# Telemonitoring for heart failure: a meta-analysis

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#### Abstract

Aims	Telemonitoring modalities in heart failure (HF) have been proposed as being essential for future organization and transition of HF care, however, efficacy has not been proven. A comprehensive meta-analysis of studies on home telemonitoring systems (hTMS) in HF and the effect on clinical outcomes are provided.
Methods and results	A systematic literature search was performed in four bibliographic databases, including randomized trials and observational studies that were published during January 1996–July 2022. A random-effects meta-analysis was carried out comparing hTMS with standard of care. All-cause mortality, first HF hospitalization, and total HF hospitalizations were evaluated as study endpoints. Sixty-five non-invasive hTMS studies and 27 invasive hTMS studies enrolled 36 549 HF patients, with a mean follow-up of 11.5 months. In patients using hTMS compared with standard of care, a significant 16% reduction in all-cause mortality was observed [pooled odds ratio (OR): 0.84, 95% confidence interval (CI): 0.77–0.93, <i>l</i> <sup>2</sup> : 24%], as well as a significant 19% reduction in first HF hospitalization (OR: 0.81, 95% CI 0.74–0.88, <i>l</i> <sup>2</sup> : 22%) and a 15% reduction in total HF hospitalizations (pooled incidence rate ratio: 0.85, 95% CI 0.76–0.96, <i>l</i> <sup>2</sup> : 70%).
Conclusion	These results are an advocacy for the use of hTMS in HF patients to reduce all-cause mortality and HF-related hospitaliza- tions. Still, the methods of hTMS remain diverse, so future research should strive to standardize modes of effective hTMS.

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#### **Structured Graphical Abstract**

#### **Key Question**

What is the efficacy of non-invasive and invasive telemonitoring systems on clinical endpoints including all-cause mortality, first heart failure hospitalization, and the total amount of heart failure hospitalizations?

#### **Key Finding**

In 36 549 patients (mean follow-up: 11.5 months), the use of (non-)invasive telemonitoring systems compared to standard of care reduced all-cause mortality by 16%, first heart failure hospitalizations by 19%, and total heart failure hospitalizations by 15%.

#### **Take Home Message**

Home telemonitoring systems can aid in outpatient management and lower all-cause mortality and heart failure hospitalization rates. This type of monitoring should therefore be strongly considered and may be integrated into current heart failure health care systems worldwide.

All-cause mortality	No. studies	Intervention	Standard of care		Odds ratio [95% CI]	2
Non-invasive	56	1337/11 472	1365/9985	-	0.85 [0.77, 0.94]	<b>9</b> %
Telemonitoring	31	656/4998	644/4454	-	0.91 [0.79, 1.05]	7%
Structured telephone support	18	375/4033	421/3421		0.75 [0.63, 0.89]	9%
Complex telemonitoring	9	306/2441	329/2355		0.88 [0.74, 1.05]	0%
Invasive	24	762/7239	584/5246	-	0.86 [0.70, 1.06]	50%
Cardiac implantable devices	17	429/4732	472/4323		0.84 [0.65, 1.08]	56%
Invasive haemodynamic monitoring	7	333/2507	112/923	-	0.96 [0.72, 1.27]	0%
Total	80	2099/18 861	1949/15 231	•	<b>0.84 [0.77</b> , 0.93]	23%
First heart failure hospitalization	า				Odds ratio [95% CI]	
Non-invasive	39	1639/7468	1766/6615		0.78 [0.70, 0.86]	26%
Telemonitoring	22	1008/3826	1091/3527		0.78 [0.67, 0.92]	39%
Structured telephone support	15	485/2947	599/2788		0.75 [0.65, 0.86]	0%
Complex telemonitoring	4	146/695	128/545		0.79 [0.50, 1.23]	48%
Invasive	15	562/2884	497/2268		0.89 [0.77, 1.03]	5%
Cardiac implantable devices	11	417/2410	440/2128		0.92 [0.79, 1.06]	1%
Invasive haemodynamic monitoring	4	145/474	57/140		0.68 [0.42, 1.09]	0%
Total	54	2201/10 352	2263/8883	•	0.81 [0.74, 0.88]	22%
Total/recurrent heart failure ho	spitalization	No. events pe	r person year		Incidence risk ratio [95% CI]	
Non-invasive	21	0.363	0.389		0.82 [0.70, 0.96]	70%
Telemonitoring	13	0.446	0.472		0.83 [0.67, 1.02]	77%
Structured telephone support	5	0.327	0.378		0.70 [0.46, 1.06]	66%
Complex telemonitoring	4	0.140	0.141		0.98 [0.79, 1.21]	0%
Invasive	13	0.385	0.296	-	0.90 [0.74, 1.10]	73%
Cardiac implantable devices	7	0.195	0.199		0.98 [0.76, 1.25]	67%
Invasive haemodynamic monitoring	6	0.605	0.584		0.75 [0.61, 0.91]	52%
Total	34	0.373	0.350		0.85 [0.76, 0.96]	70%
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Summary results for all-cause mortality, first heart failure hospitalization, and total/recurrent heart failure hospitalizations divided in invasive home telemonitoring systems and total.  $l^2$  represents heterogeneity between studies. CI, confidence interval.

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**Keywords** 

Telemonitoring • Heart failure • Non-invasive • Invasive • Mortality • Hospitalization

## Introduction

Heart failure (HF) is a chronic, complex, and progressive syndrome with a significant impact on public health. Globally, >60 million patients are affected by HF, and with the ageing of the general population, its prevalence is expected to increase in the forthcoming years.<sup>1</sup> Despite

advances in medical therapy, cardiac implantable electronic devices (CIEDs) and (long-term) mechanical circulatory support, the morbidity and mortality of HF remain high. Moreover, HF places a high burden on healthcare due to frequent outpatient follow-up and recurrent hospitalizations as a result of deterioration of HF.<sup>2</sup> The costs of HF care are projected to further increase, primarily driven by hospitalizations.

Therefore, there is a great need to develop effective strategies to reduce HF (re-)admissions and improve ambulatory HF care. Telemonitoring by means of home telemonitoring systems (hTMS) in this respect seems a promising option, which has gained even more momentum after the COVID-19 pandemic.<sup>3</sup> The hTMS is a system at home, which uses a non-invasive or invasive device to collect health data, such as vital signs and other diagnostic data.<sup>4</sup> While the number of studies—both randomized controlled trials (RCTs) and observational —reporting on hTMS has increased rapidly over the last years, their results and applicability have been uncertain due to heterogeneity. <sup>5–8</sup>

In 2015, a comprehensive Cochrane meta-analysis demonstrated a minor, albeit statistically significant reduction in all-cause mortality (ACM) through the use of structured telephone support (STS) and a significant reduction of both HF hospitalizations (HFH) and ACM by employing other non-invasive telemonitoring solutions.<sup>5</sup> However, the results are hampered by high heterogeneity between the individual studies due to the differences in methodology of the employed systems, some risk of bias, and the lack of a consistent effect in many studies in-dividually. Furthermore, there is a lack of studies pertaining to real-world data and repeated events in this meta-analysis. This conflicting evidence has led to a weak (class IIb, LoE B) recommendation for hTMS in the latest ESC Guidelines on Acute and Chronic HF.<sup>1</sup>

However, medical technology is ever evolving, and newer hTMS have been developed including invasive devices such as CIEDs incorporating new algorithms to detect deterioration of HF (e.g. Heartlogic) and invasive haemodynamic devices measuring the pulmonary artery pressure (e.g. CardioMEMS and Cordella). Also, non-invasive remote monitoring strategies have improved and are now more structured, like the system used in the TIM-HF2 trial.<sup>9</sup> Moreover, the COVID-19 pandemic has further accelerated the process of employing hTMS within the context of HF management.<sup>3</sup> In order to fill in the abovementioned knowledge gaps, it is of great importance to explore the ever-growing body of contemporary literature regarding this subject as the HF community is on the breach of an outbreak of telemonitoring integration in clinical practice. Therefore, we performed a systematic review and meta-analysis of both RCTs and observational studies up to July 2022, comparing hTMS with standard of care (SoC) in patients with HF and describe the efficacy on clinical endpoints.

## **Methods**

#### **Protocol and registration**

We performed a systematic review and meta-analysis of prospective studies (RCTs and observational studies) following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>10</sup> This review is registered in the International Prospective Register of Systematic Reviews with number CRD42022306677.

#### Search strategy and selection criteria

In collaboration with an expert librarian specialized in systematic searches, a literature search was carried out, including studies that were reported during 1996—1 July 2022, using Embase, Medline Ovid, Web of Science, and Cochrane CENTRAL. Keywords used in the search were 'heart failure', 'telemonitoring', 'implantable haemodynamic monitor', 'implantable cardioverter defibrillator', 'home monitoring', 'e-health', 'clinical trial', and 'prospective study'. The full search strategy is presented in the Supplementary material. Only published peer-reviewed original articles in the English language were included in our study. In addition, cross-referencing for any additional eligible studies was performed.

Studies were included if they contained any form of hTMS in chronic HF patients aged 18 years or older. We defined hTMS as a system in the home setting that employs a non-invasive or invasive device to remotely collect vital signs and other biometric or health-status related data (such as weight, blood pressure, heart rate, pulmonary pressure, ECG lead, and signs and symptoms with the exception of physical activity) and remotely transmits the collected data to a healthcare institution for further assessment by a healthcare provider. All other eligibility criteria are presented in Supplementary data online, *Table S1*.

Three reviewers (N.S., M.G., and D.A.) independently performed title and/or abstract screening in order to identify studies that potentially met the inclusion criteria. Results were then discussed, and any disagreement regarding eligibility was resolved by consensus. The full text of these studies was then retrieved and read independently by the same reviewers. Hereafter, each study was discussed in detail to decide upon the eligibility based on the inclusion and exclusion criteria. In case no consensus was reached, the principal investigator (J.B.) had the final say.

If eligible studies described the same population, only the study with the longest follow-up or most recent publication (with an active intervention arm) containing the entire population was included, unless different outcomes of interest were studied in each article. Studies describing a subgroup of the same population were excluded.

## Data extraction, home telemonitoring systems categories, and study endpoints

The following information was extracted from the main study reports: author, year of publication, country, study name, study design, enrollment years, sample size, age, sex, New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF) cut-off, HF aetiology, medication use, type of telemonitoring solution, comparison group, follow-up duration, and endpoints. If studies presented endpoints at more than one time point, endpoints from the latest time point were extracted. Data extraction was performed by M.G., N.S., and D.A., independently. Categories and definitions of non-invasive and invasive hTMS and subcategories are presented in Table 1. Non-invasive hTMS consisted of the following separate subcategories: telemonitoring (TM), structured telephone support (STS), and a combination of TM and STS (complex TM). Invasive hTMS consisted of the following separate subcategories: cardiac implantable electronic devices (CIED), and invasive haemodynamic monitoring (IHM) (Table 1). The primary outcomes for this meta-analysis were ACM, first HFH, and total number of HFHs.

#### Quality assessment

The Cochrane risk of bias (RoB2) and ROBINS-I were used to assess the risk of bias for RCTs and observational studies, respectively. Each article was assessed independently by at least two authors (N.S., M.G., and/or D.A.). In case no consensus was reached, a third author was available for consultation to give their conclusive opinion.

#### Statistical analysis

Continuous variables are presented as means and  $\pm$  standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate. Categorical variables are presented as counts and percentages. Random-effects methods were used to obtain an estimate of the pooled treatment effect, applying the DerSimonian and Laird procedure. For ACM and first HFH, we present the pooled treatment effect as odds ratio (OR) and corresponding 95% confidence interval (CI). The endpoint total HFHs is presented as incidence rate ratio (IRR) and 95% CI, which required person-years to be calculated. Person-years were calculated by using the mean or median follow-up time. If no mean or median follow-up time was available, the planned follow-up time was used, with the exception of patients who withdrew or died. To calculate person-years for these patients, we used half of the planned follow-up time.

Home Telemonitoring System		Definitions
Non-invasive hTMS		
– TM	Telemonitoring (individual)	Modality in which biometric data and/or health-related questionnaires are collected and sent to an HF clinic.
– STS	Structural telephone support	Modality in which HF patients are called by a HF nurse or cardiologist on a frequeness.
– Complex TM	Complex telemonitoring	Modality in which multiple TM is combined with STS and/or 24-h call center or m of other sub-modalities.
Invasive hTMS		
– CIED	Cardiac implantable electronic devices	Modality in which PM/ICD systems (optionally with impedance leads) are used to monitor the patient.
– IHM	Invasive haemodynamic monitoring	Modality in which invasive haemodynamic parameters are used, e.g. (pressure) sensor

hTMS, home telemonitoring system; TM, telemonitoring; STS, structural telephone support; HF, heart failure; CIED, cardiac implantable electronic device; PM, pacemaker; ICD, implantable cardiac defibrillator; IHM, invasive haemodynamic monitoring.

