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RESEARCH ARTICLE

Cost-effectiveness of remote haemodynamic monitoring by an implantable pulmonary artery pressure monitoring sensor (CardioMEMS-HF system) in chronic heart failure in the Netherlands

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Aims Remote haemodynamic monitoring with an implantable pulmonary artery (PA) sensor has been shown to reduce heart failure (HF) hospitalizations and improve quality of life. Cost-effectiveness analyses studying the value of remote haemodynamic monitoring in a European healthcare system with a contemporary standard care group are lacking.

Methods and results A Markov model was developed to estimate the cost-effectiveness of PA-guided therapy compared to the standard of care based upon patient-level data of the MONITOR-HF trial performed in the Netherlands in patients with chronic HF (New York Heart Association class III and at least one previous HF hospitalization). Cost-effectiveness was measured as the incremental cost per quality-adjusted life year (QALY) gained from the Dutch societal perspective with a lifetime horizon which encompasses a wide variety of costs including costs of hospitalizations, monitoring time, telephone contacts, laboratory assessments, and drug changes in both treatment groups. In the base-case analysis, PA-guided therapy increased costs compared to standard of care by €12 121. The QALYs per patient for PA-guided therapy and standard of care was 4.07 and 3.481, respectively, reflecting a gain of 0.58 QALYs. The resulting incremental cost-effectiveness ratio was €20 753 per QALY, which is below the Dutch willingness-to-pay threshold of €50 000 per QALY gained for HF.

Conclusions The current cost-effectiveness study suggests that remote haemodynamic monitoring with PA-guided therapy on top of standard care is likely to be cost-effective for patients with symptomatic moderate-to-severe HF in the Netherlands.

Keywords CardioMEMS-HF system • Implantable pulmonary artery sensor • Cost-effectiveness analysis

Introduction

Heart failure (HF) is a major and rapidly growing healthcare problem with significant clinical and economic implications considering that frequent HF hospitalizations (HFH) increase the already high burden for patients, families, hospitals and payers. Addressing this problem is urgently needed and necessitates a restructuring of HF care in order to reduce HFH, thereby containing/reducing costs

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and improving prognosis. In pursuit of this objective, a variety of telemonitoring strategies have been developed with variable efficacy.[1] Pulmonary artery pressure (PAP)-guided telemonitoring strategies have shown the most promising results, with PAP being a simple and clinically meaningful haemodynamic parameter related to fluid status and congestion.[2] PAP increases precede worsening of HF by several weeks, which makes timely and remote interventions possible.[3] The CardioMEMS-HF system (Abbott, Abbott Park, IL, USA) is an implantable PAP monitoring sensor (referred to as pulmonary artery [PA] sensor throughout this article) that is associated with a reduction in HFH in three randomized controlled trials[4–6] and several real-world studies in various healthcare systems, including UK and Germany.[7–9] The MONITOR-HF trial is the first randomized trial conducted in a European healthcare setting (the Netherlands) and showed an improvement in quality of life and reduction in HFH against a high-quality contemporary level of standard care.[5]

However, consideration of the costs of implementing PA sensor to achieve these benefits is necessary given increasingly constrained healthcare budgets and the aim of many countries to provide value-based healthcare. Consequently, conducting cost-effectiveness analyses (CEAs) has become an important step in introducing such novel therapies. Several CEAs of the PA sensor have been performed, three from a US perspective and one from a UK perspective, which has recently been updated.[10–14] These CEAs have predominantly relied on health and clinical outcome data of the North American CHAMPION trial conducted over a decade ago and cost data, which were often fairly aggregated and derived from secondary data sources.[4] However, differences in healthcare systems, costs of healthcare services, and background HF therapy caution against generalizing these results to the Netherlands or similar Western European countries.

This study aims to perform a CEA of the CardioMEMS HF system (PA sensor) compared to standard of care (SoC) based on the data of the MONITOR-HF trial.[5] Our analysis incorporates detailed information on healthcare utilization that has not been incorporated in previous CEAs, including interactions with healthcare providers through telephone consultations, outpatient clinic visits, telemonitoring time, as well as HF medication usage. This approach allowed for the calculation of more precise model input parameters and more robustly justified assumptions than in previous CEAs. The data used for this CEA were drawn from a contemporary HF population that received a SoC in accordance with up-to-date clinical guidelines, rendering it a more accurate representation of current HF care.

Methods

Study design

The CEA was performed using data from the MONITOR-HF trial, an open-label randomized clinical trial conducted in 25 centres in the Netherlands.[5] Eligible patients had chronic HF classified in New York Heart Association (NYHA) functional class III and a previous HFH, irrespective of ejection fraction. In total, 348 patients were randomly assigned (1:1) to HF management with guideline-directed medical therapy (GDMT) and diuretics (SoC group) or HF management with GDMT and diuretics plus haemodynamic monitoring by a PA sensor (PA sensor group). Daily compliance in the PA sensor group was high with 84.3%, all-cause and cardiovascular mortality rates were 0.14 and 0.08 in the PA sensor group and 0.14 and 0.10 in the SoC group. The full characteristics of the MONITOR-HF study population are included in online supplementary *Table S1*. Inclusion and exclusion criteria and more details about the MONITOR-HF trial were described elsewhere.[15]

