Efficacy of Pulmonary Artery Pressure Monitoring in Patients with Chronic Heart Failure: A Meta-Analysis of Three Randomized Controlled Trials

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ABSTRACT

Background and Aims: Adjustment of treatment based on remote monitoring of pulmonary artery (PA) pressure may reduce the risk of hospital admission for heart failure (HF). We have conducted a meta-analysis of large randomized trials investigating this question.

Methods: A systematic literature search was performed for randomized clinical trials (RCTs) with PA pressure monitoring devices in patients with HF. The primary outcome of interest

was the total number of HF hospitalizations. Other outcomes assessed were urgent visits leading to treatment with intravenous diuretics, all-cause mortality, and composites. Treatment effects are expressed as hazard ratios, and pooled effect estimates were obtained applying random effects meta-analyses.

Results: Three eligible RCTs were identified that included 1898 outpatients in New York Heart Association functional class II-IV, either hospitalized for HF in the prior 12 months or with elevated plasma NT-proBNP concentrations. Mean follow-up was 14.7 months, 67.8% of the patients were men, and 65.8% had an ejection fraction ≤40%. Compared to patients in the control group, the hazard ratio (95% confidence interval) for total HF hospitalizations in those randomized to PA pressure monitoring was 0.70 (0.58-0.86) (p=0.0005). The corresponding hazard ratio for the composite of total HF hospitalizations, urgent visits and all-cause mortality was 0.75 (0.61-0.91; p=0.0037) and for all-cause mortality 0.92 (0.73-1.16). Subgroup analyses, including ejection fraction phenotype, revealed no evidence of heterogeneity in the treatment effect.

Conclusions: The use of remote PA pressure monitoring to guide treatment of patients with HF reduces episodes of worsening HF and subsequent hospitalizations.

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Key words: heart failure, pulmonary artery pressure, sensor, monitoring, trial

Introduction

Hospital admission rates for heart failure (HF) are high, and are mainly driven by congestion.[1-3] Haemodynamic congestion, characterised by increasing pulmonary artery (PA)

pressure, often precedes signs and symptoms of clinical congestion by several weeks, which may allow early detection and treatment to prevent hospitalization.[4] Two devices that measure PA pressure are available but only one, the CardioMEMS HF System (Abbott, Illinois, USA), has efficacy data from randomized clinical trials.[5-9] The first reported trial with this device, CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association [NYHA] Class III Heart Failure Patients), was conducted exclusively in the United States of America and demonstrated a significant benefit of PA pressure-guided management in preventing HF hospitalization.[6] The second trial, GUIDE-HF (Haemodynamic-GUIDEd management of Heart Failure), carried out in the United States and Canada was neutral.[7] The 2021 European Society of Cardiology (ESC) HF guideline, published before the results of GUIDE-HF were available, gave a Class II, Level B recommendation for PA pressure monitoring in patients with HF.[1] Although the 2022 American Heart Association and American College of Cardiology guideline made a similar recommendation after GUIDE-HF, it stated that the usefulness of this approach is uncertain and that further evidence was needed before it could be recommended for routine clinical care.[10] A new and first European randomized controlled trial, MONITOR-HF, has just been published and showed that PA pressure-guided HF management resulted in a significant reduction of HF hospitalizations as compared to standard of care. A pooled analysis of these three trials is warranted and timely considering the uncertainty described above, in order to obtain more robust estimates of the effect of PA pressure-guided management on clinical endpoints with the larger number of patients and longer follow-up.

Methods

The reporting of this systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and has been registered on PROSPERO with registration number CRD42023408739.[11]

This study was set up to estimate the effects of remote PA pressure monitoring on HF hospitalizations and mortality outcomes in a meta-analysis, by combining the results of the CHAMPION, GUIDE-HF, and MONITOR-HF.[5-7] In contrast to earlier conducted meta-analyses assessing implantable haemodynamic telemonitoring devices,[12,13] the focus of this meta-analysis was on the CardioMEMS HF System as at the moment of the PROSPERO registration, no efficacy data were available from other PA pressure devices based on randomized controlled trials. Nevertheless, we performed a systematic literature search to ensure no eligible studies were missed. Studies were eligible for inclusion if they had a randomized controlled trial design, prospective, compared the CardioMEMS HF System to a control group, included at least 100 patients, and reported on HF-related clinical endpoints. Medline, Web of Science, Embase, Cochrane, and Google Scholar were searched from inception until 28 February 2023. The systematic search was built and adapted for each database by an experienced information scientist **(Supplementary Material)**.[14] No restrictions on language, study status, or time of publication were placed. Two independent teams of reviewers (PC and SR) screened the articles on eligibility in a title and abstract phase and a full-text phase.

Clinical endpoints of interest were HF hospitalizations, urgent visits with the need for intravenous diuretic therapy, all-cause mortality, and composites of these endpoints. For GUIDE-HF and MONITOR-HF, we accessed all follow-up data and for CHAMPION there were two reports, where we decided to use the extended follow-up analysis.[6] The CHAMPION trial did not include urgent HF visits with the need for intravenous diuretics, which are presently considered as a comparable endpoint to HF hospitalizations. Urgent visits were included as endpoints in both the GUIDE-HF and MONITOR-HF trials. In the analysis of the composite endpoint consisting of total HF hospitalizations, urgent visits, and all-cause mortality, the CHAMPION data only included HF hospitalizations and all-cause mortality.

Similarly, in the analysis of the composite endpoint of total HF hospitalizations and urgent visits, the CHAMPION data only included HF hospitalizations. This decision was made to ensure that data on these related endpoints were not missing, which was also the approach in an earlier meta-analysis on invasive hemodynamic monitoring.[13] A summary of the PICOTS for this study is provided in **Table 1**.

