. The pooled estimates are indicated by a diamond (fixed effects, above; random effects below). M–H, Mantel and Haenszel fixed effect method; D–L, DerSimoniam and Laird random effect method. Given the high heterogeneity between studies, random effects estimates should be considered.

The above results show that RPM is a 'dominant' approach over existing treatment as it is both cost saving and produces a positive QALY gain.

Budget impact analysis

A simulation study was performed on a hypothetical cohort of 100 patients observed for 1 year. The initial hypothesis assumed that all

Table 3 Costs per patient hospitalized for heart failure, estimated for three diagnosis-related group reimbursements (minimum, median, maximum over countries) and three different incidence rates and their lower and upper 95% CI, for a time horizon of 1 year

Reimbursement per HF hospitalization (DRG)		RPM		Usual care		Difference in costs
		Incidence rate (per person-year)	Estimated costs (€)	Incidence rate (per person-year)	Estimated costs (€)	(RPM-usual care)
Minimum DRG amount €2360[a]	Estimate of incidence rate	**0.29**	**684.4**	**0.42**	**991.2**	**−306.8**
	Lower confidence limit	0.27	637.2	0.39	920.4	−283.2
	Upper confidence limit	0.32	755.2	0.45	1062	−306.8
Median DRG amount €3473[b]	Estimate of incidence rate	**0.29**	**1007.17**	**0.42**	**1458.66**	**−451.49**
	Lower confidence limit	0.27	937.71	0.39	1354.47	−416.76
	Upper confidence limit	0.32	1111.36	0.45	1562.85	−451.49
Maximum DRG amount €7638[c]	Estimate of incidence rate	**0.29**	**2215.02**	**0.42**	**3207.96**	**−992.94**
	Lower confidence limit	0.27	2062.26	0.39	2978.82	−916.56
	Upper confidence limit	0.32	2444.16	0.45	3437.1	−992.94

Data in bold were used in the cost-effectiveness analysis.
[a]Minimum DRG reimbursement over countries from *Table 1*.
[b]Median DRG reimbursement.
[c]Maximum DRG reimbursement.
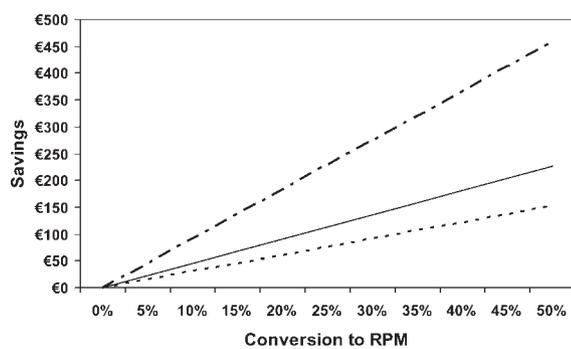
Figure 5 Budget impact analysis: a simulation study. Relationship between the percentage of patients in the remote patient monitoring arm (*x*-axis) and the hospital costs saved (*y*-axis) in a hypothetical cohort of 100 patients. The upper and lower lines correspond to the estimated differential costs for the highest and lowest diagnosis-related group tariffs in *Table 3*, while the midline corresponds to the differential cost for the median diagnosis-related group tariff.

patients were treated according to usual care; then the proportion of these patients followed using an RPM management strategy was progressively increased up to 50%. The effect of the progressive adoption of RPM on payer/healthcare system savings was computed for the three DRG tariffs from *Table 3*, using the difference in costs between patients followed-up with RPM and those followed in the usual manner (−451€, −307€, and −917€). The adoption of an RPM strategy entailed a progressive and linear increase in payer/system costs saved (*Figure 5*).

Discussion

This study shows for the first time that management of HF patients by remote monitoring is cost saving due to a substantial reduction in healthcare resource utilization mostly driven by a reduction in the number of HF hospitalizations. The cost saving expected in both European and US healthcare systems is linearly related to the implementation rate of RPM. An important caveat is the limited follow-up time of the studies considered in this meta-analysis, which restricted the time horizon for the cost-effectiveness assessment to 1 year.