The main result of a CEA is the incremental cost-effectiveness ratio (ICER), which is the difference in costs between the two groups divided by the difference in quality-adjusted life years (QALYs). In accordance with reference values used by the Dutch Healthcare Institute, an intervention in HF patients is considered cost-effective if the ICER is below €50 000 per QALY gained.[16] The CEA is conducted from two distinct perspectives: (i) a healthcare perspective which encompasses all HF-related healthcare costs and all other costs incurred within the healthcare sector, which includes costs of the intervention, medication, telephone consultations, hospitalizations (both HF- and non-HF-related), general practitioners, outpatient visits, home and long-term care; (ii) a Dutch societal perspective which takes a more comprehensive approach by also considering costs incurred outside of the healthcare system. In this case, this includes the costs associated with informal care as well as the costs associated with patient's travel to healthcare services. We report both the trial-based CEA with a 1-year time horizon and the model-based CEA with a lifetime horizon from both perspectives.

Data

Health outcomes

Health gains are expressed in QALYs, a product of length of life and quality of life. Health-related quality of life was based on the generic health-related quality of life questionnaire of the EuroQoL-group, the EQ-5D-5L, which includes five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and five levels of severity per domain. The EQ-5D-5L was administered at baseline, 3, 6, and 12 months. Responses were converted to health-related quality of life values anchored on a scale in which 1 represents perfect health and 0 death (these are called utility values) using the Dutch EQ-5D-5L value set.[17] Estimates of life years lived in both treatment arms are derived from the MONITOR-HF trial.[5]

Costs

The MONITOR-HF trial collected detailed data on clinical endpoints, frequency, and duration of telephone contacts with nurses and cardiologists, and outpatient visits to the cardiology department, and medication changes, all of which were recorded in a detailed logbook. These data on health- and social care use have been supplemented with information from the Medical Consumption Questionnaire of the Institute for Medical Technology Assessment (iMCQ).[18] This questionnaire contains information about contacts with healthcare providers outside the hospitals, home care, travel to healthcare providers and hospitals, rehabilitation and residential care centres, and informal care during the past 3 months. The questionnaire was administered at three different time points during the MONITOR-HF trial: 3, 6, and 12 months. The unit costs were mainly obtained from the Dutch list of reference prices for use in health technology assessment,[16,19] and were converted into 2022 prices using the Consumer Price Index of Statistics Netherlands.[20] Total healthcare costs, informal care, and travel costs were determined by combining resource utilization data from the iMCQ and logbooks with the associated unit costs. Intervention costs include the costs of the PA sensor,[21] which consist of the

price of the device, costs of the implant procedure, cost of a potential implantation complication. PA monitoring is defined here as logging into the system (PA uploads, Merlin.net) and checking the patient's status. Other monitoring-related tasks are directly measured from the logbooks (additional telephone contacts and time, outpatient visits, lab tests, drug changes) which were sourced from the MONITOR-HF trial and costs directly applied in the base case. The current price of the PA sensor device in the Netherlands is €10 000 (manufacturer). The intervention costs were calculated by combining the quantity of resources used based on the MONITOR-HF trial with the unit costs of the Dutch Costing Manual or DBCs, published by the Dutch Healthcare Authority (NZA). The costs of drugs and drug changes of GDMT, including angiotensin receptor–neprilysin inhibitor (ARNI) and sodium–glucose cotransporter 2 inhibitor (SGLT2i), and diuretics were taken from the Dutch medicines database 'G-Standaard'. Further details on the cost calculations are provided in online supplementary *Tables S2–S10*.

Trial-based cost-effectiveness analysis

The trial-based CEA was based on resource utilization and health outcomes of the patients in the trial and had a time horizon of 12 months. To better understand the impact of the PA sensor on healthcare costs and how that effect varies over time, we estimated a linear mixed model with a random intercept, and variables for time, treatment group and the interaction between time and treatment group. Similarly, a linear mixed model with random intercept was used to estimate the effect of the PA sensor on the utility values and how they vary over time. The details of the linear mixed models for the utilities and costs can be found in online supplementary *Tables S11* and *S12*. To calculate a trial-based ICER, we performed 1000 non-parametric bootstrapping by random sampling with replacement of the original data for QALYs and costs.

Lifetime horizon cost-effectiveness analysis

Model structure

A cohort-state transition model (Markov model) with a cycle length of 1 month was developed to assess the long-term cost-effectiveness of the PA sensor compared to SoC. The model has two health states, namely HF and death and one event, namely HFH (*Figure 1*). Patients can move from stable HF to HFH and can spend a maximum of one cycle in the HFH and then transition back to stable HF or death state at the end of the cycle. The model assumed a starting age of 70 years for all patients, which reflects the mean age observed in the MONITOR-HF trial. The model was built in RStudio version 4.2.1. Patients accrued QALYs and healthcare costs during each cycle, depending on whether they are in the stable state or hospitalized. The model's time horizon was a lifetime (maximum 30 years of follow-up) after which all patients were assumed to be dead. The primary outcomes of the model-based CEA were the costs per QALY (ICER) over the lifetime horizon. As with the trial-based CEA, the model-based CEA ICER was calculated from both a healthcare perspective and a Dutch societal perspective. The discount rates were 4.0% for costs and 1.5% for effects, in accordance with Dutch guideline for economic evaluations,[16] and half-cycle correction was applied according to previously described methodology.[22]