Data extraction was performed by the same reviewers using a standardized data extraction sheet, which included study characteristics, baseline characteristics of the included patients for each treatment group, and clinical endpoints. Patient level data were available for MONITOR-HF. Hazard ratios (HRs) were the primary measure of effect, risk ratios (RRs), and odds ratios (ORs) were considered when HRs were not available. All effect sizes were extracted and reported as point estimates with 95% confidence intervals (CIs). Data were extracted from post hoc analyses, follow-up analyses, Food and Drug Administration summary report when the included studies did not report on them.[15-17] The numbers of patients in subgroups were calculated from available data where necessary. If the HR was not reported in the literature, the incidence rate ratio (IRR) was calculated using the number of events and study cohort time at risk. Study cohort time at risk was calculated by dividing the number of events by the event rate of the primary endpoint.

The risk of bias was assessed by the same independent reviewers; disagreements were resolved in a consensus meeting. To assess the risk of bias in the included studies, the Revised Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2 tool) was used.[18]

Meta-analyses were performed when outcomes were reported by at least two studies with similar effect measures (if only one trial reported on an outcome, we show the individual study data). For the meta-analyses, we used a random effects model with the DerSimonian and Laird estimator. [19] Of note, the three trials analysed total HF hospitalizations with the

Andersen-Gill extension of the Cox model, which includes first and recurrent events. As a sensitivity analysis, we also included fixed effect models in the Supplements. The presence of heterogeneity was quantified with I^2 and p-values. The numbers of patients in subgroups were calculated from available data where necessary. The CHAMPION trial did not report on several subgroups included in this meta-analysis. If subgroups were reported, the investigators included HF hospitalizations only (deaths are not reported in subgroups). GUIDE-HF reported many subgroups on the composite endpoint of HF hospitalizations, urgent visits, and mortality only. To follow this, we aligned with subgroups of GUIDE-HF (including endpoint) with the MONITOR-HF using individual patient level data. Subgroup analyses were performed for left ventricular ejection fraction (LVEF) (≤40% and >40%; <50% and ≥50%), NYHA class, sex, age, HF aetiology, and implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) device implantation. Reported safety data on device- or system-related complications (DSRC) and sensor failures were presented and combined for total implant procedures in the trials. Complete data from all trials were used, also for the GUIDE-HF trial. Sensitivity analyses were performed using the data from the prespecified COVID-19 analysis of GUIDE-HF, which are presented in the Supplementary Appendix.[7] All calculations and analyses were performed with the Metafor package for R.[20]

Several outcomes were extracted and described in addition to the clinical endpoints described above. All trials described medication changes, changes in mean PA pressure and safety endpoints. GUIDE-HF and MONITOR-HF also used the Kansas City Cardiomyopathy Questionnaire to described patient-reported outcomes after 12-month follow-up, which was not available in CHAMPION (which used the Minnesota Living with Heart Failure Questionnaire).

Results

Study and patient characteristics

The systematic search identified a total of 840 records of which the titles and abstracts were screened. Three studies met the eligibility criteria and were included in the meta-analysis: CHAMPION, GUIDE-HF and MONITOR-HF **(Supplementary Figure 1)**, of which only aggregated data were available for CHAMPION and GUIDE-HF. The trial design features and study characteristics are summarized in **Table 1**. In short, 67.8% of patients were men, and 15.6%, 81.6% and 2.8% of patients were in NYHA functional class II, III, or IV, respectively. In CHAMPION and GUIDE-HF, all patients underwent implantation of a wireless PA pressure sensor and were subsequently randomized to receive standard HF care only or to PA pressure-guided management. In both trials, patients were blinded to the allocated treatment group while investigators were not. In MONITOR-HF, all enrolled patients were randomly allocated to either PA pressure-guided management or standard HF care without the implant. Both patients and investigators were unblinded to the allocated treatment group. All trials had an independent, masked, clinical event committee for adjudication of clinical endpoints.

Clinical efficacy of remote PA pressure-guided treatment

The studies included a total of 1,898 patients, and the mean follow-up was 14.7 months (which ranged from 10.8 months, 17.6 months and 21.4 months across the trials, respectively). Only in the GUIDE-HF trial, the follow-up period was fixed at 12 months. The meta-analyses of all clinical endpoints are summarized in **Figure 1.** For the CHAMPION trial, no data were available on urgent visits.

Composite of total HF hospitalizations, urgent HF visits and all-cause mortality: The composite endpoint of total HF hospitalization, urgent visits, and all-cause mortality occurred 644 times among 943 patients in the PA pressure monitoring group (0.56 events per patient-year), and 889 times among 955 control group patients (0.76 events per patients-year), resulting in an HR of 0.75, 95% CI 0.61-0.91; p=0.0037 (moderate heterogeneity, I^2 = 59.29%).

Composite of total HF hospitalizations and all-cause mortality: The composite endpoint of total HF hospitalizations and mortality occurred 605 times among 943 patients in the PA pressure monitoring group (0.53 events per patient-year), and occurred 845 times among 955 patients in the control group (0.73 events per patient-year), yielding an HR of 0.74, 95% CI 0.62-0.89; p=0.0010 (I^2 = 51.05%).

Total HF hospitalizations and urgent HF visits: The composite endpoint HF hospitalizations and urgent HF visits occurred 515 times among 943 patients in the PA pressure monitoring group patients (0.44 events per patient-year) and 743 times among 955 control patients (0.63 events per patient-year), yielding an HR of 0.71, 95% CI 0.57-0.88; p=0.0018 (moderate heterogeneity, I^2 = 59.60%).