Sensitivity analyses were performed based on the specified categories of hTMS (Table 1). In this meta-analysis, we use ORs as the key effect measure, since the data that are required to obtain this measure can be directly derived from the study reports. It is true that in scenarios where the time varies, the hazard ratio (HR) is the preferred effect measure. However, HRs are only presented in 30% (endpoint hospitalization) to 37% (endpoint mortality) of studies, and must thus be estimated for the other studies. Therefore, we decided to present the (pooled) HRs as a sensitivity analysis and not as main analysis. Furthermore, another sensitivity analysis was carried out, dividing studies in short- (<3 months), mid- (3 to 12 months) and long-term (>12 months) follow-up time with respect to ACM and first HFH. Heterogeneity was assessed using the  $l^2$ -statistic and classified as not important ( $l^2$ :  $\leq 25\%$ ), moderate, ( $l^2$ : 26%–50%), substantial ( $l^2$ : 51%–75%), and considerable ( $l^2$ : >75%).<sup>11</sup> Funnel plots were generated and Egger regression tests performed to assess publication bias. All analyses were carried out using R Studio version 3.0 with the Metafor 3.4–0 package. A two-sided P-value of  $\leq 0.05$  was considered as statistically significant.

## Results

## **Study characteristics**

The literature search exposed, after duplicate removal, 6112 studies. A total of 91 studies that met all the eligibility criteria were included. In addition, one study was added from cross-referencing, resulting in a total of 92 studies.<sup>9,12–102</sup> The full PRISMA-flow diagram is shown in *Figure 1*. Within the 92 included studies, 36 549 HF patients were included, with a mean follow-up of 11.5 (range: 1.0–34.9) months. A total of 23 610 HF patients were included from 65 non-invasive hTMS studies, with a mean follow-up of 9.9 (range: 1.0–32.4) months (*Table 2*; Supplementary data online, *Table S2*). In 27 invasive hTMS studies, 12 939 HF patients were included and had a mean follow-up of 15.3 (range: 5.4–34.9) months (*Table 3*; Supplementary data online, *Table S3*). In non-invasive hTMS and invasive hTMS, 8 and 11 studies, respectively, were observational (either pre–post studies, matched studies, or single arm studies). All other studies were RCTs.

#### **Patient characteristics**

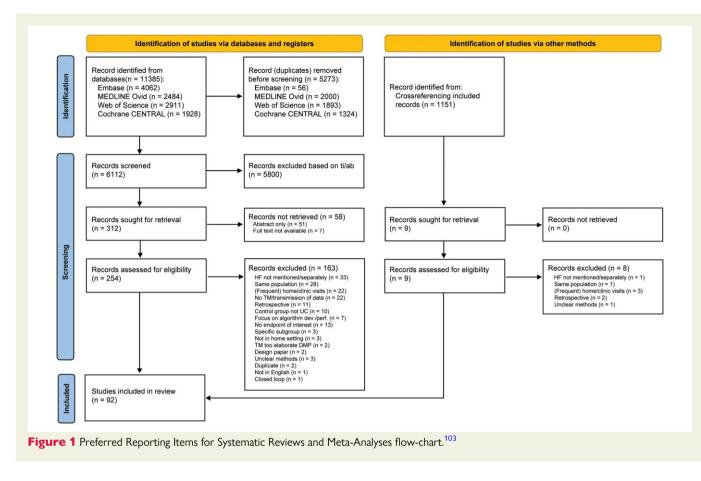
The mean age of patients in the non-invasive hTMS studies was  $68 \pm 13$  years; 67.8% were men; 46.6% were classified as NYHA classes III–IV. Of the non-invasive studies, 10 359, 8571, and 4680 patients were included in the TM, STS, and Complex TM categories, respectively (*Table 2*). In the invasive hTMS studies, the mean age was  $66 \pm 12$  years. Of these patients 75.8% were men, and 47.6% were classified as NYHA classes III–IV. In the invasive hTMS, 9445 and 3494 patients were included in CIED or IHM, respectively (*Table 3*). Details regarding the prescription of guideline-directed medical therapy (GDMT) for HF are presented in Supplementary data online, *Tables S4* and S5.

## Clinical efficacy of telemonitoring All-cause mortality

In 80 studies (both non-invasive and invasive) reporting ACM, 11.1% (2099/18 711) of the patients died in the hTMS group compared with 12.8% (1949/15 231) in the SoC group. Overall, hTMS showed a significant 16% reduction in ACM (OR: 0.84, 95% Cl: 0.77-0.93) (Figure 2). Within the treatment effect, the degree of heterogeneity across all studies was considered as not important however, significant ( $l^2 = 24\%$ ). The funnel plot and Egger's regression test showed no evidence of publication bias for this endpoint (see Supplementary data online, Figure \$1-\$6). Non-invasive hTMS showed a 15% reduction in ACM (OR: 0.85, 95% CI: 0.77–0.94,  $l^2 = 9\%$ ). This effect was primarily driven by the effect of STS. Invasive hTMS showed no significant reduction in mortality (OR: 0.86, 95% CI: 0.70–1.06,  $l^2 = 50\%$ ) (*Figure 2*). These results were consistent for both CIED and IHM studies. The results of the sensitivity analyses, in which HRs are obtained, showed similar results compared with the main analyses based on ORs (see Supplementary data online, Figure S7). Results dividing articles based on follow-up times are presented in Supplementary data online, Figure S8.

#### First heart failure hospitalization

In 54 studies reporting first HFH, 21.3% (2201/10 352) of the patients receiving hTMS and 25.5% (2263/8883) receiving SoC had at least one



HF admission. The pooled non-invasive and invasive studies showed a 19% reduction in first HFHs in patients using hTMS (OR: 0.81, 95% CI 0.74–0.88) (Figure 3). The degree of heterogeneity of these studies was considered to be not important and non-significant ( $l^2 = 22\%$ ). The funnel plot and Egger's regression test showed a significant asymmetry (see Supplementary data online, Figure S9-S13). The HF patients using non-invasive hTMS showed a 22% reduction in first HFH compared with SoC, with a moderate degree of heterogeneity (OR: 0.78, 95% CI: 0.70–0.86,  $l^2 = 26\%$ ). This effect was primarily driven by the STS and TM studies. In contrast, invasive hTMS showed no significant reduction compared with SoC, with a low degree of heterogeneity (OR: 0.89, 95% CI: 0.77–1.03,  $l^2 = 5\%$ ). These results were consistent within for both CIED and IHM studies. The results of the sensitivity analysis, in which HRs are obtained, showed similar results compared with the main analyses based on ORs (see Supplementary data online, Figure S14). Results dividing articles based on follow-up times are presented in Supplementary data online, Figure S15.

#### Total heart failure hospitalizations

In 34 studies reporting total HFHs, 3839 HFHs occurred over the course of 10 280 patient-years in patients receiving hTMS compared with 2929 HFHs over the course of 8358 patient-years in the control group. Receiving hTMS was found to be significantly associated with a 15% reduction in the occurrence of HFHs over time (IRR: 0.85, 95% CI 0.76–0.96) (*Figure 4*). Within the non-invasive studies, the use of hTMS was associated with an 18% reduction in the occurrence of HFH over time (IRR: 0.82, 95% CI 0.70–0.96). In contrast, in invasive studies, no significant effect in the occurrence of HFH was shown (IRR: 0.90, 95% CI 0.74–1.10). Within all invasive studies, the IHM

studies showed a significant reduction in the occurrence of HFH, whereas the CIED studies showed no effect. The degree of heterogeneity of both non-invasive and invasive studies was classified as substantial (non-invasive:  $l^2 = 70\%$ , invasive:  $l^2 = 73\%$ ). The funnel plot and Egger's regression test showed no evidence of publication bias for this outcome (see Supplementary data online, Figure S16–S21).

#### **Risk of bias assessment**

Quality assessment was performed using the RoB2 tool and ROBINS-I tool in 73 and 19 studies, respectively. A total of 20.5% of the RCTs were classified as high risk of bias. This was most frequently due to risk of bias in the domain 'missing outcome data' and 'deviations from the intervention' (see Supplementary data online, *Figure S22*). A total of 62.5% of the observational articles were classified as serious or critical risk of bias. This was frequently due to the high risk of confounding bias (see Supplementary data online, *Figure S23*).

## Discussion

In this state-of-the-art meta-analysis of 92 studies encompassing 36 549 patients with HF, we show that the use of hTMS modalities in HF patients is associated with a reduction in the risk of mortality, first HFH, and the total HFHs (Structured Graphical Abstract). We found a strong and consistent overall efficacy in reducing all clinical endpoints, with less heterogeneous results than previous meta-analyses on telemonitoring in chronic HF.<sup>5</sup> Overall, with our findings, the body of evidence for the use of hTMS in the management of these patients is further growing.

#### Table 2 Trial characteristics non-invasive studies

Author, year (study)	Country	Design	Enrollment	n	Age, years	Men, %	NYHA III–IV, %	LVEF cut-off	lschaemic aetiology, %
Angermann <b>et al.</b> , 2012 (INH) <sup>15</sup>	DE	RCT	2004–2007	715	68.6 <u>+</u> 12.2	71	40	ANY	58
Antonicelli <b>et al.</b> , 2008 <sup>16</sup>	IT	RCT	NA	57	78 ± 8.5	61	42	ANY	67
Baker <b>et al.</b> , 2011 <sup>17</sup>	US	RCT	2007–2009	605	60.7 ± 13.1	52	31	ANY	NA
Balk <b>et al.</b> , 2008 <sup>18</sup>	NL	RCT	2005–2006	214	66 (33–87) <sup>a</sup>	70	52	ANY	57
Bento <b>et al.</b> , 2009 <sup>19</sup>	BR	RCT	NA	40	57.5 ± 9.4	70	38	ANY	25
Blum <b>et al.</b> , 2014 (MCCD) <sup>20</sup>	US	RCT	2001–2005	203	72.5 ± 9	71	86	ANY	65
Boyne <b>et al.</b> , 2012 (TEHAF) <sup>13</sup>	NL	RCT	2007–2008	382	71.4 ± 11.2	59	43	ANY	50
Capomolla <b>et al.</b> , 2004 <sup>25</sup>	IT	RCT	2000–2001	133	57 <u>+</u> 10	88	33	ANY	41
Chaudhry <b>et al.</b> , 2010 (Tele-HF) <sup>26</sup>	US	RCT	NA	1653	61 (51–73)	58	57	ANY	51
Chen <b>et al.</b> , 2010 <sup>27</sup>	TW	NRCT	2003–2005	550	68.2 ± 15.5	71	NA	<45%	58
Cichosz <b>et al.</b> , 2018 (Danish telecare north) <sup>29</sup>	DK	RCT	NA	299	70.5	81	NA	ANY	NA
Cleland <b>et al.</b> , 2005 (TEN-HMS) <sup>30</sup>	NL/UK/ DE	RCT	2000–2002	426	67.2 <u>±</u> 11.6	77	34	<40%	78
Copeland <b>et al.</b> , 2010 <sup>32</sup>	US	RCT	2005	458	70.0 ± 10.8	99	44	ANY	35
Comin-Colet <b>et al.</b> , 2016 (iCOR) <sup>31</sup>	ES	RCT	2010–2012	178	74 <u>+</u> 11	59	54	ANY	35
Dar <b>et al.</b> , 2009 (Home HF) <sup>34</sup>	UK	RCT	2006–2007	182	71.0 ± 11.7	66	NA	ANY	55
De Lusignan <b>et al.</b> , (2001) <sup>35</sup>	UK	RCT	NA	20	75.2	NA	NA	ANY	NA
DeBusk <b>et al.</b> , 2004 <sup>37</sup>	US	RCT	1998–2001	462	72 <u>+</u> 11	51	50	ANY	51
Delaney <b>et al.</b> , 2013 <sup>38</sup>	US	RCT	2011–2012	100	NA	32	100	ANY	NA
Dendale <b>et al.</b> , 2012 (TEMA-HF) <sup>39</sup>	BE	RCT	2008–2010	160	75.8 <u>+</u> 9.7	65	NA	ANY	NA
DeWalt <b>et al.</b> , 2006 <sup>40</sup>	US	RCT	2001–2003	127	62.5 <u>+</u> 10.1	49	50	ANY	NA
Domingues <b>et al.</b> , 2010 <sup>42</sup>	BR	RCT	2005–2008	120	63 <u>+</u> 13	58	NA	<45%	NA
Galbreath <b>et al.</b> , 2004 <sup>43</sup>	US	RCT	1999–2003	1069	70.9 <u>+</u> 10.3	71	24	ANY	NA
Galinier <b>et al.</b> , 2020 (OSICAT) <sup>44</sup>	FR	RCT	2013–2016	990	70 ± 12.4	72	49	ANY	NA
Gambetta <b>et al.</b> , 2007 <sup>45</sup>	US	NRCT	NA	282	74.6 ± 13	56	NA	ANY	46
Gattis <b>et al.</b> , 1999 (PHARM) <sup>46</sup>	US	RCT	1996–1997	181	NA	68	33	<45%	NA
GESICA, Grancelli <b>et al.</b> , 2005 (DIAL)	AR	RCT	2000–2001	1518	65 ± 13.3	71	49	ANY	NA
Giordano <b>et al.</b> , 2009 <sup>47</sup>	IT	RCT	2002–2004	460	57 <u>+</u> 10	85	40	<40%	53
Gjeka <b>et al.</b> , 2021 <sup>48</sup>	US	RCT	2016–2018	62	68.6	49	NA	NA	NA
Goldberg <b>et al.</b> , 2003 (WHARF) <sup>49</sup>	US	RCT	1998–2000	280	59.1 <u>+</u> 15.3	68	100	≤35%	43
Ho <b>et al.</b> , 2007 <sup>52</sup>	TW	OBS (pre-post)	2004	247	60 ± 17	68	33	≤40%	49
Kalter-Leibovici <b>et al.</b> , 2017 <sup>55</sup>	IL	RCT	2007–2012	1360	70.7 ± 11.3	73	85	ANY	NA
Kashem <b>et al.</b> , 2008 <sup>56</sup>	US	RCT	NA	48	53.7 <u>+</u> 10.5	74	58	ANY	41
Köberich <b>et al.</b> , 2015 <sup>57</sup>	DE	RCT	2011–2013	110	61.7 ± 12.0	83	34	≤40%	53
Koehler <b>et al.</b> , 2011 (TIM-HF) <sup>58</sup>	DE	RCT	2008–2009	710	66.9 <u>+</u> 10.6	81	50	≤35%	56
Koehler <b>et al.</b> , 2018 (TIM-HF2) <sup>9</sup>	DE	RCT	2013–2017	1538	70.0 <u>+</u> 10.5	70	48	ANY	41