Model input parameters

The values of the model input parameters are shown in *Table 1*. For the SoC care group, mortality was modelled using a Weibull distribution

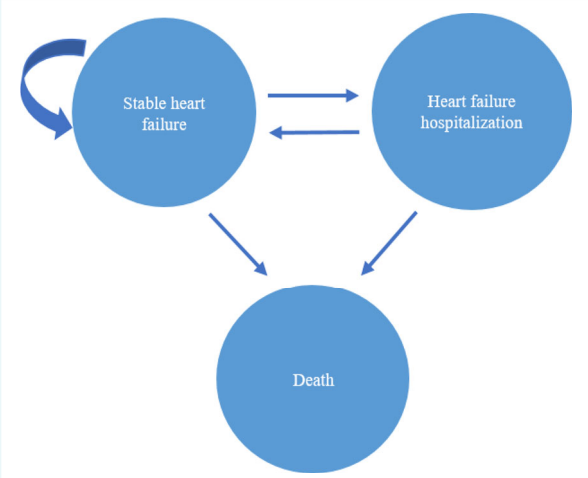

Figure 1 Structure of the Markov model used to estimate lifetime costs and quality-adjusted life years.

that was fitted to the mortality data of the MONITOR-HF trial. Because the MONITOR-HF trial was not powered on mortality, the hazard ratio (HR) associated with mortality in the PA sensor group was based on a recent meta-analysis, in which the impact of the PA sensor on all-cause mortality was estimated (HR 0.92, 95% confidence interval [CI] 0.73–1.16).[23] For the SoC group, the probability of an HFH was obtained from the MONITOR-HF trial. The effect of the PA sensor on HFH was derived from the MONITOR-HF trial, which showed an HR of 0.56 (95% CI 0.38–0.84). The definition of HFH in the MONITOR-HF trial was a composite of hospital admissions (88%), defined as unscheduled HFHs longer than 6 h with or without the need for intravenous diuretics for decongestion of the patient, and urgent visits defined as unscheduled HFHs shorter than 6 h during which the patient received intravenous diuretics (12%). In the base-case analysis, we assumed that the effect of the PA sensor on mortality and HFH remains constant over time.

The model-based CEA included all cost categories that were also included in the trial-based CEA. The PA sensor device and implantation costs were allocated to the first cycle. The monthly costs of stable HF included all costs that were not related to HFH and were estimated separately for each treatment group, based on the 12-month iMCQ and the 24-month logbook data of the MONITOR-HF trial. The mean costs of HFH were derived from the logbooks of the MONITOR-HF trial. The mean duration of an HFH was 10.4 days in the SoC group and 12.9 days in the PA sensor group, resulting in a cost per HFH of €9182 and €11 357, respectively (*Table 1*). The monthly costs of HFH included the costs of stable HF for the remaining days of the monthly cycle that patients did not stay in the hospital. The monthly costs of stable HF and the costs per HFH were kept constant over time.

Utility values in the different states are also shown in *Table 1*. During the days spent in hospital, we applied a disutility of 0.10.[24] We also took into account that quality of life gradually declines as individuals age by reducing the utility index scores by 0.004 each year.[25]

To translate uncertainty surrounding the input parameters of the model into uncertainty surrounding the outcomes, we conducted a probabilistic sensitivity analysis (PSA) using a combination of 1000 Monte Carlo simulations and bootstrapping. The distributions of all parameters included in the Monte Carlo are shown in *Table 1*. We

Table 1 Input values used in the model

Variable group	Distribution used in PSA	Values	Source
Age of patients entering the model		70	MONITOR-HF
Model time horizon		30	
Baseline mortality	Log-normal	Weibull Shape parameter: 1.131 Scale parameter: 2206.28 Uncertainty derived from covariance matrix	MONITOR-HF
Hazard ratio reduction in mortality	Log-normal	0.92 (95% CI 0.73–1.16)	Meta-analysis of RCTs
Hazard ratio reduction in HFH	Log-normal	0.56 (95% CI 0.38–0.84)	MONITOR-HF
Monthly risk of HFH	Poisson	0.055 (95% CI 0.049–0.064)	MONITOR-HF
Risk of implant complications	Fixed	See online supplementary *Table S2*	MONITOR-HF
Total cost of implant procedure including cost of equipment and device	Non-parametric bootstrap using MONITOR-HF data	12 397 in the base-case 11 845 (95% CI 11 459–12 231)	MONITOR-HF
Monthly costs of stable HF in treatment group (including monitoring costs)	Bootstrap using MONITOR-HF data		MONITOR-HF
First year		1158 (95% CI 895–1420)	
From the second year		928 (95% CI 671–1186)	
Monthly monitoring (PA uploads) costs per patient[a]	Bootstrap using MONITOR-HF data		MONITOR-HF
First year		7.4 (95% CI 7.22–7.53)	
From the second year		3.7 (95% CI 3.39–4.09)	
Monthly costs of stable HF in SoC	Bootstrap using MONITOR-HF data		
First year		1015 (95% CI 825–1206)	
From the second year		895 (95% CI 698–1094)	
HFH costs for treatment group (mean LOS 12.9 days)	Bootstrap using MONITOR-HF data	€11 357 (95% CI 10 875-13 278)	MONITOR-HF
HFH costs for SoC (mean LOS 10.4 days)		€9182 (95% CI 8973–12 296)	MONITOR-HF
Utility at baseline for PA sensor	Bootstrap using MONITOR-HF data	0.716 (95% CI 0.716–0.716)	MONITOR-HF
Utility at 3 months for PA sensor		0.725 (95% CI 0.726–0.727)	
Utility at 6 months for PA sensor		0.726 (95% CI 0.724–0.728)	
Utility at 12 months for PA sensor		0.735 (95% CI 0.733–0.738)	
Utility at baseline for SoC	Bootstrap using MONITOR-HF data	0.716 (95% CI 0.716–0.716)	MONITOR-HF
Utility at 3 months for SoC		0.680 (95% CI 0.678–0.682)	
Utility at 6 months for SoC		0.669 (95% CI 0.667–0.682)	
Utility at 12 months for SoC		0.668 (95% CI 0.666–0.670)	
Reduction in utility after 12 months in stable HF state for both treatment groups	Fixed	0.004	Heijink *et al.*
Disutility during days spent in hospital for an HFH	Beta	0.10 (standard error 0.01)	Klersy *et al.*