The efficacy of RPM was further supported by several sensitivity analyses which all consistently indicated that neither duration of follow-up nor the country in which RPM was tested would influence the obtained benefit. Hospitalizations for any cause were also significantly reduced indicating that close follow-up of HF patients is a key element for achieving improved quality and quantity[5] of life. An intriguing finding was the similar length of inhospital stay once the patient had been hospitalized in both the RPM and usual care groups. One would indeed expect that early detection of signs and symptoms of decompensation by RPM would be reflected by a less severe decompensated status resulting in a shorter hospital stay. A possible explanation for this observation is a methodological bias introduced in RCTs, with inconsistencies between studies in the reporting of LOS. Thus, only an individual-data meta-analysis could give a definite answer on the real effect of RPM on LOS.

Despite consensus among health economists about the standardized methodological approach for evaluating cost-effectiveness of RPM,[12] economic data collected in RCTs are scanty and more importantly, there is no uniform approach to the economic analysis. To overcome this important limitation, we combined the

results of the present meta-analysis with the expected DRG reimbursements for HF hospitalizations to populate the economic model. This is an extremely conservative approach because the indirect costs which are usually carried by society (loss in productivity for either morbidity and/or mortality) or by individual (reduced/loss in income, travel costs for follow-up visits, etc.) are not considered. Also, no costs of monitoring were considered here, since no RCT reported sufficiently homogeneous information. Despite the substantial criticism that this third-party payer view has recently received,[36] this approach is relatively simple and easy to assess. Our model was further conservative because only costs related to HF hospitalization were considered, based on the assumption that HF hospitalization dominated the expenditure for these patients.[1,3,4,37]

Remote patient monitoring was associated with a relevant economic benefit with savings per patient of about €450 (but in some countries it reached up to €1000) over a time horizon of 1 year. Although this saving may be considered marginal, it is not when the public health relevance of HF is taken into account.[1–3] Moreover when including health state utilities (QALY) in the economic analysis, the RPM technology proved dominant, and hence superior to that of other well established management strategies of chronic disease, such as diabetes, chronic obstructive pulmonary disease, and asthma.[38–40] The BIA elicited the progressive increase in payer/healthcare system savings that would follow a progressive conversion to RPM in a hypothetical population of HF patients.

As mentioned previously, the costs of the implementation of the various RPM systems are not accounted for in this analysis due to a lack of data in the literature and high cost-structure variability (Supplementary material online, *Table B*). It is however evident that the savings generated for the third-party payer by implementing the RPM approach could be used to partly or completely cover the implementation costs. However, as recently indicated by the Heart Rhythm Society/European Heart Rhythm Association joint expert consensus document on monitoring of cardiovascular implantable electronic devices,[41] the lack of reimbursement in the vast majority of European countries is currently a disincentive to the implementation of RPM; this may have a significant impact on patient safety and disease management, as well as hindering the realization of cost savings associated with RPM. Today in the absence of appropriate reimbursement, the burden of implementation of RPM strategies lies totally within the providers (hospitals, ambulatory HF patient services) and the benefits lie with the third-party payers (local authorities, regional authorities, insurance companies, ministries of health, etc.). Various hypotheses of reimbursement modalities could be considered depending on the particularities of each healthcare system, such as creation of virtual ambulatory patient control tariffs that provide a reimbursement per single patient control, per capita monthly reimbursement of a service contract to an external provider for the lifetime of a patient, or device-specific reimbursement of technological automated devices.

Technology is advancing rapidly, and the RPM strategies currently being evaluated in RCTs will undergo a gradual technological transformation. Expert system and sophisticated algorithm event (heart failure hospitalization and other major cardiovascular events) prediction algorithms based on multiple physiological information derived from exosensors, implantable devices, and external monitors are on the horizon. These data will form the basis for electronic patient records, which may be accessed by all of those involved in a patient's management including the patient himself who may be actively engaged in his own disease management. Such integration of implantable device management with 'conventional' RPM will most likely further improve the efficient use of healthcare resources.