Author, year (study)	Country	Design	Enrollment	n	Age, years	Men, %	NYHA III–IV, %	LVEF cut-off	lschaemic aetiology, %
Kotooka <b>et al.</b> , 2018 (HOMES-HF) <sup>59</sup>	JP	RCT	2012–2013	181	66.2 ± 14.2	59	22	ANY	30
Krum <b>et al.</b> , 2013 (CHAT) <sup>60</sup>	AU	RCT	2003 -?	405	73.0 ± 10.5	63	41	<40%	NA
Laramee <b>et al.</b> , 2003 <sup>63</sup>	US	RCT	1999–2001	287	70.7 ± 11.8	54	36	<40%	71
Lyngå <b>et al.</b> , 2012 (WISH) <sup>67</sup>	SE	RCT	NA	319	73.6 ± 10.1	75	100	<50%	46
Mo <b>et al.</b> , 2021 <sup>68</sup>	CN	OBS	2019	300	53.1 ± 11.4	67	52	<40%	NA
Morguet <b>et al.</b> , 2008 <sup>70</sup>	DE	OBS (matched)	2004–2006	128	60.8 ± 10.2	88	25	≤60%	69
Mortara <b>et al.</b> , 2009 (HHH) <sup>71</sup>	UK/IT/PL	RCT	2002–2004	461	60 <u>±</u> 12	85	40	≤40%	56
Negarandeh <b>et al.</b> , 2019 <sup>73</sup>	IR	RCT	2016	80	NA	60	NA	NA	NA
Nouryan <b>et al.</b> , 2019 <sup>74</sup>	US	RCT	NA	89	83.2	32	NA	NA	NA
Nunes-Ferreira <b>et al.</b> , 2020 <sup>75</sup>	РТ	OBS (matched)	2016–2018	125	65.9 <u>+</u> 11.9	68	8	≤40%	38
Olivari <b>et al.</b> , 2018 (RENEWING HEALTH) <sup>76</sup>	EU	RCT	2011–2014	339	80.0 ± 7.0	63	52	ANY	43
Ong <b>et al.</b> , 2016 (BEAT-HF) <sup>77</sup>	US	RCT	2011–2013	1437	73	54	75	ANY	NA
Pedone <b>et al.</b> , 2015 <sup>78</sup>	IT	RCT	NA	96	80 ± 7	39	68	ANY	NA
Pekmezaris <b>et al.</b> , 2019 <sup>79</sup>	US	RCT	2014–2016	104	59.9 <u>+</u> 15.1	57	70	ANY	NA
Pérez-Rodríguez <b>et al.</b> , 2015	MX	RCT	2011–2012	40	68.2 <u>+</u> 7.5	65	100	NA	NA
Ramachandran <b>et al.</b> , 2007 <sup>80</sup>	IN	RCT	2005	50	44.6 <u>+</u> 11.9	78	26	<40%	12
Riegel <b>et al.</b> , 2002 <sup>81</sup>	US	RCT	NA	358	73.8 <u>+</u> 12.4	51	97	ANY	49
Ritchie <b>et al.</b> , 2016 <sup>82</sup>	US	RCT	2010–2011	346	63.3 <u>+</u> 13.1	51	NA	NA	NA
Roth <b>et al.</b> , 2004 <sup>84</sup>	IL	OBS	NA	118	74 <u>+</u> 9	70	78	<50%	NA
Scherr <b>et al.</b> , 2009 <sup>86</sup>	AU	RCT	2003–2008	120	NA	73	87	NA	NA
Schwarz <b>et al.</b> , 2008 <sup>87</sup>	US	RCT	NA	102	78.1 ± 7.1	48	79	ANY	NA
Seto <b>et al.</b> , 2012 <sup>88</sup>	CA	RCT	2009–2010	100	53.7 <u>+</u> 13.7	79	46	<40%	33
Soran <b>et al.</b> , 2008 (HFHC trial) <sup>92</sup>	US	RCT	2002–2005	315	76 ± 7	35	42	≤40%	55
Villani <b>et al.</b> , 2014 <sup>96</sup>	IT	RCT	NA	80	72 ± 3	74	NA	<40%	NA
Völler, <b>et al.</b> , 2022 <sup>97</sup>	DE	RCT	2010–2013	621	63.0 <u>+</u> 11.5	88	31	<40%	59
Vuorinen <b>et al.</b> , 2014 (Heart at Home) <sup>98</sup>	FI	RCT	2010–2012	94	58.1 ± 11.8	83	62	≤35%	NA
Wagenaar <b>et al.</b> , 2019 (e-VITA HF) <sup>99</sup>	NL	RCT	2013–2014	450	66.8 ± 11.0	74	20	NA	NA
Wakefield <b>et al.</b> , 2008 <sup>100</sup>	US	RCT	2002–2005	148	69.3 ± 9.6	99	72	NA	NA
Ware <b>et al.</b> , 2020 <sup>101</sup>	CA	OBS (pre-post)	2016–2019	315	58.3 ± 15.5	78	31	ANY	NA
Wita <b>et al.</b> , 2022 <sup>102</sup>	PL	RCT	2014–2017	63	66.1 ± 10.5	87	NA	NA	29

SD, standard deviation; IQR, interquartile range; NYHA, New York Heart Association classification; LVEF, left ventricular ejection fraction; DE, Germany; IT, Italy; US, United States; NL, The Netherlands; BR, Brazil; TW, Taiwan; DK, Denmark; UK, United Kingdom; ES, Spain; BE, Belgium; FR, France; AR, Argentina; IL, Israel; JP, Japan; AU. Australia; SE, Sweden; CN, China; PL, Poland; IR, Iran; PT, Portugal; EU, Europe; MX, Mexico; IN, India; CA, Canada; TH, Thailand; FI, Finland; RCT, randomized controlled trial; OBS, observational study; NRCT, non-randomized controlled trial; NA, not available. <sup>a</sup>Median (range).

Author, year (study)	Country	Design	Enrollment	n	Age, years	Men %	NYHA III–IV, %	LVEF cut-off	lschaemic aetiology, %
Abraham <b>et al.</b> , 2016 (CHAMPION) <sup>12</sup>	US	RCT	2007–2009	550	61.6 <u>+</u> 12.8	73	100 <sup>a</sup>	ANY	61
Adamson <b>et al.</b> , 2011 (REDUCEhf) <sup>13</sup>	US	RCT	NA	400	55 <u>+</u> 15	69	51	ANY	45
Angermann <b>et al.</b> , 2020 (MEMS-HF) <sup>14</sup>	NL/DE/IE	NRCT	2016-2018	234	67.9 <u>+</u> 10.7	78	100	ANY	53
Böhm <b>et al.</b> , 2016 <sup>21</sup>	DE	RCT	2008–2013	1002	66.3 ± 10.4	80	87 <sup>a</sup>	<35%	54
Boriani <b>et al.</b> , 2016 (MORE-CARE)	IT	RCT	2009–2014	918	66 <u>+</u> 10	76	62	ANY	44
Bourge et al., 2008 (COMPASS-HF) <sup>23</sup>	US	RCT	NA	274	58 ± 13.5	65	100	<50%	81
Chiu <b>et al.</b> , 2021 (REMOTE-CIED)	NL/DK	RCT	2013–2016	595	65 (59–73)	78	33 <sup>a</sup>	ANY	55
Cowie <b>et al.</b> , 2022 (COAST) <sup>33</sup>	UK	OBS	2017–2018	100	69 <u>±</u> 11.9	70	100	ANY	39
De Simone <b>et al.</b> , 2015 (EFFECT) <sup>36</sup>	IT	NRCT	2011–2013	987	66 ± 12.5	77	44	ANY	55
Domenichini <b>et al.</b> , 2015 (LIMIT-CHF) <sup>41</sup>	UK	RCT	2010–2013	80	67.9 <u>+</u> 11.4	94	NA	<50%	NA
Hansen <b>et al.</b> , 2018 (InContact) <sup>50</sup>	DE	RCT	2010–2014	210	63.8 ± 11.1	84	43	≤35%	59
Hindricks <b>et al.</b> , 2014 (IN-TIME) <sup>51</sup>	AU/EU/IL	RCT	2007–2010	664	65.5 ± 9.4	81	57	≤35%	NA
Jermyn <b>et al.</b> , 2017 <sup>54</sup>	US	OBS	2014–2016	66	NA	NA	100	NA	NA
Kurek <b>et al.</b> , 2017 (COMMIT-HF) <sup>61</sup>	PL	OBS (matched)	2009–2013	574	NA	84	41	≤35%	71
Landolina <b>et al.</b> , 2012 (EVOLVO) <sup>62</sup>	IT	RCT	2008–2009	200	NA	79	88	≤35%	46
Liberska <b>et al.</b> , 2016 <sup>64</sup>	PL	OBS	2006–2012	305	62.6	76	NA	≤35%	57
Lindenfeld <b>et al.</b> , 2021 (GUIDE-HF) <sup>65</sup>	US	RCT	2018–2019	1000	NA	63	70	ANY	40
Lüthje <b>et al.</b> , 2015 <sup>66</sup>	DE	RCT	2007–2011	176	65.9 <u>+</u> 12.0	77	43	ANY	51
Morgan <b>et al.</b> , 2017 (REM-HF) <sup>69</sup>	UK	RCT	2011–2014	1650	69.5 <u>+</u> 10.17	86	31	ANY	NA
Mullens <b>et al.</b> , 2010 <sup>72</sup>	BE/US	OBS	2007–2007	194	62.0 <u>±</u> 14.0	59	NA	NA	45
Sardu <b>et al.</b> , 2016 <sup>85</sup>	IT	RCT	2010–2014	191	72.2 ± 7.2	76	55	<35%	NA
Sharif <b>et al.</b> , 2022 (SIRONA 2) <sup>89</sup>	BE	OBS	2019–2021	70	71.0 ± 10.0	71	100	ANY	NA
Shavelle <b>et al.</b> , 2020 <sup>90</sup>	US	OBS (pre-post)	2014–2017	1200	69 <u>+</u> 12	62	NA	ANY	41
Smeets <b>et al.</b> , 2017 <sup>91</sup>	BE	OBS (registry)	2010–2013	282	71 ± 12	82	18	ANY	61
Tajstra <b>et al.</b> , 2020 (RESULT) <sup>93</sup>	PL	RCT	2015–2017	608	NA	81	22	<35%	64
Treskes <b>et al.</b> , 2021 <sup>94</sup>	BE/NL/ CH	NRCT (pre-post)	2018–2019	74	67.2 ± 10.3	84	32	ANY	36
Van Veldhuisen <b>et al.</b> , 2011 (DOT-HF) <sup>95</sup>	EU/AF/ ME/AS	RCT	NA	335	64 <u>±</u> 10	86	37	≤ 35%	56

SD, standard deviation; IQR, interquartile range; NYHA, New York Heart Association classification; LVEF, Left Ventricular Ejection Fraction; US, United States; NL, The Netherlands; DE, Germany; IE, Ireland; IT, Italy; DK, Denmark; AU, Australia; EU, Europe; PL, Poland; UK, United Kingdom; BE, Belgium; AT, Austria; CH, Switzerland; AF, Africa; ME, Middle East; AS, Asia; RCT, randomized controlled trial; OBS, Observational study; NRCT, non-randomized controlled trial; NA, not available. <sup>a</sup>Only NYHA III patients.