Total HF hospitalizations: HF hospitalizations occurred 473 times among 943 patients in the PA pressure monitoring group (0.41 events per patient-year) and 699 times among 955 control patients (0.59 events per patient-year), yielding an HR of 0.70 (95% CI 0.58-0.86; p=0.0005) in favour of the PA pressure monitoring group (moderate heterogeneity, I^2 = 53.60%).

All-cause mortality: Among 943 patients in the PA pressure monitoring group, 132 patients died (14.0%, 0.12 events per patient-year) and among 955 patients in the control group, 146

patients (15.3%, 0.13 events per patient-year) died, resulting in an HR of 0.92, 95% CI 0.73-1.16; p=0.495 (I^2 = 0%).

Subgroup analyses (HF hospitalizations, urgent visits, and all-cause mortality)

For the subgroup analyses, CHAMPION only included data on HF hospitalizations and reported on relatively few subgroups as compared to GUIDE-HF and MONITOR-HF. Pooled analyses of all three trials showed a consistent treatment benefit of remote PA pressure monitoring across the full spectrum of LVEF: among patients with LVEF ≤40% (n=1248, 65.8%), we calculated an HR of 0.76 (95% CI 0.63-0.91), and an HR of 0.69 (95% CI 0.47-0.996) among patients with LVEF >40% (n=650, 34.2%) (**Figure 2)** (P-value for interaction 0.65). Despite the presence of moderate heterogeneity, the effects of remote PA pressure monitoring were found to be largely consistent across clinically relevant subgroups **(Figure 2, Supplementary Table 2,3)**.

Exploratory endpoints

The results for these endpoints are summarized in **Table 2.** Freedom from DSRC was 98.9% and freedom from sensor failure was 99.7% in the pooled analysis.

The full risk of bias assessment is included in **Supplementary Figure 2**. Sensitivity analyses incorporating only the data from the pre-COVID-19 period of the GUIDE-HF trial (instead of all data in the main analysis) were performed. These analyses did not alter our overall findings (**Supplementary Figures 3 and 4)**. Sensitivity analyses were performed with fixed

effect models for the main and subgroup analyses, and are presented in **Supplementary Tables 2 and 3.**

Discussion

This meta-analysis of three large randomized clinical trials including 1898 patients showed that adjusting treatment based on remote monitoring of PA pressures led to a 30% reduction in total HF hospitalizations. This beneficial effect of PA pressure-guided treatment was apparent in patients with LVEF ≤40% and >40%. However, PA pressure-guided treatment did not lead to a reduction in overall mortality. Importantly, the implantation of a PA sensor was safe and durable with a low number of device-related complications and sensor failures (**Structured Graphical Abstract**).

Although the CHAMPION trial suggested that PA pressure-guided management could substantially reduce rates of HF hospitalizations, that trial included a selected high-risk cohort enrolled exclusively in the USA. Moreover, CHAMPION was conducted between 2007 and 2011 when guideline-recommended therapy was different than today. [21] GUIDE-HF, conducted between 2018 and 2021, extended the eligibility to patients in NYHA functional class II and patients with elevated NT-proBNP concentrations in case there was no HF hospitalization in the previous 12 months.[7] However, the use of the same PA pressure-monitoring system to guide treatment did not lead to a significant reduction in the primary outcome or HF hospitalizations in GUIDE-HF compared to CHAMPION. While this may have been due to the impact of the COVID-19 pandemic on the conduct of GUIDE-HF, as suggested by the pre-specified COVID-19 sensitivity analysis of the trial that confirmed a significant treatment benefit, there were also concerns that this management approach might not work in a broader and lower-risk HF population. One of the potential reasons for the smaller difference between the treatment and control groups in GUIDE-HF as compared to

CHAMPION, is that the control group in GUIDE-HF had two weekly calls with their healthcare provider, which may not properly reflect the usual care HF patients receive.

MONITOR-HF is the first European trial using the same implantable PA pressure monitor and its results were largely consistent with CHAMPION and the pre-COVID-19 data from GUIDE-HF. MONITOR-HF differed in that the control group did not have an implanted sensor that was not monitored (as in both prior trials) and did not receive two weekly calls (as in GUIDE-HF). Background pharmacological and device therapy in MONITOR-HF was excellent compared to both prior trials with high use of renin-angiotensin system blockers (81% versus 64% in GUIDE-HF), mineralocorticoid receptor antagonists (82% versus 45% in GUIDE-HF), and an ICD (56% versus 42% in GUIDE-HF). Also, the uptake of angiotensin receptor–neprilysin inhibitor (ARNI) (47% versus 28% in GUIDE-HF) and sodium-glucose cotransporter 2 inhibitors (12% versus <1% in GUIDE-HF) was high and increased substantially to 60% and 30%, respectively, at 12 months in MONITOR-HF (which enrolled longer after the guideline updates). Interestingly, MONITOR-HF also showed the greatest effect of treatment on PA pressure. In GUIDE-HF, the impact on PA pressure was smaller, especially during the COVID-19 pandemic.[22,23] In all three trials, there was a substantially higher number of cumulative drug changes during follow-up in the PA pressure monitoring arm, especially in diuretics, which likely explains the effect on PA pressure and congestion to avoid HF hospitalizations.