Costs are expressed in price indexed year 2022 in euros.
CI, confidence interval; HF, heart failure; HFH, heart failure hospitalization; LOS, length of stay; PA, pulmonary artery; PSA, probabilistic sensitivity analysis; RCT, randomized clinical trial; SoC, standard of care.
[a]PA upload time (Merlin.net) is estimated (see online supplementary *Table S3* for the outline of monitoring schedule) and therefore presented separately here. Other monitoring activities/costs are directly measured (logbooks) and applied in the base-case.

plotted the results of the PSA in a cost-effectiveness plane and created a cost-effectiveness acceptability curve. We performed a one-way sensitivity analysis to investigate the ICER sensitivity to change in costs and treatment effects. We used the upper and lower bound of the 95% CI for the model input parameters on costs and treatment effects. Further, we implemented different scenarios regarding the mortality rates and HFHs, the price of the PA sensor device, the costs of monitoring, reduction in the number of outpatient visits, and the model's time horizon. Finally, we provided an exploratory analysis of a more pronounced longer-term mortality benefit of PA-guided therapy, including best and worst case scenarios.

Results

Trial-based cost-effectiveness analysis

In the trial-based CEA and from the Dutch societal perspective the total QALYs were 0.72 and 0.67 in the PA sensor and SoC groups, respectively (online supplementary *Figure S1*). The total costs were €30 690 and €19 100. This resulted in a 1-year trial-based ICER of €186 481 per QALY. This is an overestimation as the time horizon of only 12 months is not long enough to capture the full benefits whereas it does capture the full costs of the PA sensor, which is why a model-based CEA is necessary.

Model-based cost-effectiveness analysis: Base-case analysis

Figure 2 shows the difference in discounted QALYs, life years, HFH costs, and other costs per patient between the PA sensor and SoC groups over time from a societal perspective. The other cost category consists of all costs related to the stable state, excluding the device and implantation procedures costs (€12 397 per patient). Over a lifetime horizon, the model estimated a mean discounted life expectancy of 5.72 years in the PA sensor arm and 5.35 years in the SoC arm (*Table 2*). This represents an increase of 0.38 years in discounted life expectancy. In the PA sensor arm, the mean number of discounted QALYs was 4.07, while in the SoC group, it was 3.48, which is an increase of 0.58 QALYs. The total