# Non-invasive home telemonitoring systems

This comprehensive meta-analysis is the first to demonstrate a significant consistent benefit of non-invasive hTMS in HF patients on reducing ACM, first HFH, and the total HFHs. However, considering the

separate modalities within non-invasive hTMS, limited power precluded the robustness that is needed to evaluate if each individual modality would reduce total HFHs. When dissecting the results of the different non-invasive hTMS modalities, we demonstrate that TM had a significant reduction in first HFH, while a tendency towards a reduced risk of ACM and total HFHs was observed. This is in contrast to a

Author(s) and Year	Events	vention Patients	Usua Events	ll care Patients	Weights		Odds Ratio [95% C
Non-invasive hTMS							
A. Telemonitoring							
- Boyne 2012 (TEHAF)	18	197	12	185	1.2%		1.41 [0.66, 3.00]
- Capomolla 2004	5	67	7	66	0.5%	<b>⊢</b>	0.70 [0.21, 2.33]
- Chaudhry 2010	92	826	94	827	4.1%	H#H	0.98 [0.72, 1.33]
- Cichosz 2018 (Danish TeleCare North)	7	145	8	154	0.7%	<b>⊢</b> •−−1	0.93 [0.33, 2.63]
- Cleland 2005 (TEN-HMS)*	28	168	20	85	1.6%	<b>⊢</b> ∎÷-	0.71 [0.38, 1.33]
- Comín-Colet 2016 (iCOR)	5	81	12	97	0.6%	<b>⊢</b>	0.50 [0.17, 1.48]
- Dar 2009 (Home-HF)	17	91	5	91	0.7%	·	3.40 [1.20, 9.61]
- De Lusignan 2001	2	10	3	10	0.2%		0.67 [0.09, 4.89]
- Dendale 2012 (TEMA-HF)	4	80	14	80	0.6%		0.29 [0.09, 0.91]
- Domingues 2010	8	57	13	63	0.8%	<b>⊢</b> •;-1	0.68 [0.26, 1.76]
- Galinier 2020 (OSICAT)	91	482	89	455	3.9%	ŀ≢⊣	0.97 [0.70, 1.33]
- Goldberg 2003 (WHARF)	11	138	26	142	1.2%	<b>├──</b>	0.44 [0.21, 0.92
- Kalter-Leibovici 2017	232	682	218	678	5.3%	H#H	1.06 [0.85, 1.31]
- Kashem 2008	1	24	1	24	0.1%		1.00 [0.06, 16.93
- Kotooka 2018 (HOMES-HF)	10	90	13	91	0.9%		0.78 [0.32, 1.86
- Lyngå 2012 (WISH)	5	166	8	153	0.6%		0.58 [0.18, 1.80]
- Nunes-Ferreira 2020	1	25					Not estimable
<ul> <li>Olivari 2018 (RENEWING HeALTH)</li> </ul>	55	229	24	110	2.1%	<b>⊢</b> ,∎	1.10 [0.65, 1.87]
- Pedone 2015	3	43	7	47	0.4%	<b>→</b>	0.47 [0.11, 1.93]
- Pérez-Rodríguez 2015	0	20	0	20			Not estimable
- Ritchie 2016	4	168	5	178	0.4%		0.85 [0.22, 3.21]
- Scherr 2009	0	66	1	54	0.1%	• • •	0.27 [0.01, 6.84]
- Schwarz 2008	4	51	7	51	0.5%		0.57 [0.16, 2.07]
- Seto 2012	3	50	0	50	0.1%		<ul> <li>7.00 [0.35, 139.03]</li> </ul>
- Soran 2008 (HFHC)	11	160	17	155	1.1%		0.63 [0.28, 1.38]
- Villani 2014 (ICAROS)	5	40	9	40	0.6%		0.56 [0.17, 1.80]
- Völler 2022	20	302	26	319	1.7%	⊢∎÷-1	0.81 [0.44, 1.49]
- Vuorinen 2014 (Heart at Home)	0	47	0	47			Not estimable
- Wagenaar 2019 (e-Vita HF)	8	150	4	150	0.5%		2.00 [0.59, 6.78]
- Ware 2020	5	315					Not estimable
- Wita 2022	1	28	1	32	0.1%	· · · · · · · · · · · · · · · · · · ·	I.14 [0.07, 19.13]
							-
Subtotal TM (95% CI)		4998		4454	30.6%	•	0.91 [0.79, 1.05]
Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 27.88, df = 26 (P = 0 Test for overall effect: $Z = -1.33$ (P = 0.18)	656 (.36); l <sup>2</sup> = 7%		644				
B. Structured Telephone Support							A / B / B / B
- Angermann 2012 (INH)	32	352	52	363	2.5%	⊢∎⊣	0.63 [0.40, 1.01]
- Baker 2011	0	303	2	302	0.1% 🗲	-	0.20 [0.01, 4.17
- Bento 2009	0	20	1	20	0.1%		0.33 [0.01, 8.67
- Cleland 2005 (TEN-HMS)*	27	173	20	85	1.6%	<b>⊢</b> •-∹{	0.66 [0.35, 1.25]
- Copeland 2010	20	220	56	238	2.0%	┝━━┤┊	0.39 [0.22, 0.66]
	21	228	29	234	1.8%	<b>⊢</b> ∎÷-1	0.74 [0.41, 1.34]
- DeBusk 2004	41			65	0.2%		
- DeWalt 2006	3	62	4		0.3%		0.79 [0.17, 3.66]
- DeWalt 2006 - Galbreath 2004		710	39	359	2.8%	⊢ ⊢∎-i	0.70 [0.45, 1.08]
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM)	3						0.70 [0.45, 1.08]
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL)	3 54	710	39	359	2.8%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25]
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009	3 54 3	710 90	39 5	359 91	2.8% 0.4%	<b>⊢</b>	0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13]
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007	3 54 3 116	710 90 760	39 5 122	359 91 758	2.8% 0.4% 4.5%	<b>⊢</b>	0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009	3 54 3 116 20	710 90 760 230	39 5 122	359 91 758	2.8% 0.4% 4.5%	<b>⊢</b>	0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007	3 54 3 116 20 13	710 90 760 230 247	39 5 122 32	359 91 758 230	2.8% 0.4% 4.5% 1.8%	<b>⊢</b>	0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49]
- DeValt 2006 - Galbreath 2004 - Gatis: 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015	3 54 3 116 20 13 1	710 90 760 230 247 64	39 5 122 32 3	359 91 758 230 64	2.8% 0.4% 4.5% 1.8% 0.2%		0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95]
- DeVValt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT)	3 54 3 116 20 13 1 17	710 90 760 230 247 64 188	39 5 122 32 3 16	359 91 758 230 64 217	2.8% 0.4% 4.5% 1.8% 0.2%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.33]
- DeVvalt 2006 - Galbreath 2004 - Gatis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003	3 54 116 20 13 1 17 13	710 90 760 230 247 64 188 141 106	39 5 122 32 3 16 15	359 91 758 230 64 217 146 160	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.33]
- DeValt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)*	3 54 3 116 20 13 1 17 13 9 1	710 90 760 230 247 64 188 141 106 40	39 5 122 32 3 16 15 9 5	359 91 758 230 64 217 146 160 40	2.8% 0.4% 4.5% 1.8% 0.2% ↓ 1.3% 1.2% 0.8% 0.2% ↓		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79
- DeValt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008	3 54 3 116 20 13 1 17 13 9	710 90 760 230 247 64 188 141 106 40 99	39 5 122 32 3 16 15 9	359 91 758 230 64 217 146 160 40 49	2.8% 0.4% 4.5% 1.8% 0.2% ↓ 1.3% 1.2% 0.8% 0.2% ↓ 1.1%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.93] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47]
- DeValt 2006 - Galbreath 2004 - Gatisi 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal STS (95% CI)	3 54 3 116 20 13 1 17 13 9 1 25	710 90 760 230 247 64 188 141 106 40	39 5 122 32 3 16 15 9 5 11	359 91 758 230 64 217 146 160 40	2.8% 0.4% 4.5% 1.8% 0.2% ↓ 1.3% 1.2% 0.8% 0.2% ↓		0.70 [0.45, 1.08] 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.93] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47]
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HIHL) <sup>®</sup> - Negarandeh 2019 - Wakefield 2008	3 54 3 116 20 13 1 17 13 9 1 25 375	710 90 760 230 247 64 188 141 106 40 99	39 5 122 32 3 16 15 9 5	359 91 758 230 64 217 146 160 40 49	2.8% 0.4% 4.5% 1.8% 0.2% ↓ 1.3% 1.2% 0.8% 0.2% ↓ 1.1%		0.33 [0.03, 3.29]
- DeWalt 2006 - Galbreath 2004 - Gatzis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring	3 54 3 116 20 13 1 17 17 17 13 9 1 25	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b>	39 5 122 32 3 16 15 9 5 11 421	359 91 758 230 64 217 146 160 40 49 <b>3421</b>	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% 1.1%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Net estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.44] 0.90 [0.41, 1.95] 1.51 [0.58, 3.33] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89]
- DeWalt 2006 - Galbreath 2004 - Gatis; 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtocal STS (95% CI) Subtocal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008	3 54 3 116 20 13 1 17 13 9 1 25 25 0.34); l <sup>2</sup> = 9%	710 90 760 230 247 64 188 141 141 106 40 99 <b>4033</b>	39 5 122 32 3 16 15 9 5 11 421	359 91 758 230 64 217 146 160 40 49 <b>3421</b> <b>3421</b>	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.93] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89]
- DeWalt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal STS (95% CI) Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Balk 2008	3 54 3 116 20 13 1 17 13 9 1 25 0.34); l <sup>2</sup> = 9%	710 90 760 220 247 64 188 141 106 40 99 <b>4033</b> 28 101	39 5 122 32 3 16 15 9 5 11 421 5 8	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% 1.1% 22.7%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Net estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.93] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89] 0.62 [0.14, 2.85] 1.26 [0.47, 3.39]
- DeWalt 2006 - Calbreath 2004 - Gatirs 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH) <sup>®</sup> - Negarandeh 2019 - Wakefield 2008 <b>Subtocal STS (9% CI)</b> Subtoral events Heterogeneity:Tau <sup>2</sup> = 0.01: Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Bilum 2014 (MCCD)	3 54 3 116 20 13 17 13 9 1 25 25 0.34); l <sup>2</sup> = 9%	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> 28 101 102	39 5 122 32 3 16 15 9 5 11 421 5 8 45	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.93] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89] 0.62 [0.14, 2.85] 1.26 [0.47, 3.39] 1.11 [0.68, 1.81]
- DeWalt 2006 - Galbreath 2004 - Gartis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH) <sup>e</sup> - Negarandeh 2019 - Wakefield 2008 <b>Subtotal STS (95% CI)</b> Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balk 2008 - Balk 2008 - Bilum 2014 (MCCD) - Koehler 2011 (TIM-HF)	3 54 3 116 20 13 1 17 13 9 1 25 25 375 25 3.34); l <sup>2</sup> = 9%	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> 28 101 102 334	39 5 122 32 3 16 15 9 5 11 421 5 8 45 55	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 3356	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% 1.1% 22.7%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 (003, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.68, 1.81 0.99 [0.66, 1.48
- DeWalt 2006 - Galbreath 2004 - Gattis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 <b>Subtotal events</b> Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balk 2008 - Bilum 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2)	3 54 3 116 20 13 1 17 13 9 1 25 0.34); l <sup>2</sup> = 9% 3 9 49 54 61	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> 28 101 102 354 796	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 9	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.33 0.20 [0.02, 1.79 1.12 [0.51, 2.47] 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.66, 1.81 0.67 [0.47, 0.34
- DeWalt 2006 - Galbreath 2004 - Garsis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HIHH)* - Wakefield 2008 Subtotal STS (95% Cl) Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0 Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Balk 2008 - Bilm 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2) - Morguet 2008	3 54 3 16 20 13 1 17 13 9 1 25 25 375 25 375 375 375 375 375 49 49 54 61 0	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> 28 101 102 354 796 32	39 5 122 32 3 16 15 9 5 11 421 5 8 8 45 55 89 4	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 0.3% 0.8% 2.4% 3.0% 3.7% 0.1% ⊢		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 (0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.33 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 1.26 [0.47, 3.39 1.11 [0.66, 1.48 0.97 [0.66, 1.48 0.67 [0.47, 0.34 0.33 [0.02, 6.29