It is however necessary to clearly distinguish between 'device checking' and 'patient monitoring' through the device. Device checking is only about monitoring device functionalities and reading device records, whereas patient monitoring allows control of physiological parameters (key clinical indicators of disease progression). As concerns device checking, the recently concluded TRUST (Lumos-T Safely Reduces Routine Office Device Follow-Up) trial clearly demonstrated that remote monitoring ensured continuity of follow-up in a large number of patients, avoided unnecessary inhospital patient evaluation (thus reducing clinic load), but maintained continuous surveillance to rapidly identify patients requiring attention.[42] Thus, when combining remote device monitoring with heart failure management, a significant cost saving on an individual patient-basis may be anticipated. Also a sizeable reduction in the number of follow-up visits for device monitoring, and associated travelling costs for HF patients treated with implantable cardioverter-defibrillator and/or cardiac resynchronization therapy devices, has already been reported.[10,11] In these two observational studies, the authors reported estimated savings of about $950 over 5 years (including the additional system costs)[10] and €500 over 9 months,[11] respectively.

To objectively assess the impact of technology-based monitoring vs. telephone contact-based patient monitoring, a comparative evaluation of measurement of the quality-of-life, patient's satisfaction, adherence, and adaptations between technology-based monitoring vs. telephone contact-based patient monitoring would be required. However, very limited data are currently available and these have been in part addressed in the recent work by Inglis *et al.*[43] Taken together, the scant data available do not indicate major differences between the two disease management strategies.

Conclusions

This novel cost-effectiveness data coupled with the demonstrated clinical efficacy of RPM compared with usual care, should encourage the acceptance of RPM amongst clinicians and consideration by third-party payers when defining reimbursement strategies. At the same time, the scientific community should acknowledge the lack of prospectively and uniformly collected economic data and should request new studies incorporating full economic analyses.

Supplementary material

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

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References

1. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, Ford E, Furie K, Gillespie C, Go A, Greenlund K, Haase N, Hailpern S, Ho PM, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott MM, Meigs J, Mozaffarian D, Mussolino M, Nichol G, Roger VL, Rosamond W, Sacco R, Sorlie P, Stafford R, Thom T, Wasserthiel-Smoller S, Wong ND, Wylie-Rosett J, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation* 2010;**121**:e46–e215.

2. Zannad F, Agrinier N, Alla F. Heart failure burden and therapy. *Europace* 2009; **11**(Suppl. 5):v1–v9.

3. Berry C, Murdoch DR, McMurray JJ. Economics of chronic heart failure. *Eur J Heart Fail* 2001;**3**:283–291.

4. Seto E. Cost comparison between telemonitoring and usual care of heart failure: a systematic review. *Telemed J E Health* 2008;**14**:679–686.

5. Klersy C, De Silvestri A, Gabutti G, Regoli F, Auricchio A. A meta-analysis of remote monitoring of heart failure patients. *J Am Coll Cardiol* 2009;**54**:1683–1694.

6. Clark RA, Inglis SC, McAlister FA, Cleland JG, Stewart S. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis. *BMJ* 2007;**334**:942.

7. Polisena J, Tran K, Cimon K, Hutton B, McGill S, Palmer K, Scott RE. Home telemonitoring for congestive heart failure: a systematic review and meta-analysis. *J Telemed Telecare* 2010;**16**:68–76.

8. Burri H, Senouf D. Remote monitoring and follow-up of pacemakers and implantable cardioverter defibrillators. *Europace* 2009;**11**:701–709.

9. Crossley GH, Chen J, Choucair W, Cohen TJ, Gohn DC, Johnson WB, Kennedy EE, Mongeon LR, Serwer GA, Qiao H, Wilkoff BL, PREFER Study Investigators. Clinical benefits of remote versus transtelephonic monitoring of implanted pacemakers. *J Am Coll Cardiol* 2009;**54**:2012–2019.

10. Fauchier L, Sadoul N, Kouakam C, Briand F, Chauvin M, Babuty D, Clementy J. Potential cost savings by telemedicine-assisted long-term care of implantable cardioverter defibrillator recipients. *Pacing Clin Electrophysiol* 2005;**28**(Suppl. 1):S255–S259.

11. Raatikainen MJ, Uusimaa P, van Ginneken MM, Janssen JP, Linnaluoto M. Remote monitoring of implantable cardioverter defibrillator patients: a safe, time-saving, and cost-effective means for follow-up. *Europace* 2008;**10**:1145–1151.