The combined evidence from the three trials indicates a significant and consistently positive outcome of PA pressure-guided treatment in reducing HF hospitalizations. The effects of PA pressure-guided therapy, observed across the three trials conducted in different periods with evolving background guideline-recommended medical therapy (and during the pandemic), demonstrates strong agreement in outcomes. These findings provide substantial support for PA pressure-guided HF management. Furthermore, this benefit remained

consistent among patients with HF with reduced ejection fraction and those with an LVEF >40%. The aggregated data revealed a notable treatment effect in patients classified as NYHA class III, who are known to have high rates of HF hospitalizations. Based on the GUIDE-HF data, neither the NYHA class II nor IV patient groups exhibited a significant treatment effect on the primary outcome (HF hospitalization, urgent visits, and mortality), nor did NYHA class show a significant interaction of treatment effect. However, in GUIDE-HF, a significant reduction in the primary outcome was observed when combining patients in NYHA class II and III. The accuracy of assigning NYHA class has its limitations, which should be kept in mind while interpreting these results. Although no reduction in mortality was observed, it is important to note that the overall number of deaths was relatively small, and even this meta-analysis had limited statistical power to detect an effect on mortality. We acknowledge that none of the trials were specifically designed or powered to assess mortality as a singular endpoint, and the follow-up time was limited.

Remote monitoring triggers an interaction between patient and healthcare provider to proactively optimize diuretic therapy based upon invasive markers of volume status. The potential benefit of this technique lies in optimizing and tailoring background therapy in patients, which is reflected by the higher rates of medication changes in the PA pressure-guided group. Although an important clinical question is in which patients PA pressure monitoring should be considered, the present meta-analysis shows consistent findings across subgroups tested including ejection fraction. While this reflects relative risk reductions related to PA pressure-guided treatment, higher risk groups such as NYHA class III patients and patients with recent HF hospitalization will most likely receive the larger absolute risk reductions. Despite the observed consistency in treatment effect, we underline that the procedure investigated is not without risk, although the complication rate was very low. The few complications were all easily manageable, and sensor failures were few, with a high

reliability of the technology over several years.[5-7] Similar rates of system-related adverse events were reported based upon post-marketing surveillance data in the U.S.[24]

The current meta-analysis has several limitations. First, individual data were only available from MONITOR-HF and aggregate published data from CHAMPION and GUIDE-HF were used. Second, the overall neutral results from the full data of the GUIDE-HF trial were used in this meta-analysis and not the COVID-19 sensitivity analysis (Supplements). Third, the trials included were performed in Northern America (predominantly USA, 4 sites Canada) and in the Netherlands and the technology and associated management may not be generalizable to all countries. Still, the additive effect on top of high levels of guideline-recommended medical therapy are reassuring for generalisability of these findings. Fourth, the three trials were underpowered to assess mortality, even combined in this meta-analysis. Fifth, moderate heterogeneity was present within the main and subgroup analyses. Nevertheless, the benefit of PA pressure monitoring remained consistent across most subgroups. Sixth, the lack of blinding in the three trials could have impacted the results through performance bias. Finally, successful use of the technology depends on two factors: 1) an adherent patient performing measurements at least several times a week, and 2) an involved physician or healthcare provider responding to these pressure measurements.

In conclusion, the current meta-analysis of three randomized clinical trials demonstrated a substantial benefit of remote monitoring of PA pressures in patients with chronic HF. Total HF hospitalizations were reduced by 30%. This benefit was consistent among subgroups and independent of ejection fraction.

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Figure legends

Figure 1. Meta-analyses of clinical endpoints

PA: Pulmonary Artery; RE: Random Effects; CI: Confidence Interval.

All rates are reported as events per patient-year.

*CHAMPION did not report data on urgent visits; †Calculated and included as Incidence Rate Ratio (IRR).

Figure 2. Subgroup analysis - Meta-analyses of clinical endpoints (Heart failure hospitalizations, urgent visits, and all-cause mortality)

All rates are reported as events per patient-year.

PA: Pulmonary Artery; RE: Random Effects; CI: Confidence Interval.

*CHAMPION did not report data on urgent visits; †Calculated and included as Incidence Rate Ratio (IRR); ‡CHAMPION only reported data for LVEF ≥40%.

Structured graphical abstract

The X-axis present the risk ratio. The Y-axis the data points of clinical endpoints as addressed. The dot is the point estimate of the hazard ratio pooled estimate and the bars corresponds to the 95% confidence interval. CI = confidence interval. EF = ejection fraction. HR = hazard ratio. HF = heart failure. HFH = heart failure hospitalization. M = months. NT-proBNP = N-terminal pro-B-type natriuretic peptide. NYHA = New York Heart Association. PA = pulmonary artery.

Table 1. Characteristics of included trials and patients

	CHAMPION	**GUIDE-HF**	**MONITOR-HF**
Enrolment period	2007 – 2009	2018 – 2019	2019-2022
Number of randomized patients	550	1000	348

Number of participating sites	64 in 1 country (U.S.)	140 in 2 countries (U.S. and Canada)	25 in 1 country (the Netherlands)
Design	Single-blind randomized clinical trial, all patients received the device	Single-blind randomized clinical trial, all patients received the device	Open-label randomized clinical trial, allocation to CM or SC (no device)
Blinding	Patients only	Patients only	None
Key inclusion criteria	NYHA III HFH <12 months Treatment according to guidelines (GRMT and/or device)	NYHA II-IV HFH <12 months and/or elevated natriuretic peptides levels Treatment according to guidelines (GRMT and/or device)	NYHA III HFH <12 months Treatment according to guidelines (GRMT and/or device)
Key exclusion criteria	eGFR <25 Recurrent PE/DVT CRT implantation <3 months	eGFR <25 Intolerance to all neurohormonal antagonists Current /recurrent PE/DVT CRT <3 months	eGFR <25 Recurrent PE/DVT CRT implantation <3 months
Mean follow-up time	17.6 months	10.8 months	21.4 months
Follow-up period	Entire study (randomized access period)	Fixed 12-month time-point	Entire study