- DeWalt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0 Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Bluk 2008 - Blum 2014 (MCCD) - Koehler 2018 (TIM-HF) - Koehler 2018 (TIM-HF2) - Mortara 2009 (HHH)*	3 54 3 116 20 13 1 17 13 9 1 25 3.34); l <sup>2</sup> = 9% 3 9 49 54 61 0 15	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 0.1% ⊢ 1.0%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.33 0.20 [0.02, 1.79 1.12 [0.51, 2.47, 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.68, 1.88 0.67 [0.47, 0.94 0.33 [0.02, 6.79 1.37 [0.58, 3.21]
- DeWalt 2006 - Calbreath 2004 - Gatirs 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)# - Negarandeh 2019 - Wakefield 2008 Subtotal STS (9% CI) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0 Test for overall effect: Z = -3.26 (P = 0.01) C. Complex Telemonitoring - Antonicelli 2008 - Balt 2008 Blum 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2) - Mortara 2009 (HHH)# - Mortara 2009 (HHH)#	3 54 3 16 20 13 1 17 13 9 1 25 25 375 25 375 375 375 375 375 49 49 54 61 0	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> 28 101 102 354 796 32	39 5 122 32 3 16 15 9 5 11 421 5 8 8 45 55 89 4	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 0.3% 0.8% 2.4% 3.0% 3.7% 0.1% ⊢		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.33] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89] 0.75 [0.63, 0.89] 0.75 [0.64, 1.48] 0.67 [0.47, 0.34] 0.79 [0.66, 1.48] 0.67 [0.47, 0.34] 0.33 [0.02, 6.79] 1.37 [0.58, 3.21] 0.89 [0.66, 1.48]
- DeWalt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0 Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Bluk 2008 - Blum 2014 (MCCD) - Koehler 2018 (TIM-HF) - Koehler 2018 (TIM-HF2) - Mortara 2009 (HHH)*	3 54 3 116 20 13 1 17 13 9 1 25 3.34); l <sup>2</sup> = 9% 3 9 49 54 61 0 15	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 0.1% ⊢ 1.0%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.33 0.20 [0.02, 1.79 1.12 [0.51, 2.47, 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.68, 1.88 0.67 [0.47, 0.94 0.33 [0.02, 6.79 1.37 [0.58, 3.21]
- DeWalt 2006 - Galbreath 2004 - Gartis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HIHH) <sup>e</sup> - Negarandeh 2019 - Wakefield 2008 Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Bilum 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2011 (TIM-HF) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2) - Morguez 2008 - Mortara 2009 (HIH) <sup>a</sup> - Ong 2016 (BEAT-HF) - Roth 2004 Subtotal Complex TM (95% CI)	3 54 3 116 200 13 1 17 13 9 1 25 25 375 25 375 25 375 375 375 375 375 137 49 54 61 0 15	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9 114	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 3366 775 96 160	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 0.1% ⊢ 1.0%		0.70 [0.45, 1.08 0.61 [0.14, 2.61] 0.95 [0.72, 1.25] 0.62 [0.35, 1.13] Not estimable 0.33 [0.03, 3.29] 1.23 [0.60, 2.49] 0.90 [0.41, 1.95] 1.51 [0.58, 3.33] 0.20 [0.02, 1.79] 1.12 [0.51, 2.47] 0.75 [0.63, 0.89] 0.75 [0.63, 0.89] 0.75 [0.64, 1.48] 0.67 [0.47, 0.34] 0.79 [0.66, 1.48] 0.67 [0.47, 0.34] 0.33 [0.02, 6.79] 1.37 [0.58, 3.21] 0.89 [0.66, 1.48]
- DeWalt 2006 - Galbreath 2004 - Gastics 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHHH)* - Negarandeh 2019 - Wakefield 2008 Subtotal events Heterogeneity-Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0 Test for overall effect: Z = -3.26 (P = 0.001) C. Complex Telemonitoring - Antonicelli 2008 - Ballu 2004 Blum 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2) - Morguet 2008 - Mortara 2009 (HHH)* - Ong 2016 (BEAT-HF) - Roth 2004	3 54 3 16 20 13 17 13 9 1 25 25 2.34); l <sup>2</sup> = 9% 3 9 49 54 61 0 15 100 15	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> <b>28</b> 101 102 354 796 32 195 715 118	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9	339 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160 722	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 0.8% 0.8% 0.8% 0.8% 0.8% 1.0% 1.0% 4.3%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.48, 1.81 0.97 [0.66, 1.14 0.33 [0.02, 6.29 1.37 [0.58, 3.21] 0.89 [0.66, 1.16]
- DeWalt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH) <sup>®</sup> - Negarandeh 2019 - Wakefield 2008 <b>Subtocal STS (9% CI)</b> Subtocal events Heterogeneity:Tau <sup>1</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balte 2008 Bilum 2014 (MCCD) - Koehler 2011 (TIM-HF) - Koehler 2018 (TIM-HF2) - Morgara 2009 (HHH) <sup>®</sup> - Ong 2016 (BEAT-HF) - Roth 2004 Subtocal events Heterogeneity:Tau <sup>2</sup> < 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) Subtocal Non-invasive hTMS (95% CI)	$\begin{array}{c} 3\\ 54\\ 3\\ 116\\ 20\\ 13\\ 17\\ 13\\ 9\\ 1\\ 25\\ 3.34); \ l^2=9\%\\ \begin{array}{c} 375\\ 9\\ 49\\ 54\\ 61\\ 0\\ 15\\ 100\\ 15\\ 5); \ l^2=0\%\\ \end{array}$	710 90 760 230 247 64 188 141 106 40 99 <b>4033</b> <b>28</b> 101 102 354 796 32 195 715 118	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9 114	339 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160 722	2.8% 0.4% 4.5% 1.8% 0.2% 1.3% 1.2% 0.8% 0.2% ⊢ 1.1% 22.7% 0.3% 0.8% 0.8% 0.8% 0.8% 0.8% 0.8% 1.0% 1.0% 4.3%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.48, 1.81 0.97 [0.66, 1.14 0.33 [0.02, 6.29 1.37 [0.58, 3.21] 0.89 [0.66, 1.16]
- DeValt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH) <sup>a</sup> - Negarandeh 2019 - Wakefield 2008 <b>Subtocal STS (9% CI)</b> Subtoral events Heterogeneity:Tau <sup>2</sup> = 0.01: Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balta 2008 - Mortara 2009 (HHH) <sup>a</sup> - Ong 2016 (BEAT-HF) - Roth 2004 <b>Subtocal events</b> Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - 1.43 (P = 0.15) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events - Lastria - L	$\begin{array}{c} 3\\ 54\\ 3\\ 116\\ 20\\ 13\\ 17\\ 13\\ 9\\ 1\\ 25\\ 3.34); \ l^2=9\%\\ \begin{array}{c} 375\\ 9\\ 49\\ 54\\ 61\\ 0\\ 15\\ 100\\ 15\\ 5); \ l^2=0\%\\ \end{array}$	710 90 760 220 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195 715 118 <b>2441</b>	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9 114	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160 722 <b>2355</b>	2.8% 0.4% 4.5% 1.3% 1.3% 1.2% 0.8% 0.2% 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 1.5.6%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 (003, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.68, 1.48 0.97 [0.66, 1.48 0.67 [0.47, 0.94 0.33 [0.02, 6.29 1.37 [0.58, 3.21] 0.89 [0.64, 1.18 Not estimable 0.88 [0.74, 1.05
- DeWalt 2006 - Galbreath 2004 - Gastis 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HIHI)* - Wakefield 2008 <b>Subtotal STS (95% CI)</b> Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balk 2008 - Balk 2008 - Bum 2014 (MCCD) - Koehler 2018 (TIM-HF2) - Koehler 2018 (TIM-HF2) - Koehler 2018 (TIM-HF2) - Morguet 2008 - Mortara 2009 (HIH)* - Ong 2016 (BEAT-HF) - Roth 2004 <b>Subtotal Complex TM (95% CI)</b> Subtotal events Heterogeneity:Tau <sup>2</sup> < 0.001; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) Test for overall effect: Z = -1.43 (P = 0.15)	$\begin{array}{c} 3\\ 54\\ 3\\ 116\\ 20\\ 13\\ 17\\ 13\\ 9\\ 1\\ 25\\ 3.34); \ l^2=9\%\\ \begin{array}{c} 375\\ 9\\ 49\\ 54\\ 61\\ 0\\ 15\\ 100\\ 15\\ 5); \ l^2=0\%\\ \end{array}$	710 90 760 220 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195 715 118 <b>2441</b>	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9 114	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160 722 <b>2355</b>	2.8% 0.4% 4.5% 1.3% 1.3% 1.2% 0.8% 0.2% 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 1.5.6%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13] Not estimable 0.33 (0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.33 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 1.26 [0.47, 3.39 1.11 [0.68, 1.64 0.67 [0.47, 0.94 1.37 [0.58, 3.21] 0.99 [0.66, 1.16 0.96 [0.66, 1.16 Not estimable 0.88 [0.74, 1.05]
- DeValt 2006 - Galbreath 2004 - Gatris 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Köberich 2015 - Krum 2013 (CHAT) - Laramee 2003 - Mortara 2009 (HHH) <sup>a</sup> - Negarandeh 2019 - Wakefield 2008 <b>Subtocal STS (9% CI)</b> Subtoral events Heterogeneity:Tau <sup>2</sup> = 0.01: Chi <sup>2</sup> = 17.67, df = 16 (P = 0) Test for overall effect: Z = -3.26 (P = 0.001) <b>C. Complex Telemonitoring</b> - Antonicelli 2008 - Balta 2008 - Mortara 2009 (HHH) <sup>a</sup> - Ong 2016 (BEAT-HF) - Roth 2004 <b>Subtocal events</b> Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - 1.43 (P = 0.15) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events Heterogeneity:Tau <sup>2</sup> - 0.01; Chi <sup>2</sup> = 5.88, df = 7 (P = 0.5) - Subtocal events - Lastria - L	$\begin{array}{c} 3\\ 54\\ 3\\ 116\\ 20\\ 13\\ 17\\ 13\\ 9\\ 1\\ 25\\ 3.34 ); \ l^2 = 9\%\\ \begin{array}{c} 375\\ 9\\ 49\\ 54\\ 61\\ 0\\ 15\\ 100\\ 15\\ 5); \ l^2 = 0\%\\ \end{array}$	710 90 760 220 247 64 188 141 106 40 99 <b>4033</b> <b>4033</b> <b>4033</b> <b>28</b> 101 102 354 796 32 195 715 118 <b>2441</b>	39 5 122 32 3 16 15 9 5 11 421 421 5 8 8 45 55 89 4 9 114	3359 91 758 230 64 217 146 160 40 49 <b>3421</b> 29 113 104 356 775 96 160 722 <b>2355</b>	2.8% 0.4% 4.5% 1.3% 1.3% 1.2% 0.8% 0.2% 1.1% 22.7% 0.3% 0.8% 2.4% 3.0% 3.7% 1.5.6%		0.70 [0.45, 1.08 0.61 [0.14, 2.61 0.95 [0.72, 1.25 0.62 [0.35, 1.13 Not estimable 0.33 [0.03, 3.29 1.23 [0.60, 2.49 0.90 [0.41, 1.95 1.51 [0.58, 3.93 0.20 [0.02, 1.79 1.12 [0.51, 2.47 0.75 [0.63, 0.89 0.62 [0.14, 2.85 1.26 [0.47, 3.39 1.11 [0.66, 1.48 0.97 [0.66, 1.48 0.67 [0.47, 0.39 1.37 [0.58, 3.21] 0.89 [0.74, 1.05

Odds Ratio (log scale)

**Figure 2** Forest plot all-cause mortality. TM, telemonitoring; STS, structured telephone support; complex TM, complex telemonitoring; hTMS, home telemonitoring systems; CIED, cardiac implantable electronic devices; IHM, invasive haemodynamic monitoring. \*The studies of Mortara *et al.*<sup>71</sup> and Cleland *et al.*<sup>30</sup> have multiple intervention arms. Therefore, those articles are presented more than once in the forest plot. In the subtotal non-invasive home telemonitoring systems and the total pooled analysis, event rates of each study arm are added together. \*\*From the article of Lindenfeld *et al.*, the post-COVID analysis was used, to avoid bias in observed outcomes due to the COVID pandemic.