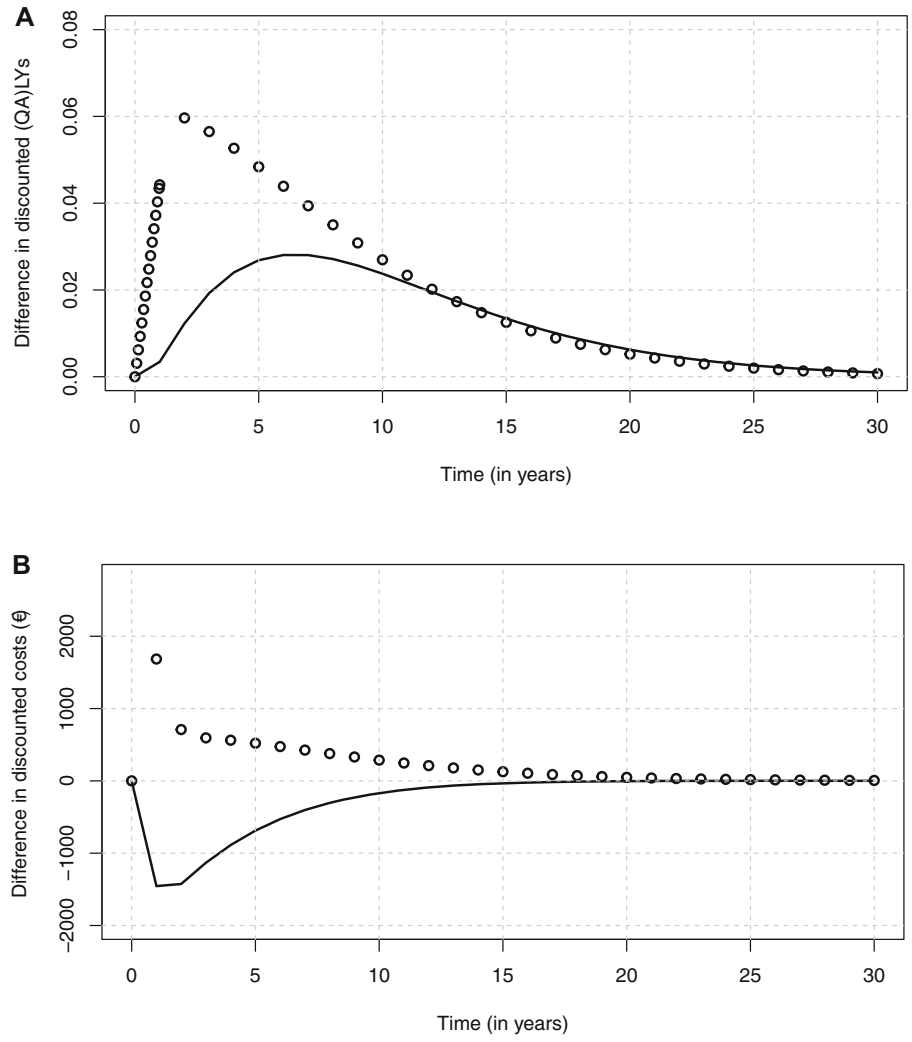

Figure 2 (*A*) Difference in quality-adjusted life years (QALYs) and life years per patient between the pulmonary artery (PA) sensor and standard of care groups in the Netherlands over time. The line represents discounted life years; the dots represent discounted QALYs. Both the line and the dots are plotted as the difference between the PA sensor group and the standard of care group over time in the model. A positive number improves the cost-effectiveness of the PA sensor, and a negative number worsens the cost-effectiveness of the PA sensor. (*B*) Difference in heart failure hospitalization and other costs (excluding intervention costs) per patient between the PA sensor and standard of care groups in the Netherlands over time. The line represents the difference in heart failure hospitalizations and the dots represent the difference in other costs. Both the line and the dots are plotted as the difference between the PA sensor group and the standard of care group over time in the model. A positive number worsens the cost-effectiveness of the PA sensor, and a negative number improves the cost-effectiveness of the PA sensor.

discounted lifetime costs were €91 646 in the PA sensor group and €79 525 in the SoC group, an increase of €12 121, mainly driven by the device and implantation procedure costs.

In the base case, the ICER was €20 753 per QALY, which is below the Dutch willingness-to-pay (WTP) threshold of €50 000 per QALY for HF. Repeating the base-case scenario from the Dutch healthcare perspective, which excludes the costs of informal care and travelling, led to an ICER of €10 406 per QALY.

A more detailed break-down of the cost-differences between the groups in the trial is shown in online supplementary *Tables S13* and *S14* and *Figure S2*.

One-way sensitivity analysis

The results of sensitivity analyses are shown in *Figure 3*. They do not change the finding that the PA sensor is cost-effective at a WTP threshold of €50 000 per QALY. Changing the HR of mortality from 0.92 to the upper and lower limits of the 95% CI changes the ICER to €18 616 per QALY and SoC being dominant, respectively. Changing the HFH HR of 0.56 to the upper and lower limits of the 95% CI changes the ICER to € 37 442 and € 9856 per QALY, respectively. Increasing and decreasing the device costs by 20%, the ICER changed to €24 178 per QALY and €17 329 per QALY,

Table 2 Results of cost-effectiveness analysis

	PA sensor	SoC	Incremental
Base-case scenario from the societal perspective			
Life years	5.72	5.35	0.38
QALYs	4.07	3.48	0.58
Total costs	€91 646	€79 525	€12 121
Stable state	€57 328	€49 958	
HFH state	€21 921	€29 567	
Implantation and device	€12 397	€0	
ICER	–	–	€20 753 per QALY (€15 888 per QALY in probabilistic analysis)
Base-case scenario from the healthcare perspective			
Life years	5.72	5.35	0.38
QALYs	4.07	3.48	0.58
Total costs	€75 088	€69 010	€6077
Stable state	€41 083	€39 833	
HFH state	€21 608	€29 177	
Implantation and device	€12 397	€0	
ICER	–	–	€10 406 per QALY (€ 6562 per QALY in probabilistic analysis)

All results are discounted.
ICER, incremental cost-effectiveness ratio; PA, pulmonary artery; QALY, quality-adjusted life year; SoC, standard of care.

respectively. Increasing the costs of an HFH by 20%, decreased the ICER to €18 414 per QALY. Finally, changing the monthly probability of an HFH from 0.055 to the lower limit of the 95% CI the ICER increased to €21 871 per QALY. The input parameters are provided in online supplementary *Table S15*.

Probabilistic sensitivity analysis

The PSA results are shown in *Figure 4*; the reference line represents the WTP threshold of €50 000 per QALY. The probability of the PA sensor being cost-effective at a WTP threshold of €50 000 per QALY is approximately 87% (i.e. 87% of dots are located below the reference line).

Scenario analysis

The various scenario analyses show that the ICER is particularly sensitive to the mortality effect and time horizon as presented in *Table 3*. Results of additional sensitivity analyses are shown in online supplementary *Tables S16* and *S17*.