Primary clinical endpoint	Total HFH (first and recurrent events)		Composite of total HF events (first and recurrent, including urgent HF visits) and mortality at 12 months.		Quality of life (KCCQ) Secondary: total HFH (first and recurrent events), urgent visits, mortality	
Reports on the following clinical endpoints	HFH Death		HFH Urgent visits with IV diuretics Death		HFH Urgent visit with IV diuretics Death	
Subgroup data available on	Total HFH only		Composite of HFH, urgent HF visits and death		Composite of HFH, urgent HF visits and death	
Control group	Sensor implant, but no monitoring		Sensor implant, but no monitoring		No sensor implanted	
Adjudication of clinical endpoints	Independent and masked CEC		Independent and masked CEC		Independent and masked CEC	
Baseline characteristics	**Treatment (N=270)**	**Control (N=280)**	**Treatment (N=497)**	**Control (N=503)**	**Treatment (N=176)**	**Control (N=172)**
Age, years (mean with SD, or median with IQR)	61 (13)	62 (13)	71 (64-76)	70 (64-77)	69 (61-75)	70 (61-75)
Male sex	194 (72%)	205 (73%)	310 (62%)	315 (63%)	138 (78%)	125 (73%)
NYHA functional						

class II III IV	0 (0%) 270 (100%) 0 (0%)	0 (0%) 280 (100%) 0 (0%)	146 (29%) 322 (65%) 29 (6%)	150 (30%) 328 (65%) 25 (5%)	0 (0%) 176 (100%) 0 (0%)	0 (0%) 172 (100%) 0 (0%)
Median EF	N.A.	N.A.	38% (25-55)	40% (25-55)	30% (23-40)	30% (22-43)
LVEF ≤40% >40%	222 (82%) 48 (18%)	234 (84%) 46 (16%)	273 (55%) 224 (45%)	258 (51%) 245 (49%)	134 (76%) 42 (24%)	127 (74%) 45 (26%)
NT-proBNP (pg/mL)	N.A.	N.A.	1480 (686-2743)	1274 (661-2318)	2377 (837-5153)	1905 (691-4444)
eGFR, mean (SD) or median (IQR)	60 (23)	62 (23)	51 (39-65)	49 (38-65)	48 (35-60)	48 (38-63)
Ischaemic aetiology	158 (59%)	174 (62%)	207 (42%)	190 (38%)	93 (53%)	81 (47%)
GRMT (all patients)						
ACEi/ARB/ARNi	205 (76%)	222 (79%)	319 (64%)	320 (64%)	144 (82%)	139 (81%)
ARNI	N.A.	N.A.	145 (29%)	139 (28%)	81 (46%)	81 (47%)
Beta-blocker	243 (90%)	256 (91%)	444 (89%)	442 (88%)	150 (85%)	142 (83%)
MRA	117 (43%)	114 (41%)	237 (48%)	216 (43%)	143 (81%)	144 (84%)

Diuretics*	248 (92%)	258 (92%)	474 (95%)	478 (95%)	168 (96%)	167 (97%)
SGLT2 inhibitor	N.A	N.A.	2 (<1%)	2 (<1%)	12 (7%)	21 (12%)
Device therapy						
ICD	88 (33%)	98 (35%)	213 (43%)	205 (41%)	94 (53%)	102 (59%)
CRT	91 (34%)	99 (35%)	142 (29%)	163 (32%)	46 (26%)	46 (27%)

CEC = Clinical Event Committee; ACEi= angiotensin-converting enzyme inhibitor; ARB= angiotensin-receptor blocker; ARNI = angiotensin-receptor-neprilysin inhibitor, MRA = mineralocorticoid receptor antagonist; ICD = implantable cardioverter defibrillator; CRT = cardiac resynchronisation therapy; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association; EF = ejection fraction; LVEF = left ventricular ejection fraction; PE = pulmonary embolism; DVT= deep venous thrombosis; NT-proBNP = N-terminal pro-B-type natriuretic peptide; HF = heart failure; HFH = heart failure hospitalization; SGLT2 = sodium-glucose cotransporter 2; SC = standard care; GRMT = guideline-recommended medical therapy; IV = intravenous; N.A. = not available; SD = standard deviation; IQR = interquartile range; KCCQ = Kansas City Cardiomyopathy Questionnaire

*Loop diuretics for CHAMPION and MONITOR-HF, unknown for GUIDE-HF

Table 2. Overview of exploratory endpoints

	CHAMPION		**GUIDE-HF**		**MONITOR-HF**	
	Treatment	**Control**	**Treatment**	**Control**	**Treatment**	**Control**
Endpoint						
Change in mean PAP (AUC)	-156 mmHg.days (6 months)	33 mmHg.days (6 months)	-792.7 mmHg.days (12 months)	-582.9 mmHg.days (12 months)	-1623.8 mmHg.days (12 months)	N.A.
Change in average daily mean PAP	-0.6 mmHg	0.1 mmHg	-2.4 mmHg	-1.8 mmHg	-4.4 mmHg	N.A.
Average mean PAP at 12 months	N.A.	N.A.	N.A.	N.A.	24.9 mmHg	N.A.