Cochrane review,<sup>5</sup> which demonstrated a significant benefit for both ACM and HFH. This difference could be explained by the reclassification of the Tele-HF study from STS to TM.<sup>26</sup> The benefits on first HFHs are in line with Inglis et al.<sup>5</sup> For complex TM, this review was

not able to demonstrate a clear benefit, which may be due to the lower number of studies in this category. Nevertheless, complex TM systems may prove beneficial as shown in the TIM-HF2 trial.<sup>9</sup> Within this RCT, patients were monitored using a combination of TM and STS and

Events	Patients	Events	Patients	Weights		
	1120-030 0421 19:0-03 12		racients			Odds Ratio [95%
7	202	9	198	0.7%	i	0.76 [0.28, 2.0
						0.92 [0.63, 1.3
						1.15 [0.72, 1.8
						0.89 [0.47, 1.6
					1.5.1	0.70 [0.41, 1.
						1.27 [0.27, 6.
						1.35 [0.25, 7.
					· · · · · · · · · · · · · · · · · · ·	0.37 [0.18, 0.
						0.22 [0.12, 0.
		8	101	0.7%		0.89 [0.31, 2.
40	305					Not estimat
8	87	6	89	0.6%		1.36 [0.45, 4.
128	824	152	826	4.8%	Hei	0.84 [0.65, 1.
					· · · · ·	0.92 [0.32, 2.
		7				2.22 [0.91, 5.
						1.01 [0.51, 1.
						1.26 [0.62, 2.
19	168	15	16/	1.3%		1.20 [0.02, 2.
120	4732	470	4323	24.4%	•	0.84 [0.65, 1.
04); I <sup>z</sup> = 56%						
50	270	64	280	3.0%		0.81 [0.54, 1.
		04	200	3.0%		Not estimat
			1.40	1.00/		1.23 [0.53, 2.
		11	140	1.0%		
						Not estimat
		37	503	2.5%		1.09 [0.69, 1.
						Not estimat
186	1200					Not estimal
333 I <sup>2</sup> =0%	2507	112	923	6.5%	•	0.96 [0.72, 1.
	0000		22/22	1000000		
762	7239	584	5246	30.9%	•	0.86 [0.70, 1.
1- = 50%						
10.01014	18711		15231	100%	•	0.84 [0.77, 0.
2099   <sup>2</sup> = 24%		1949				
				-		7
				0.01	0.1 I	10
					Odds Ratio (log scale)	
	128 7 19 18 19 04); $1^2 = 56\%$ 50 31 13 10 40 3 186 $1^2 = 0\%^{333}$ $1^2 = 0\%^{23}$	$\begin{array}{c} 40 & 437 \\ 19 & 300 \\ 25 & 499 \\ 4 & 41 \\ 5 & 102 \\ 10 & 333 \\ 14 & 287 \\ 7 & 99 \\ 40 & 305 \\ 8 & 87 \\ 128 & 824 \\ 7 & 89 \\ 19 & 155 \\ 128 & 824 \\ 7 & 89 \\ 19 & 155 \\ 18 & 299 \\ 19 & 168 \\ 4732 \\ 429 \\ 19 & 168 \\ 4732 \\ 429 \\ 19 & 168 \\ 4732 \\ 429 \\ 19 & 168 \\ 4732 \\ 429 \\ 19 & 168 \\ 10 & 100 \\ 40 & 497 \\ 3 & 70 \\ 10 & 100 \\ 40 & 497 \\ 3 & 70 \\ 10 & 100 \\ 40 & 497 \\ 3 & 70 \\ 186 & 1200 \\ 12 \\ 12 \\ 12 \\ 10 \\ 12 \\ 10 \\ 10$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

Figure 2 Continued

provided with 24/7 telemedical support. This complex intervention led to a reduction in the percentage of days lost due to HFH and ACM. Nevertheless, one potential limitation of complex TM systems is that they are labour-intensive and therefore probably not feasible in every healthcare system. The modality described in the TIM-HF2 study requires extra personnel due to the large amount of provided data in combination with continuous accessibility of telemedical support. A desirable solution to this would be automated interpretation of such data, which, obviously, is challenging. In addition, the effects of less labour-intensive alternatives as STS and TM were overall stronger than complex TM. This observation might be explained by differences in the healthcare system and therefore the SoC of the included studies. The CHAMP-HF and CHECK-HF registries, both containing quality-of-care data from two developed western countries (USA and the Netherlands), show substantial differences regarding guideline adherence, prescription levels, and target dose levels of GDMT and devices, which can be related to differences in healthcare system, insurance, and care access.<sup>104</sup>

Our results show a significant overall reduction in the incidence of endpoints in patients with HF through the use of non-invasive hTMS. There is, however, some heterogeneity present between studies. On the other hand, the degree of heterogeneity, regarding ACM and first HFH, of the studies included in this meta-analysis is considerably lower as compared with previous meta-analyses. Interestingly, the effect on the outcomes attenuates in the period after publication of Inglis *et al.*<sup>5</sup> A potential explanation for this heterogeneity is that studies that include chronic 'stable' HF patients (NYHA classes I–II), who

experience less events and have a better overall prognosis, will show a smaller effect size on the short term than studies including unstable HF patients who recently had an HF admission and therefore are at a greater risk of a recurrent event. Unfortunately, as these data were not always presented in detail, we were unable to analyse these differences in the context of the current study. Also, we selected many new studies (up to July 2022) especially from the last 5 years with a more structured and integrated approach of hTMS, and this time window is important with the expansion of GDMT between guidelines.

#### Invasive home telemonitoring systems

This meta-analysis was not able to demonstrate an overall benefit of invasive hTMS on all outcomes. Sensitivity analysis of the different invasive hTMS modalities showed no benefit of CIED monitoring on ACM and HFHs, while IHM showed a significant reduction in total HFHs. The lack of effect of CIED monitoring is important to note. In our meta-analysis, we did not differentiate between CIED with or without impedance measurements to investigate the potential differences in effect. However, a recent meta-analysis by Zito *et al.*<sup>105</sup> showed no reduction in risk of ACM and HFH using CIED with or without impedance measurements. Additionally, this meta-analysis presented similar results regarding IHM, with several studies showing a remarkably strong result especially those with specifically designed sensors. These findings can be explained by the pathogenesis of HF deterioration. It is well known that increasing filling pressures is one of the first parameters for deterioration of HF, even before overt clinical Author(s) and Year