Discussion

The current CEA suggests that remote haemodynamic monitoring in patients with moderate-to-severe HF is cost-effective in the Netherlands from the societal perspective with an estimated ICER of €20 753 per QALY and a probability of 87% that the ICER is below the threshold of €50 000 per QALY at which interventions in HF patients are considered cost-effective in the Netherlands. From the healthcare perspective, the ICER was €10 435/QALY. Comparison of the trial-based and model-based analyses and sensitivity analyses on the time horizon in the model makes clear that most savings in costs due to fewer hospitalizations are obtained in the years beyond the trial.

The efficacy of remote haemodynamic monitoring has been studied intensively. Currently, eight studies have shown a consistent treatment benefit in reducing HFH with PA-guided therapy in

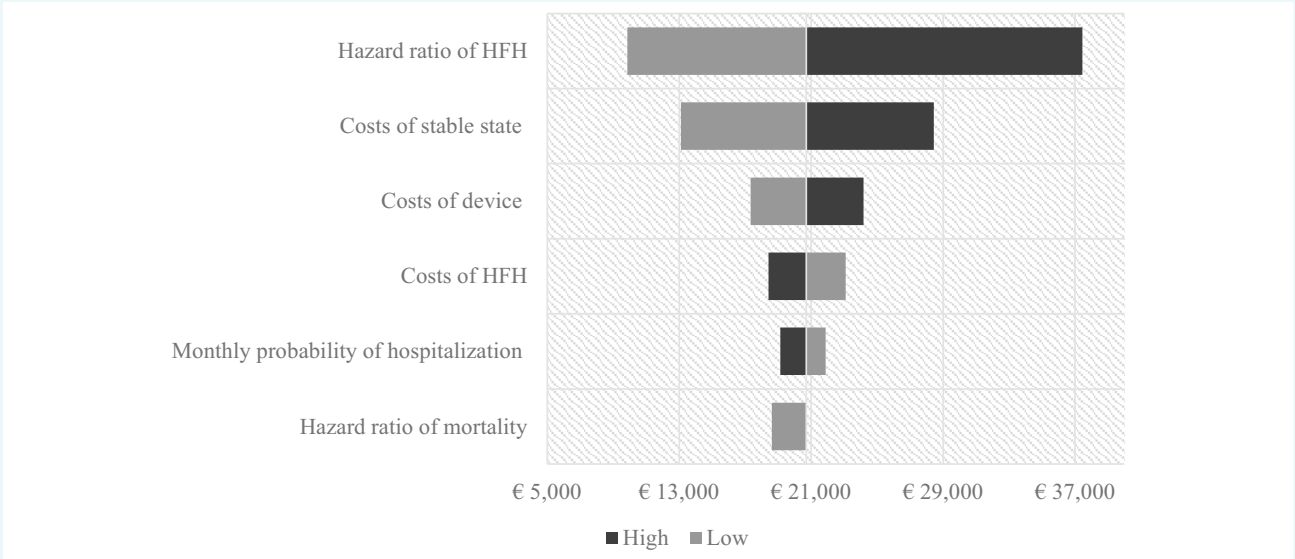

Figure 3 Tornado diagram presenting the one-way sensitivity analysis results. The tornado diagram ranks the parameters listed on the left in order of their influence on the incremental cost-effectiveness ratio, which is portrayed on the *x*-axis. The black and grey bars indicated the range or 95% confidence interval for each variable. The input ranges are provided in online supplementary *Table S15*. HFH, heart failure hospitalization.