Mean change in KCCQ at 12 months (SD)	N.A.	N.A.	5 (21)	4 (23)	7 (25)	-1 (23)
Mean change in MLHFQ at 6 months (SD)*	-11 (25)	-7 (25)	N.A.	N.A	N.A.	N.A.
Freedom from device or system related complications (%)	98.6%		99%		97.7%	
Freedom from sensor failure (%)	100%		N.A.		98.8%	
Medication changes rate/month	1.52	0.63	1.03	0.61	0.93†	0.55

KCCQ = Kansas City Cardiomyopathy Questionnaire; MLHFQ = Minnesota Living with Heart Failure Questionnaire; PAP = pulmonary artery pressure; AUC = area under the curve; SD = standard deviation; N.A. = not available.

*Retrieved from the Food and Drug Administration Executive Summary (change not reported in main article). † Changes in guideline-recommended medical therapy and diuretics only (until 12 months of follow-up).

In combined analysis of the three trials, the freedom from device or system related complications was 98.9% and freedom from sensor failure was 99.7% in implanted patients.

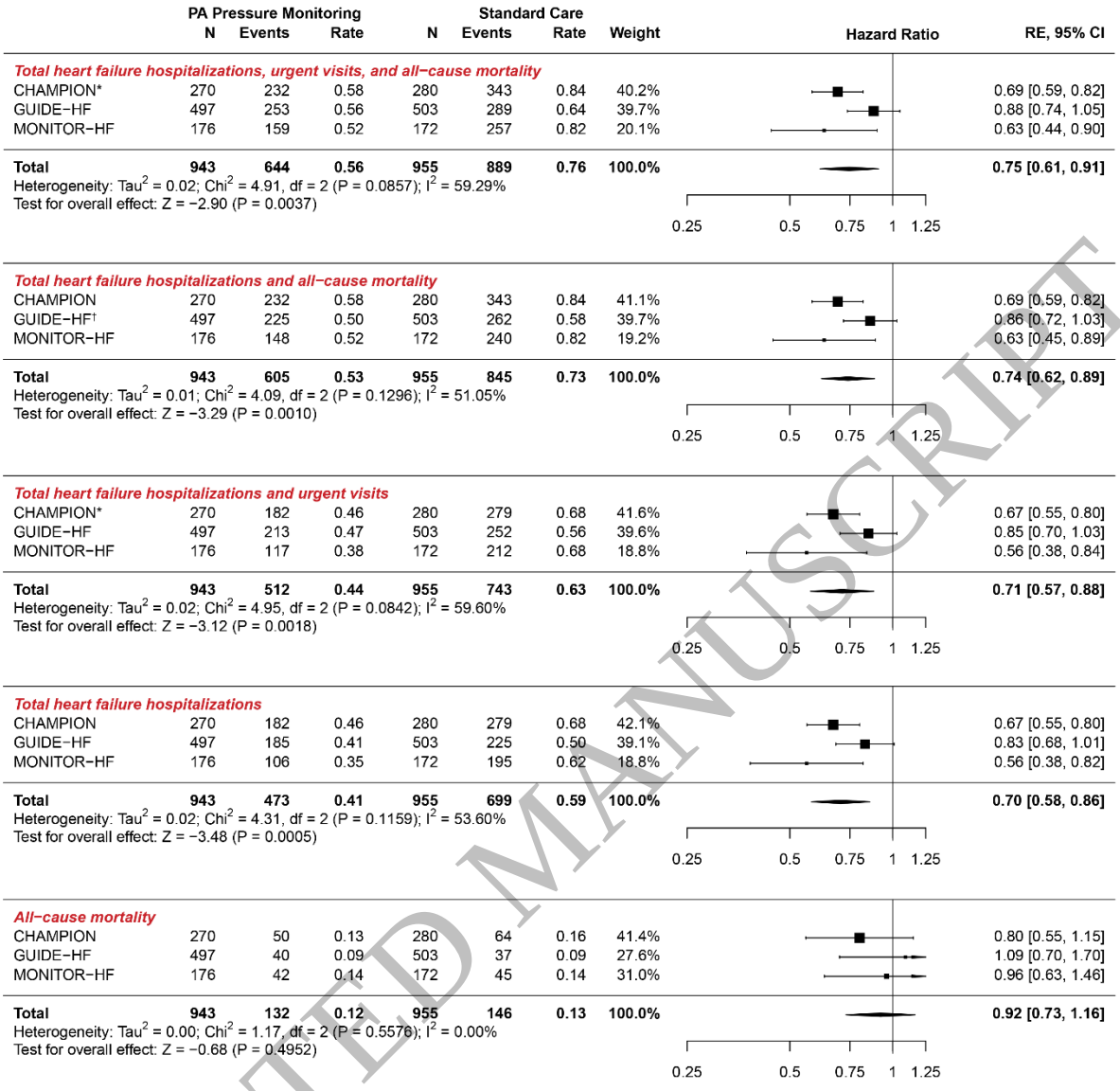

Figure 1
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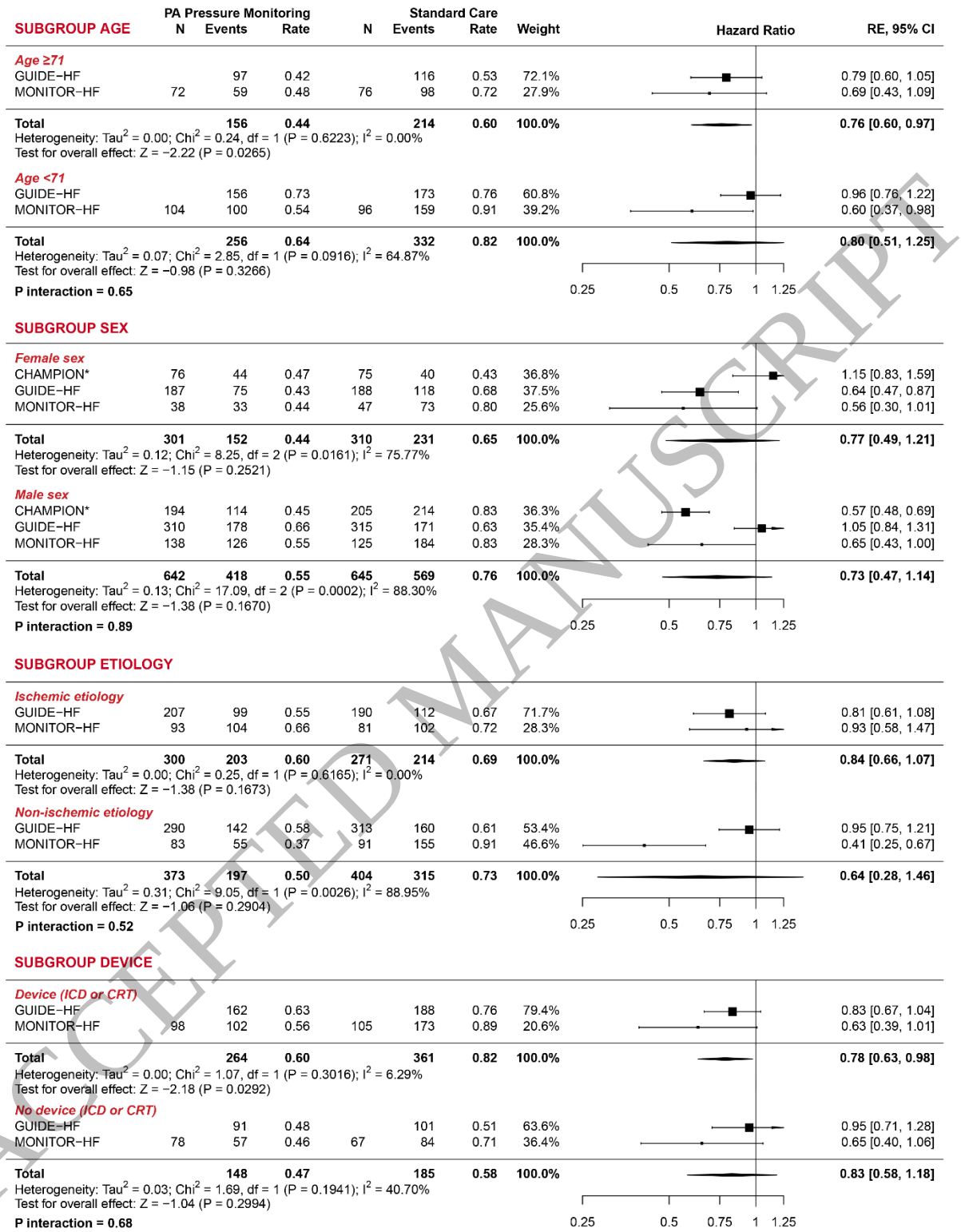


Figure 2a
159x209 mm (x DPI)