ithor(s) and Year	Events	Patients	Events	Patients	Weights		Odds Ratio [95% C
on-invasive hTMS						1	
A. Telemonitoring           Boyne 2012 (TEHAF)           - Chaudhry 2010           - Cleand 2005 (TEN-HMS)*           - Comin-Colet 2016 (ICOR)           - Dar 2009 (Home-HF)           - Delaney 2013           - Galmiert 2003 (OSICAT)           - Gamberta 2007           - Gaite 2007           - Gaite 2017							
- Boyne 2012 (TEHĂF)	18	197	25 223	185 827	1.5%	H=	0.68 [0.36, 1.2 1.02 [0.83, 1.2
- Chaudhry 2010	227	826	223	827	7.0%	H	1.02 0.83, 1.2
- Cleland 2005 (TEN-HMS)*	40	168	24 32	85 97	1.8%		0.84 [0.48, 1.4
Dar 2009 (Hemory HE)	11	81 91	32	97	0.9%		102 (0.83, 12) 0.84 (0.48, 14) 0.41 (0.20, 0.6 1.70 (0.74, 3.9) 0.43 (0.10, 74, 3.9) 0.43 (0.10, 74, 3.9) 0.26 (0.06, 1.0) 0.26 (0.06, 1.0) 0.26 (0.06, 1.0) 0.92 (0.76, 1.1) 0.20 (0.04, 1.0) 0.96 (0.48, 1.9) 1.21 (0.51, 2.8) Not estimable 0.88 (0.57, 1.3) 0.79 (0.24, 1.5) 0.53 (0.23, 1.2) 0.92 (0.38,
- Dal 2009 (Home Hr)	3	50	7	50	0.9%		0.43 [0.10, 1.7
- Galinier 2020 (OSICAT)	141	482	160	455	0.3% 5.6%	HEA	0.83 0.64. 1.0
- Gambetta 2007	19	158	48	455 124	1.8%		0.31 0.17, 0.5
- Gjeka 2021	4	47 682	5 326	15	0.3% 7.5%		0.26 0.06, 1.0
- Kalter-Leibovici 2017	302	682	326	678	7.5%	H	0.92 0.76, 1.1
- Kashem 2008 - Kotooka 2018 (HOMES-HF)	2 19	24 90	10	24	0.3%	·	0.20 [0.04, 1.0
- Kotooka 2018 (HOMES-HF)	19	90	20	91	1.3%	<b>⊢</b> •−1	0.96 [0.48, 1.9
- Nouryan 2019	14	42 25 229	13	47	0.9%		1.21 [0.51, 2.8
- Nunes-Ferreira 2020 - Olivari 2018 (RENEWING HeALTH) - Pekmezaris 2019	3 79	25	43	110	2.8%		0.99 [0.57 ] 3
- Pekmezaris 2019	5	46	8	58	0.5%		0.79 [0.24 2 5
- Scherr 2009	ú	66	17	54	0.9%		0.53 0.23, 1.2
- Schwarz 2008	12	51	13	51	0.9%	· · · · · · · · · · · · · · · · · · ·	0.92 0.38, 2.2
- Schwarz 2008 - Soran 2008 (HFHC)	29	155	36	155	2.0%	<b>⊢</b> ∎→	0.81 0.47, 1.3
- Völler 2022	39	241	44 13	251 47	2.6% 0.7%	<b>⊢</b> ∎1	0.92 [0.58, 1.4
- Vuorinen 2014 (Heart at Home)	8	47	13	47	0.7%		0.62 [0.23, 1.6
- Wita 2022	5	28	14	32	0.5%		0.41 [0.13, 1.2
Subtotal TM (95% CI)		3826		3527	41.2%		0.78 [0.67, 0.9
Subtotal events	1008	3826	1091	3527	41.2%	•	0.78 [0.87, 0.9
Heterogeneity: $Tau^2 = 0.04$ : Chi <sup>2</sup> = 32.83, df = 20 (P = 0	$(04): 1^2 = 39\%$		1071				
Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 32.83, df = 20 (P = 0 Test for overall effect: Z = $-3.05$ (P = 0.002)							
· · · · ·							
B. Structured Telephone Support							
- Angermann 2012 (INH)	36	352	46	363	2.6%	H=	0.81 [0.51, 1.2
- Cleland 2005 (TEN-HMS)*	34 38	352 173 228	24 43	85	1.8%	H	0.81 [0.51, 1.2 0.70 [0.39, 1.2 0.91 [0.57, 1.4 0.09 [0.01, 0.7
- DeBusk 2004	38	228	43	234	2.5%	H.	0.91 [0.57, 1.4
- Gattis 1999 (PHARM)	100	90		91	0.2% H		0.09 [0.01, 0.7
Giordana 2009	128	760	169	758	5.8%	HER	0.76 [0.59, 0.9
B. Structured Telephone Support Angermann 2012 (INH) - Cleand 2005 (TEN-HMS)* DeBusk 2004 - Gatus 1999 (PHARM) - GESICA 2005 (DIAL) - Giordano 2009 - Ho 2007 - Krum 2013 (CHAT)	43 42	230	73	230	3.0%	H	0.09 (0.01 0. 0.76 (0.59, 0.9 0.59 (0.39, 0.9 Not estimab 0.76 (0.43, 1. 0.89 (0.45, 1. 0.81 (0.47, 1. 0.97 (0.51, 1.8 0.50 (0.18, 1.) 1.50 (0.38, 50)
- Ho 2007 - Krum 2013 (CHAT)	42	247	25	217	1.9%		0 74 r0 42 1 3
Laramee 2003	23 18	188	35 21	217 146	1.9%		0.89 10.45
- Laramee 2003 - Mo 2021	27	141	29	146	2.0%		0.81 10 47 14
- Mortara 2009 (HHH)* - Negarandeh 2019 - Ramachandran 2007	18	106	39 28	160	1.5%		0.97 [0.5] 18
Negarandeh 2019	7	40	14	40	1.5% 0.7%		0.50 0.18, 1.3
- Ramachandran 2007	6	25	4	25	0.4%	· · · · · · · · · · · · · · · · · · ·	1.50 0.38, 5.9
- Riegel 2002 - Wakefield 2008	23	130	63	228	2.1%	<b>⊢</b> ∎i	0.64 0.38, 1.0
- Wakefield 2008	41	99	29	49	1.8%	<b>⊢</b> •+1	1.50 [0.38, 5. 0.64 [0.38, 1.0 0.70 [0.39, 1.1
Subtotal STS (95% CI)	105	2947	500	2788	27.7%	•	0.75 [0.65, 0.8
Subtoral events Heterogeneity: Tau <sup>2</sup> = 0.00: Chi <sup>2</sup> = 8.96. df = 13. (P = 0.7	(485)		599				
Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 8.96, df = 13 (P = 0.7 Test for overall effect: Z = $-4.19(P < 0.001)$	0),1 -0/8						
C. Complex Telemonitoring							
- Antonicelli 2008	9	28	26	29	0.8%		0.36 [0.14, 0.9 0.87 [0.60, 1.2
- Koehler 2011 (TIM-HF)	64	354	74 28	356	3.7% 2.0%	H-	0.87 0.60, 1.2
- Mortara 2009 (HHH)*	35	195	28	160	2.0%		1.03 [0.60, 1.7
C. Complex Telemonitoring - Antonicelli 2008 - Koehler 2011 (TIM-HF) - Mortara 2009 (HHH)* - Roth 2004	38	118					Not estimab
					6 50/		0 70 50 50 1 2
Subtotal Complex TM (95% CI) Subtotal events	147	695	128	545	6.5%	-	0.79 [0.50, 1.2
Heterogeneity: $Tau^2 = 0.08$ : $Chi^2 = 3.86$ . df = 2 (P = 0.15)	$1^2 = 48\%$		120				
Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 3.86, df = 2 (P = 0.15) Test for overall effect: $Z = -1.05$ (P = 0.30)	,,,						
btotal Non-invasive hTMS (95% CI)		7468		6615	75.3%	♦ ±	0.78 [0.70, 0.8
btotal events	1639		1818				
btotal events terogeneity:Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 47.53, df = 35 (P = 0.08 it for overall effect: Z = -4.71 (P < 0.001)	s); l <sup>2</sup> = 26%						
it for overall effect: $Z = -4.71$ (P < 0.001)							
vasive hTMS							
A. Cardiac Implantable Electronic Devices Böhm 2016 Boriani 2016 (MORE-CARE) - Domenichini 2015 (LIMIT-CHF) + Hansen 2018 (InContact) - Hindricks 2014 (IN-TIME) - Lüchic 2015 - Lüchic 2016 - Sardu 2016 - Sardu 2016 - Sardu 2016	119	505	128	497	5.2%	HEH	0.91 [0.69, 1. 1.03 [0.70, 1.] 0.95 [0.26, 3.] 0.77 [0.28, 2. 0.79 [0.47, 1.] 0.93 [0.47, 1.] 0.93 [0.47, 1.]
- Boriani 2016 (MORE-CARE)	63	437	60	428	5.2% 3.5%	H.	1.03 10.70
- Domenichini 2015 (LIMIT-CHF)	63 5	41	5	39	0.4%		0.95 0.26 3
- Hansen 2018 (InContact)	io	102	5	39 55	0.6%	i	0.77 0.28. 2.
- Hindricks 2014 (IN-TIME)	27	333	34	331	2.1%		0.79 0.47. 1.
- Lüthje 2015	20	87	22	89	1.4%		0.93 0.47, 1.
- Mullens 2010	6	194					Not estimab
- Sardu 2016	14 23	89	27 17	94	1.3%	<b>⊢</b> •i	0.55 [0.27, 1.
	23	155	17	127	1.4%	<b>⊢</b> ∎−1	0.75 [0.47, 1.4 Not estimab 0.55 [0.27, 1. 1.11 [0.57, 2. 0.77 [0.56, 1.0 1.70 [0.98, 2.9
- Tajstra 2020 (RESULT) - Van Veldhuisen 2011 (DOT-HF)	89	299	116	301	4.4% 2.0%	H <b>H</b>	0.77 [0.56, 1.
van veidhuisen zurr (DOT-HF)	41	168	24	167	2.0%	⊢∎1	1.70 [0.98, 2.9
Subtotal CIED (95% CI)		2410		2128	22.3%	4	0.92 [0.79, 1.0
Subtotal events	417	2410	440	2120	22.3%	•	0.72 [0.77, 1.9
Subtotal events Heterogeneity:Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 9.11, df = 9 (P = 0.43 Test for overall effect: Z = -1.15 (P = 0.25)	$3);  ^2 =  \%$		140				
Test for overall effect: $Z = -1.15$ (P = 0.25)	10100 - 10100						
B. Invasive Hemodynamic Monitoring							
- Angermann 2020 (MEMS-HF)	91	236		10000	12.12.00		Not estimab
Bourge 2008 (COMPASS-HF)	37	134 34	57	140	2.5%	H=	0.68 [0.42, 1.
- Jermyn 2017 Sharif 2022 (SIRONA2)	6	34					Not estimab
Sharn 2022 (SINONAZ)	11	70					Not estimab
Subtotal IHM (95% CI)		474		140	2.5%		0.68 [0.42, 1.0
Subtotal events	145	-/-	57	140	2.3/0		0.00 [0.12, 1.0
Subtotal events Heterogeneity:Tau² = 0.00; Chi² = 0.00, df = 0 (P = 1.00 Test for overall effect: Z = -1.60 (P = 0.11)	$); l^2 = 0\%$		24				
Test for overall effect: Z = -1.60 (P = 0.11)	663 - C						
btotal Invasive hTMS (95% CI)	(gales)	2884	ganes.	2268	24.7%	•	0.89 [0.77, 1.0
btotal events	562		497				
The second secon	j; i* = 5%						
terogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 10.48, df = 10 (P = 0.40)							
terogeneity:Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 10.48, df = 10 (P = 0.40 t for overall effect: Z = -1.52 (P = 0.13)						•	0.81 [0.74, 0.8
		10757					
terogeneity:Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 10.48, df = 10 (P = 0.40 st for overall effect: Z = -1.52 (P = 0.13) tal (95% CI) tal events	2201	10352	2263	8883	100%	•	0.01 [0.74, 0.0
tal (95% CI)	2201	10352	2263	8883	100%	•	0.01 [0.14, 0.0
tal (95% CI)	2201	10352	2263	8883	100%		
tal (95% CI)	2201	10352	2263	8883			_
tal (95% CI)	2201	10352	2263	8883	0.01	0.1 1	

Standard of Care Events Patients

Weights

Intervention Events Patients

Figure 3 Forest plot first hospitalization. TM, telemonitoring; STS, structured telephone support; complex TM, complex telemonitoring; hTMS, home telemonitoring systems; CIED, cardiac implantable electronic devices; IHM, invasive haemodynamic monitoring. \*The studies of Mortara et al.<sup>71</sup> and Cleland et al.<sup>30</sup> have multiple intervention arms. Therefore, those articles are presented more than once in the forest plot. In the subtotal non-invasive home telemonitoring systems and the total pooled analysis, event rates of each study arm are added together.

symptoms are present.<sup>106</sup> By measuring this clinically intuitive parameter (which leads to proactive early interventions), hospitalizations due to HF deterioration can be avoided.<sup>12</sup> These haemodynamic-guided monitoring techniques are very promising. Still, due to their costs, these devices are most likely targeted for those patients who are at higher risk of (re-)admission due to HF and require more intensive monitoring.

Odds Ratio [95% CI]