12. Ramsey S, Willke R, Briggs A, Brown R, Buxton M, Chawla A, Cook J, Glick H, Liljas B, Petitti D, Reed S. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force report. *Value Health* 2005;**8**:521–533.

13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;**151**:W65–W94.

14. Hebert PL, Sisk JE, Wang JJ, Tuzzio L, Casabianca JM, Chassin MR, Horowitz C, McLaughlin MA. Cost-effectiveness of nurse-led disease management for heart failure in an ethnically diverse urban community. *Ann Intern Med* 2008;**149**:540–548.

15. Jerant AF, Azari R, Nesbitt TS. Reducing the cost of frequent hospital admissions for congestive heart failure: a randomized trial of a home telecare intervention. *Med Care* 2001;**39**:1234–1245.

16. Blue L, Lang E, McMurray JJ, Davie AP, McDonagh TA, Murdoch DR, Petrie MC, Connolly E, Norrie J, Round CE, Ford I, Morrison CE. Randomised controlled trial of specialist nurse intervention in heart failure. *BMJ* 2001;**323**:715–718.

17. Riegel B, Carlson B, Kopp Z, LePetri B, Glaser D, Unger A. Effect of a standardized nurse case-management telephone intervention on resource use in patients with chronic heart failure. *Arch Intern Med* 2002;**162**:705–712.

18. Kasper EK, Gerstenblith G, Hefter G, Van Anden E, Brinker JA, Thiemann DR, Terrin M, Forman S, Gottlieb SH. A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission. *J Am Coll Cardiol* 2002;**39**:471–480.

19. Krumholz HM, Amatruda J, Smith GL, Mattera JA, Roumanis SA, Radford MJ, Crombie P, Vaccarino V. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. *J Am Coll Cardiol* 2002; **39**:83–89.

20. Laramee AS, Levinsky SK, Sargent J, Ross R, Callas P. Case management in a heterogeneous congestive heart failure population: a randomized controlled trial. *Arch Intern Med* 2003;**163**:809–817.

21. Galbreath AD, Krasuski RA, Smith B, Stajduhar KC, Kwan MD, Ellis R, Freeman GL. Long-term healthcare and cost outcomes of disease management in a large, randomized, community-based population with heart failure. *Circulation* 2004;**110**:3518–3526.

22. DeBusk RF, Miller NH, Parker KM, Bandura A, Kraemer HC, Cher DJ, West JA, Fowler MB, Greenwald G. Care management for low-risk patients with heart failure: a randomized, controlled trial. *Ann Intern Med* 2004;**141**:606–613.

23. Cleland JG, Louis AA, Rigby AS, Janssens U, Balk AH, TEN-HMS Investigators. 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**:1654–1664.

24. Dunagan WC, Littenberg B, Ewald GA, Jones CA, Emery VB, Waterman BM, Silverman DC, Rogers JG. Randomized trial of a nurse-administered, telephone-based disease management program for patients with heart failure. *J Card Fail* 2005;**11**:358–365.

25. Riegel B, Carlson B, Glaser D, Romero T. Randomized controlled trial of telephone case management in Hispanics of Mexican origin with heart failure. *J Card Fail* 2006;**12**:211–219.

26. Sisk JE, Hebert PL, Horowitz CR, McLaughlin MA, Wang JJ, Chassin MR. Effects of nurse management on the quality of heart failure care in minority communities: a randomized trial. *Ann Intern Med* 2006;**145**:273–283.

27. Ramachandran K, Husain N, Maikhuri R, Seth S, Vij A, Kumar M, Srivastava N, Prabhakaran D, Airan B, Srinath Reddy K. Impact of a comprehensive telephone-based disease management programme on quality-of-life in patients with heart failure. *Natl Med J India* 2007;**20**:67–73.

28. Kashem A, Droogan MT, Santamore WP, Wald JW, Bove AA. Managing heart failure care using an internet-based telemedicine system. *J Card Fail* 2008;**14**:121–126.