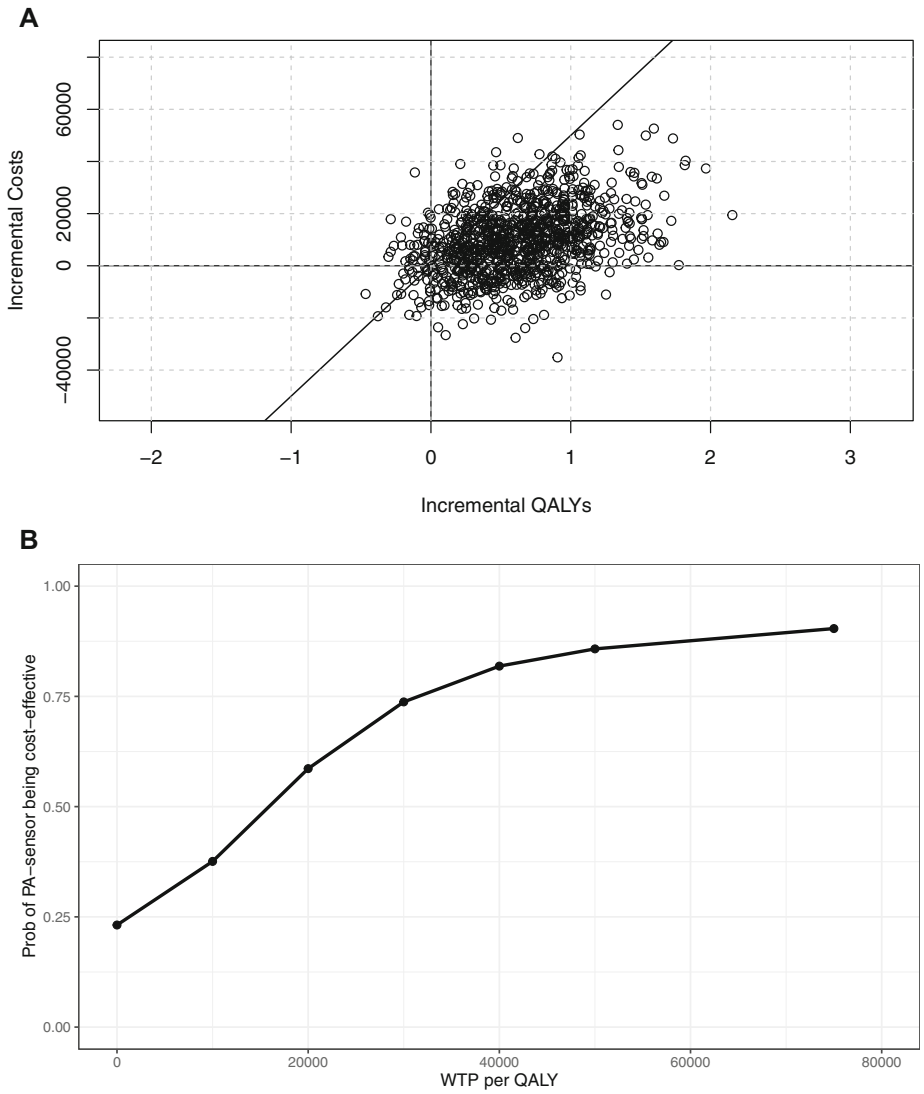

Figure 4 Cost-effectiveness results. (*A*) Cost-effectiveness plane, (*B*) Cost-effectiveness acceptability curve. The black line in (*A*) indicates the willingness-to-pay (WTP) threshold of €50 000 per quality-adjusted life years (QALYs). PA, pulmonary artery.

Table 3 Results of scenario analyses (societal perspective)

Scenario description	Difference in QALYs	Difference in costs	ICER
Mortality			
Mortality impact from the CHAMPION trial (HR 0.80)	1.6	€20 162	€19 148/QALY
Mortality impact from the MONITOR-HF trial (HR 0.96)	0.45	€9782	€21 777/QALY
No impact on mortality (HR 1)	0.33	€7588	€23 470/QALY
Time horizon			
5-year horizon	0.26	€10 805	€40 174/QALY
10-year horizon	0.44	€11 075	€25 304/QALY
15-year horizon	0.53	€11 623	€22 129/QALY

HR, hazard ratio, ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.
Additional scenario analyses are included in online supplementary *Table S16*.

different settings, areas, and against different levels of background therapy.[4–9,26,27] Recently, the MONITOR-HF trial added European randomized clinical trial data and comparison to an actual SoC group at long-term follow-up.[5] In general, the PA sensor has shown a good safety profile and durability with few complications (despite the invasive procedure) and sensor failures.[4–6] The costs of remote haemodynamic monitoring systems are relatively high and are mainly determined by the device and implantation costs, and to a lesser extent, by the workload associated with monitoring activities. The current implementation in Europe is limited as the 2021 European Society of Cardiology guideline gives a class IIb recommendation,[28] and in most countries, including the Netherlands, it is currently not reimbursed. The clinical profile applies only to symptomatic (NYHA class III), moderate-to-severe HF patients with a previous HFH, an elevated risk for future HFH despite optimal GDMT, irrespective of left ventricular ejection fraction. This clinical profile restricts the eligibility for this innovative technology. For context, in the US, the number of implants is above the 30 000 implants to date. When considering a UK perspective, the initial CEA produced an ICER of £19 274 (€22 190), and in the recently updated analysis, this figure increased to £19 761 (€22 750).[10,11] In the initial CEA, cost data from the UK were replaced by estimated cost data from several European countries, resulting in an estimated ICER of €24 500 for the Netherlands over a 10-year time horizon, with similar values for other European countries.[10] The current study confirms and complements the findings of previous CEAs, demonstrating consistency in the results.

The current CEA differs in several aspects from previous analyses. The current analysis uses patient-level data from the trial, the first trial outside the US, which allowed to estimate many parameters for the health economic model directly. Also, the comparator group in the trial was an actual contemporary SoC group with high levels of GDMT. The analysis includes adjudicated HFH as well as non-HFH. Unique to this project is the detail and extent of information on resource utilization with dedicated logbooks on outpatient visits, telephone contacts for monitoring, monitoring time, laboratory assessments, and medication changes in addition to the recorded medical consumption questionnaires adding information on informal care, general practitioners, contact with (para)medical specialists, travelling to healthcare providers, and home care. These cost data are integrated into our analysis and of additive value over previous CEAs. In previous studies, usually, only a smaller set of cost categories was included. By having patient-level data, we discovered that while the PA sensor led to fewer hospitalizations the average length of stay was somewhat higher. In previous studies, the costs per hospitalization were equal in both groups, leading to an overestimation in the savings by preventing hospitalizations. Previous CEAs could not study detailed data on medication changes, especially not on all four components of GDMT, which were unavailable. Our analysis contains the four main components of GDMT and diuretics as well as the changes therein. Also, the uptake of ARNI and SGLT2i during follow-up was accounted for, including the associated costs in both treatment groups. We observed that medication costs were substantially higher in the PA sensor group because the improved decongestive stage might have opened up the opportunity for treatment with GDMT, which are more recent and more expensive HF drugs.