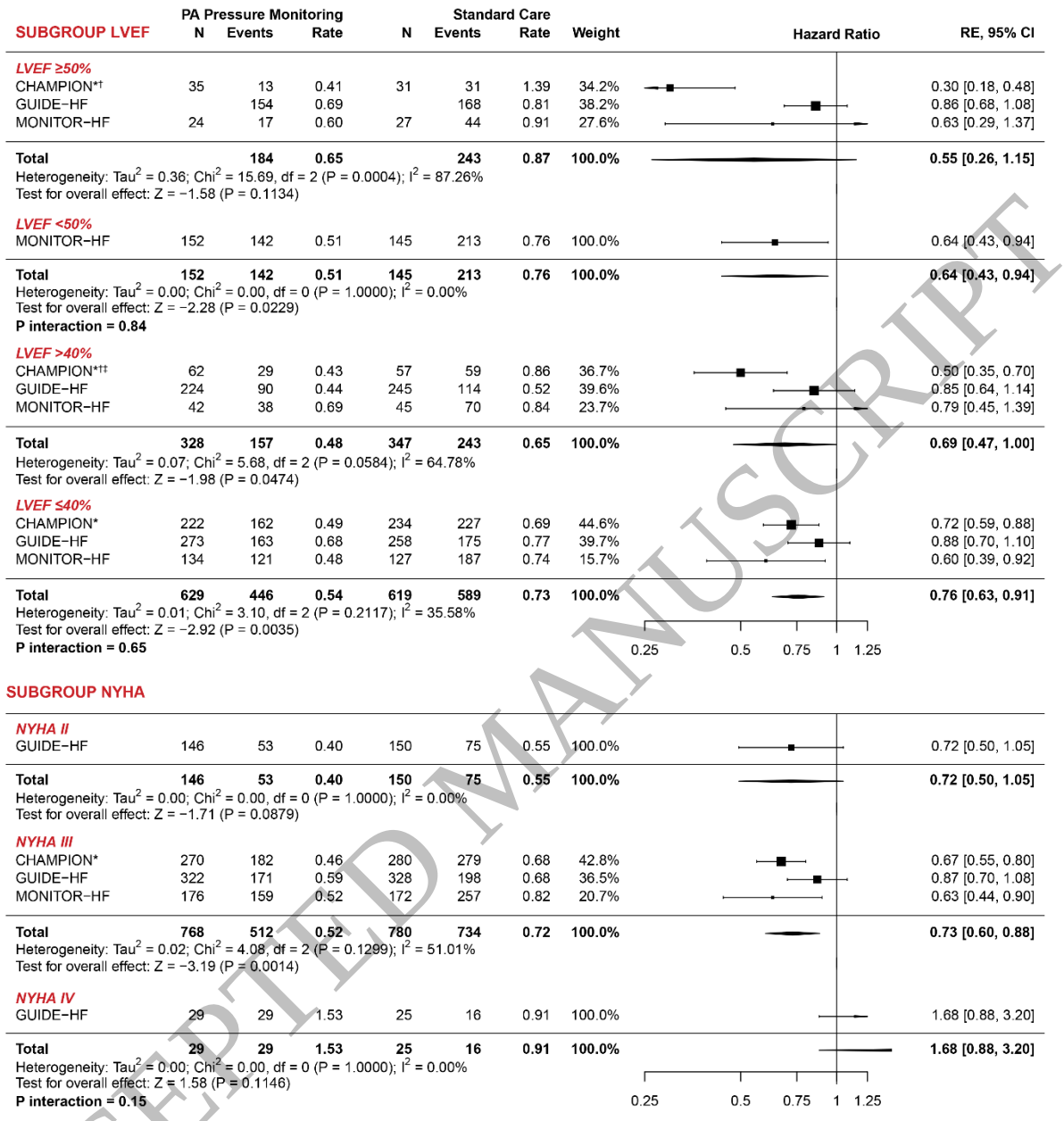


Figure 2b
159x170 mm (x DPI)

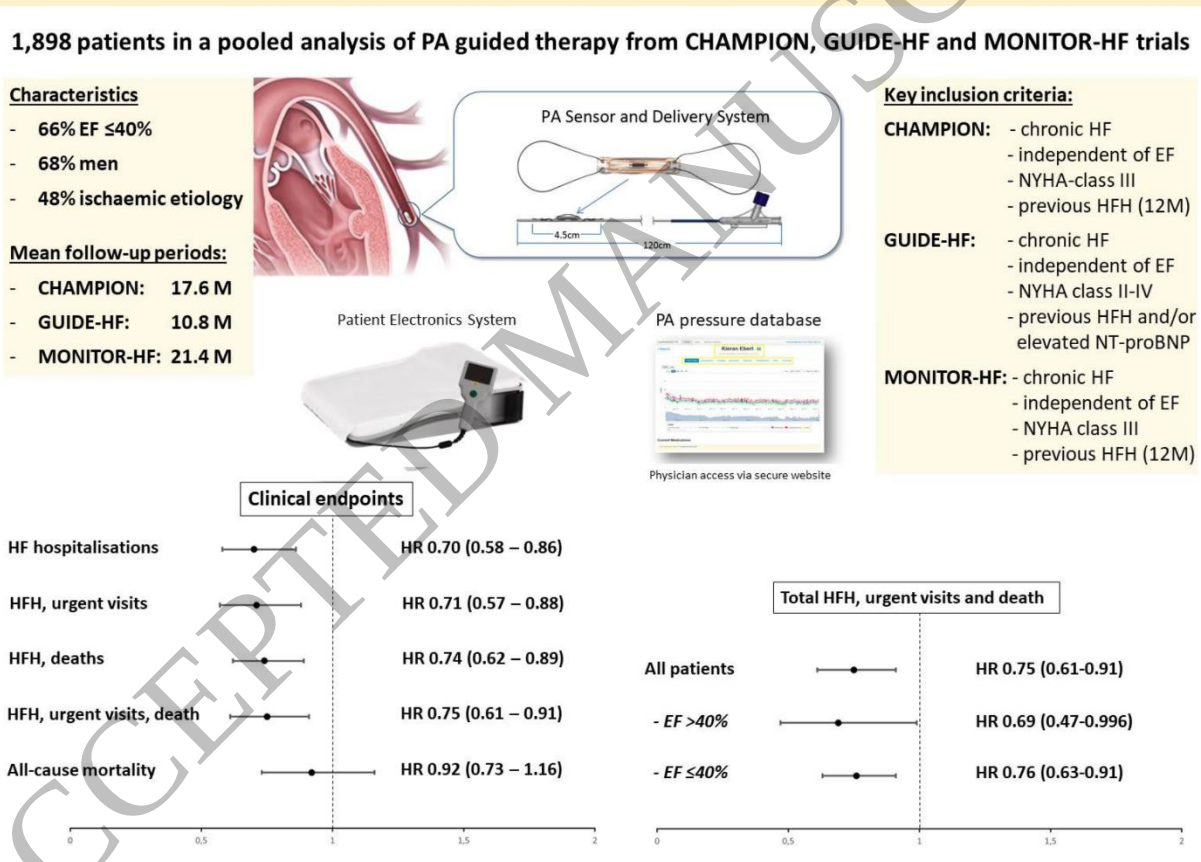
Structured graphical abstract

The X-axis present the risk ratio. The Y-axis the data points of clinical endpoints as addressed. The dot is the point estimate of the hazard ratio pooled estimate and the bars corresponds to the 95% confidence interval. CI = confidence interval. EF = ejection fraction. HR = hazard ratio. HF = heart failure. HFH = heart failure hospitalization. M = months. NT-proBNP = N-terminal pro-B-type natriuretic peptide. NYHA = New York Heart Association. PA = pulmonary artery.

Key question: What is the efficacy of management guided by remote pulmonary artery (PA) pressure monitoring in patients with heart failure (HF)?

Key finding: In a pooled analysis of 1,898 patients with chronic HF, PA pressure-guided management reduced the number of HF hospitalizations (HFH) by 30% but not mortality.

Take home message: Proactive management based on remote PA pressure monitoring reduces the risk of worsening HF and HFH.



Graphihcal Abstract
159x188 mm (x DPI)