29. Soran OZ, Pina IL, Lamas GA, Kelsey SF, Selzer F, Pilotte J, Lave JR, Feldman AM. A randomized clinical trial of the clinical effects of enhanced heart failure monitoring using a computer-based telephonic monitoring system in older minorities and women. *J Card Fail* 2008;**14**:711–717.

30. Dar O, Riley J, Chapman C, Dubrey SW, Morris S, Rosen SD, Roughton M, Cowie MR. A randomized trial of home telemonitoring in a typical elderly heart failure population in North West London: results of the Home-HF study. *Eur J Heart Fail* 2009;**11**:319–325.

31. Mortara A, Pinna GD, Johnson P, Maestri R, Capomolla S, La Rovere MT, Ponikowski P, Tavazzi L, Sleight P, HHH Investigators. Home telemonitoring in heart failure patients: the HHH study (Home or Hospital in Heart Failure). *Eur J Heart Fail* 2009;**11**:312–318.

32. Giordano A, Scalvini S, Zanelli E, Corra U, Longobardi GL, Ricci VA, Baiardi P, Glisenti F. Multicenter randomised trial on home-based telemanagement to prevent hospital readmission of patients with chronic heart failure. *Int J Cardiol* 2009;**131**:192–199.

33. Goldberg LR, Piette JD, Walsh MN, Frank TA, Jaski BE, Smith AL, Rodriguez R, Mancini DM, Hopton LA, Orav EJ, Loh E, WHARF Investigators. 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**:705–712.

34. Schwarz KA, Mion LC, Hudock D, Litman G. Telemonitoring of heart failure patients and their caregivers: a pilot randomized controlled trial. *Prog Cardiovasc Nurs* 2008;**23**:18–26.

35. Barrth V. A nurse-managed discharge program for congestive heart failure patients:outcomes and costs. *Home Health Care Manag Pract* 2001;**13**:436–443.

36. Lipscomb J, Yabroff KR, Brown ML, Lawrence W, Barnett PG. Health care costing: data, methods, current applications. *Med Care* 2009;**47**:S1–S6.

37. Boriani G, Diemberger I, Martignani C, Biffi M, Valzania C, Bertini M, Domenichini G, Saporito D, Ziacchi M, Branzi A. Telecardiology and remote monitoring of implanted electrical devices: the potential for fresh clinical care perspectives. *J Gen Intern Med* 2008;**23**(Suppl. 1):73–77.

38. Handley MA, Shumway M, Schillinger D. Cost-effectiveness of automated telephone self-management support with nurse care management among patients with diabetes. *Ann Fam Med* 2008;**6**:512–518.

39. Griffiths TL, Phillips CJ, Davies S, Burr ML, Campbell IA. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax* 2001;**56**: 779–784.

40. Steuten L, Palmer S, Vrijhoef B, van Merode F, Spreeuwenberg C, Severens H. Cost-utility of a disease management program for patients with asthma. *Int J Technol Assess Health Care* 2007;**23**:184–191.

41. Wilkoff BL, Auricchio A, Brugada J, Cowie M, Ellenbogen KA, Gillis AM, Hayes DL, Howlett JG, Kautzner J, Love CJ, Morgan JM, Priori SG, Reynolds DW, Schoenfeld MH, Vardas PE, Heart Rhythm Society, European Heart Rhythm Association, American College of Cardiology, American Heart Association, European Society of Cardiology, Heart Failure Association of ESC, Heart Failure Society of America. HRS/EHRA expert consensus on the monitoring of cardiovascular implantable electronic devices (CIEDs): description of techniques, indications, personnel, frequency and ethical considerations. *Heart Rhythm* 2008;**5**:907–925.

42. Varma N, Epstein AE, Irimpen A, Schweikert R, Love C, for the TRUST Investigators. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up the Lumos-T Safely Reduces Routine Office Device Follow-Up (TRUST) trial. *Circulation* 2010;**122**: 325–332.

43. Inglis SC, Clark RA, McAlister FA, Ball J, Lewinter C, Cullington D, Stewart S, Cleland JGF. Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database Syst Rev* 2010;**8**. Art. No.: CD007228. DOI:10.1002/14651858.CD007228.pub2