While the current analysis provides valuable data on resource utilization and monitoring workload, our analysis also encounters a level of uncertainty surrounding the mortality effect estimates, as discussed in previous analyses. The clinical trials performed so far are not powered to detect mortality differences due to the limited sample size and follow-up duration. Previous CEAs used mortality rates from the literature and mortality effect estimates of the CHAMPION trial.[10,11] We decided to use the estimates of the treatment effect on mortality (HR 0.92) from the combined data of the three randomized clinical trials containing 1898 patients.[23] When the effect on reducing mortality increases (up to HR 0.80 of the CHAMPION trial), the ICER would change to €19 197 per QALY. Additionally, a recent meta-analysis demonstrated a more pronounced longer-term benefit on mortality after the first year of follow-up (up to HR 0.75), which would reduce the ICER to €17.754 per QALY.[29] As there is no evidence whatsoever that the PA sensor would increase mortality, the sensitivity analysis with an HR above 1 is not realistic.

In this CEA, we used the results of EQ-5D-5L to measure quality of life which is standard practice in CEA. However, it is essential to recognize that this measure of quality of life may not have captured all health benefits with regard to HF-related symptoms, which are better captured with the Kansas City Cardiomyopathy Questionnaire. As the benefits of haemodynamic monitoring in the MONITOR-HF trial were primarily effectuated by changes in diuretics and—on top of—high-level GDMT, we consider the mechanism leading to the benefits and savings in hospital costs applicable to different countries with similar healthcare systems. We postulate that the effects of better decongestion and proactive responses to pressures triggered by a remote interaction between patient and caregiver are generalizable to other European countries to prevent HFH, as already shown in MEMS-HF (Germany) and COAST (UK).[7–9] As in previous CEAs, we have no data available or measured costs for other countries, and data are country-specific. However, a previous analysis that modelled the comparative costs between countries reported comparable ranges in the calculated ICER between countries.[10,11]

Finally, as with every study, this CEA also has limitations. MONITOR-HF had an open-label design without a sham-controlled group. Nevertheless, MONITOR-HF therefore also included a true and contemporary SoC and a high-level GDMT control group. It should also be noted that MONITOR-HF had a modest sample size, and that the clinical outcomes assessed in this CEA were secondary endpoints. Another limitation of this CEA is common to all Markov models, namely the 'lack of memory', meaning that the probability to transition to a future state does not depend on the history of previous states. This limits the model's ability to capture the cumulative effects of past hospitalizations. However, because HFH is treated as an event in our model rather than a state, we have opted not to implement tunnel states in our model. Furthermore, our model is not a microsimulation model in which we model the patient journeys of different subgroups or individual patients, but a cohort model

which directly calculates the expected value of the outcomes of that cohort. We chose for this structure as the available data did not allow us to estimate heterogeneity in the effects of the intervention on mortality and hospital (re)admissions. Our model does implicitly incorporate the higher readmission probability of more frail persons into the overall average admission probability. Also, our model accounts for increasing frailty by decreasing the utility with 0.004 per year in both groups and increasing mortality rates with age. Moreover, as previously discussed, the limitations also include uncertainty regarding the effect of PA sensor on (long-term) mortality, the use of the EQ-5D-5L which may not capture all effects of the intervention on HF-specific quality of life, and the potentially limited generalizability to other healthcare systems where quality of care may be different. However, as HF care in the Netherlands is similar to many high-income countries in terms of access and guidelines, we do expect the results to be applicable to these countries. Lastly, the generalizability of the results are determined by the clinical profile of the study population (online supplementary *Table S1*) and limited to the in- and exclusion criteria of the MONITOR-HF trial.

Clinical perspective

For patients with moderate-to-severe HF (NYHA class III and one previous HFH), additional means on top of GDMT are important considering the residual risk for HF events that produce a huge toll on hospital resources and available hospital beds. The transition of hospital care to the patient at home, is a transition that is very important for a sustainable healthcare organization of the future. Tools such as haemodynamic sensors can impact the lives of these patients as well as provide important means of prevention to lower the burden on hospitals. Considering the rapid developments in the field of telemonitoring and e-health, these devices are likely to evolve. For the coming years, we expect a further reduction in costs by (i) effective integration in workflows using artificial intelligence, treatment algorithms, and greater patient involvement in self-care with monitoring apps reducing the workload on the hospital side; (ii) reducing the actual number of physical outpatient visits (in stable remotely-monitored patients); and potentially (iii) reducing device costs with more companies involved in PA sensor or other relevant haemodynamic sensor technologies (more competition). These aspects can further improve the ICER and the budget impact, especially as the initial purchase costs of the device remains the main determinant. Despite costs, these technologies are designed to transform care delivery to the patient's home with proactive patient-centred remote management, and this trend can have a broader impact on healthcare organizations in the future.

Conclusion

The current analysis suggests that remote haemodynamic monitoring could provide a cost-effective means for HF physicians to optimize patient care remotely, prevent HFH, and thereby improve quality of life in patients with moderate-to-severe HF.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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