ithor(s) and Year		ention		of Care	M/ 1 - 41 -		Incidence
	Events	<b>Patients</b> Years	Events	Patients Years	Weigths		Rate Ratio [95% C
on-invasive hTMS							
A. Telemonitoring							
- Boyne 2012 (TEHAF)	24	178	43	163.5	3.1%	⊢•	0.51 [0.31, 0.8
- Capomolla 2004	17	55.8	58	55	2.8%	H=H	0.29 [0.17, 0.5
- Comin-Colet 2016 (iCOR)	15	18.4	40	131.6	2.5%		
- Dar 2009 (Home-HF) - Dendale 2012 (TEMA-HF)	22	41.2	16	44.2	2.2%		1.48 [0.77, 2.8 0.52 [0.30, 0.9
- Galinier 2020 (OSICAT)	19 284	39 578.4	34 341	36.5 580.1	2.7%		0.84 [0.71, 0.9
- Kalter-Leibovici 2017	857	1841.4	850	1830.6	6.1% 6.6%	-	1.00 [0.91, 1.
- Olivari 2018 (RENEWING HeALTH)	161	201.5	93	98	5.2%	H	0.84 [0.65, 1.0
- Schwarz 2008	14	11.8	13	11.5	1.8%		1.05 [0.49, 2.
Völler 2022	60	207.6	72	240.8	4.3%	1.1	0.97 [0.69, 1.
Vuorinen 2014 (Heart at Home)	8	23.2	13	23.5	1.4%		0.62 [0.26, 1.
Wagenaar 2019 (e-Vita HF)	7	142.5	12	145.5	1.3%	i i i i i i i i i i i i i i i i i i i	0.60 [0.23, 1.
Ware 2020	71	156.2					Not estimat
Subtotal TM (95% CI)		3495.0		3360.8	40.0%	•	0.83 [0.67, 1.
Subtotal events	1559		1585				1. A A
Heterogeneity:Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 48.17, df = 11 (P < 0.0 Test for overall effect: Z = -1.74 (P = 0.08)	01); l <sup>2</sup> = 77%						
3. Structured Telephone Support Angermann 2012 (INH)	32	157.8	52	163.2	3.5%	<b>⊢</b> ∎i	0.64 [0.41, 0.
Bento 2009	5	10	22	9.8	1.2%		0.22 [0.08, 0.
DeBusk 2004	76	213.5	86	212	4.7%	H	0.88 [0.64, 1.
Ho 2007	47	94.7					Not estimat
Mortara 2009 (HHH)*	29	102.5	44	154.7	3.3%	H.	0.99 [0.62, 1.
		F70 F		F30 7	10 70/		0 70 10 44
Subtotal STS (95% CI) Subtotal events	189	578.5	204	539.7	12.7%	-	0.70 [0.46, 1.
Heterogeneity:Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 8.81, df = 3 (P = 0.032 Test for overall effect: Z = -1.70 (P = 0.09)	$ 189 $ ; $ ^2 = 66\%$		204				
C. Complex Telemonitoring							
Antonicelli 2008	3	23.3	5	24.2	0.6%		0.62 [0.15, 2.
Blum 2014 (MCCD)	3	234.6	2	217.5	0.4%		1.39 [0.23, 8.
Koehler 2011 (TIM-HF)	113	767	114	771.3	5.2%	HÉH	1.00 [0.77, 1.
Mortara 2009 (HHH)*	51	188.5	44	154.7	3.8%	⊢ <b>∔</b> ⊣	0.95 [0.64, 1.
Subtotal Complex TM (95% CI) subtotal events deterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.57, df = 3 (P = 0.90). Test for overall effect: Z = $-0.20$ (P = $0.84$ )	170; 1 <sup>2</sup> = 0%	1213.4	165	1167.7	10.0%	•	0.98 [0.79, 1.
							0.07.07.00
htotal Non-invasive hTMS (95% CI)		5786 9		49135	62.7%	÷	
total events terogeneity:Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001)	1918 ); l² = 70%	5286.9	1910	4913.5	62.7%	•	0.82 [0.70, 0.
total events terogeneity:Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001)		5286.9	1910	4913.5	62.7%	•	0.82 [0.70, 0.
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = $-2.43$ (P = 0.02) vasive hTMS		5286.9	1910	4913.5	62.7%	•	0.82 [0.70, 0.
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) rasive hTMS A. Cardiac Implantable Electronic Devices	); l <sup>2</sup> = 70%					•	
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) <b>asive hTMS</b> A. Cardiac Implantable Electronic Devices Adamson 2011 (REDUCEhf)		5286.9 195.3	1910 78	<b>4913.5</b> 191.4	62.7% 4.6%	▲	0.90 [0.66, 1.
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> A. Cardiac Implantable Electronic Devices Adamson 2011 (REDUCEhf) Böhm 2016	72 220	195.3 993.2	78 218	191.4 923.6	4.6% 5.9%	► F#H	0.90 [0.66, 1. 0.94 [0.78, 1.
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> A. Cardiac Implantable Electronic Devices Adamson 2011 (REDUCEhf) Böhm 2016 Boriani 2016 (MORE-CARE)	72 220 1 1 1	195.3 993.2 874	78 218 103	191.4 923.6 856	4.6% 5.9% 5.1%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEhf) Boriani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF)	72 220 111	195.3 993.2 874 42	78 218 103 6	191.4 923.6 856 40	4.6% 5.9% 5.1% 1.2%	₩ +#+ 	0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 4.
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> A. Cardiac Implantable Electronic Devices Adamson 2011 (REDUCEhf) Böhm 2016 Boriani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME)	72 220 111 11 44	195.3 993.2 874 42 305.2	78 218 103 6 47	191.4 923.6 856 40 295.1	4.6% 5.9% 5.1% 1.2% 3.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 4. 0.91 [0.60, 1]
total events erogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) for overall effect: Z = -2.43 (P = 0.02) <b>asive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEhf) Boriani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021	72 220 111 11 44 7	195.3 993.2 874 42 305.2 68	78 218 103 6 47 27	191.4 923.6 856 40 295.1 68	4.6% 5.9% 5.1% 1.2% 3.7% 1.5%		0.90 [0.66, 1 0.94 [0.78, 1 1.06 [0.81, 1 1.75 [0.65, 4 0.91 [0.60, 1 0.26 [0.11, 0
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEhf) Bohani 2016 (MORE-CARE) Domenichini 2015 (LINIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021	72 220 111 11 44	195.3 993.2 874 42 305.2	78 218 103 6 47	191.4 923.6 856 40 295.1	4.6% 5.9% 5.1% 1.2% 3.7%	₩ +#+ 	0.90 [0.66, 1 0.94 [0.78, 1 1.06 [0.81, 1 1.75 [0.65, 4 0.91 [0.60, 1 0.26 [0.11, 0
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Böhm 2016 (MORE-CARE) Bornani 2016 (MORE-CARE) Bornani 2016 (MORE-CARE) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF)	72 220 111 11 44 7	195.3 993.2 874 42 305.2 68 208.6	78 218 103 6 47 27	191.4 923.6 856 40 295.1 68 207.4	4.6% 5.9% 1.2% 3.7% 1.5% 3.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 1. 0.26 [0.11, 0. 1.66 [1.10, 2.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEhf) Bohrain 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2016 (INOTE-CHF) Hindricks 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> ubtotal events	72 220 111 11 44 7 60 525	195.3 993.2 874 42 305.2 68	78 218 103 6 47 27	191.4 923.6 856 40 295.1 68	4.6% 5.9% 5.1% 1.2% 3.7% 1.5%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 1. 0.26 [0.11, 0. 1.66 [1.10, 2.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Böhm 2016 Boriani 2016 (MORE-CARE) Domenichini 2015 (LIMT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> Subtotal events eterorgeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01)	72 220 111 11 44 7 60 525	195.3 993.2 874 42 305.2 68 208.6	78 218 103 6 47 27 36	191.4 923.6 856 40 295.1 68 207.4	4.6% 5.9% 1.2% 3.7% 1.5% 3.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 1. 0.26 [0.11, 0. 1.66 [1.10, 2.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) t for overall effect: Z = $-2.43$ (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Bohrani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtocal CIED (95% CI)</b> Subtocal events <sup>4</sup> eterorgeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Fest for overall effect: Z = $-0.18$ (P = 0.86)	72 220 111 11 44 7 60 525	195.3 993.2 874 42 305.2 68 208.6	78 218 103 6 47 27 36	191.4 923.6 856 40 295.1 68 207.4	4.6% 5.9% 1.2% 3.7% 1.5% 3.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 1. 0.26 [0.11, 0. 1.66 [1.10, 2.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Böhm 2016 Boriani 2016 (MORE-CARE) Domenichin 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> Subtotal events feterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = -0.18 (P = 0.86) <b>B. Invasive Hemodynamic Monitoring</b>	72 220 111 44 7 60 ); l <sup>2</sup> = 67%	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b>	78 218 103 6 47 27 36 515	191.4 923.6 855 40 295.1 68 207.4 <b>2581.5</b>	4.6% 5.9% 1.2% 3.7% 3.7% 25.7%		0.90 [0.66, 1, 0.94 [0.78, 1, 1.06 [0.81, 1, 1.75 [0.65, 4, 0.91 [0.60, 1, 0.26 [0.11, 0, 1.66 [1.10, 2, 0.98 [0.76, 1,
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Böhm 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DCT-HF) <b>Subtotal events</b> Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = -0.18 (P = 0.86) <b>B. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAMPION)	); l <sup>2</sup> = 70% 72 220 111 11 44 7 60 ); l <sup>2</sup> = 67% 182	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7	78 218 103 6 47 27 36	191.4 923.6 856 40 295.1 68 207.4	4.6% 5.9% 1.2% 3.7% 1.5% 3.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 4 1.75 [0.65, 4. 0.91 [0.60, 1. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.68 [0.56, 0.
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = $-2.43$ (P = 0.02) rasive hTMS A. Cardiac Implantable Electronic Devices A damson 2011 (REDUCEhf) Böhm 2016 Boriani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) Subtotal CIED (95% CI) Subtotal events deterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = $-0.18$ (P = 0.86) 8. Invasive Hemodynamic Monitoring Abraham 2016 (CHAMPION) Angermann 2020 (MEMS-HF)	); l <sup>2</sup> = 70% 72 220 111 11 44 7 60 ); l <sup>2</sup> = 67% 182 363	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5	78 218 103 6 47 27 36 515	191.4 923.6 855 40 295.1 68 207.4 <b>2581.5</b>	4.6% 5.9% 1.2% 3.7% 3.7% 25.7%		0.90 [0.66, 1, 0.94 [0.78, 1, 1.06 [0.8], 1, 1.75 [0.65, 4, 0.91 [0.60, 1, 1.66 [1.10, 2, 0.98 [0.76, 1, 0.68 [0.56, 0, Not estimat
total events errogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = $-2.43$ (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEM) Bohma 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> Subtotal <b>Vents</b> Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01) Test for overall effect: Z = $-0.18$ (P = 0.86) <b>8. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAYHPION) Angermann 2020 (MEMS-HF) Cowie 2022 (COAST)	72 220 111 11 44 7 60 ): l <sup>2</sup> = 525 182 363 27	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100	78 218 103 6 47 27 36 515 279	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 1.2% 3.7% 1.5% 3.7% 25.7%		0.90 [0.66, 1 0.94 [0.78, 1 1.06 [0.81, 1 4 1.75 [0.65, 4 0.91 [0.60, 1 0.26 [0.11, 0 1.66 [1.10, 2 0.98 [0.76, 1. 0.68 [0.56, 0 Not estimal Not estimal
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Bohrani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> Subtotal events -deterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Fest for overall effect: Z = -0.18 (P = 0.86) 8. Invasive Hemodynamic Monitoring Abraham 2016 (CHAMPION) Angermann 2020 (MENS-HF) Cowie 2022 (COAST) Lindenfeld 2021 (GUIDE-HF)**	); l <sup>2</sup> = 70% 72 220 111 11 44 7 60 ); l <sup>2</sup> = 525 60 ); l <sup>2</sup> = 67% 182 363 27 185	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2	78 218 103 6 47 27 36 515	191.4 923.6 855 40 295.1 68 207.4 <b>2581.5</b>	4.6% 5.9% 1.2% 3.7% 3.7% 25.7%		0.90 [0.66, 1, 0.94 [0.78, 1, 1.06 [0.81, 1, 1.75 [0.65, 4, 0.91 [0.60, 1, 1.66 [1.10, 2, 0.98 [0.76, 1, 0.98 [0.76, 1, 0.68 [0.56, 0, Not estimal 0.82 [0.68, 1, 0.68 [0.56, 0,
total events terrogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = -2.43 (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEHf) Böhm 2016 Bornani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2021 Treskes 2021 Treskes 2021 Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal event</b> <b>Subtotal event</b> <b>B. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAMPION) Angermann 2020 (MEMS-HF) Cowie 2022 (COAST) Lindenfeld 2021 (GUIDE-HF)* <sup>8</sup> Shari 2022 (SIRONA2)	72 220 111 11 44 7 60 ): l <sup>2</sup> = 525 182 363 27	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100	78 218 103 6 47 27 36 515 279	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 1.2% 3.7% 1.5% 3.7% 25.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 9 [0.65, 4. 0.91 [0.60, 1. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) t for overall effect: Z = $-2.43$ (P = 0.02) <b>rasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Böhm 2016 Borlani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) <b>Subtotal CIED (95% CI)</b> Subtotal events <b>deterogeneity:</b> Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = $-0.18$ (P = 0.86) <b>B. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAMPION) Angermann 2020 (MEMS-HF) Cowie 2022 (COAST) Lindenfeld 2021 (GUIDE-HF)** Shartf 2022 (SIRONA2) Shavelle 2020 (CardioMEMS PAS)	72 220 111 11 44 7 60 ); l <sup>2</sup> = 525 ); l <sup>2</sup> = 67% 182 363 27 185 11	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4 1107	78 218 103 6 47 27 36 515 279	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 5.1% 1.2% 3.7% 25.7% 5.9%		0.90 [0.66, 1, 0.94 [0.78, 1, 1.06 [0.81, 1.75 [0.65, 4, 0.91 [0.60, 1, 1.66 [1.10, 2, 0.98 [0.76, 1, 0.98 [0.76, 1, 0.68 [0.56, 0, Not estimal 0.82 [0.68, 1, Not estimal
total events errogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 59,98, df = 18 (P < 0.001); t for overall effect: Z = $-2.43$ (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> Adamson 2011 (REDUCEhf) Böhn 2016 Bornani 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veidhuisen 2011 (DOT-HF) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = $-0.18$ (P = 0.86) <b>3. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAMPION) Angermann 2020 (MEMS-HF) Cowie 2022 (COAST) Lindenfeld 2021 (GUIDE-HF)** Sharif 2022 (SIRONA2) Sharelf 2020 (Cardio/HEMS PAS) Subtotal IHM (95% CI)	); l <sup>2</sup> = 70% 72 220 111 11 44 7 60 ); l <sup>2</sup> = 525 60 ; l <sup>2</sup> = 67% 182 363 27 185 11 628	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4	78 218 103 6 47 27 36 515 279 225	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 1.2% 3.7% 1.5% 3.7% 25.7%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 4. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat Not estimat
total events errogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001); t for overall effect: Z = $-2.43$ (P = 0.02) <b>vasive hTMS</b> <b>A. Cardiac Implantable Electronic Devices</b> A damson 2011 (REDUCEhf) Bohma 2016 (MORE-CARE) Domenichini 2015 (LIMIT-CHF) Hindricks 2014 (IN-TIME) Treskes 2021 Van Veldhuisen 2011 (DOT-HF) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.07: Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01 Test for overall effect: Z = $-0.18$ (P = 0.86) <b>B. Invasive Hemodynamic Monitoring</b> Abraham 2016 (CHAPHOIN) A angermann 2020 (MEMS-HF) Cowie 2022 (COAST) Lindenfeld 2021 (GUIDE-HF)** Shavefle 2020 (Cardio/MEMS PAS) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.08, df = 1 (P = 0.15)	); l <sup>2</sup> = 70% 72 220 111 44 7 60 ); l <sup>2</sup> = 67% 182 363 27 185 11 628 1396	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4 1107	78 218 103 6 47 27 36 515 279	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 5.1% 1.2% 3.7% 25.7% 5.9%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 1.75 [0.65, 4. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat Not estimat
stotal events terrogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001); t for overall effect: Z = $-2.43$ (P = 0.02) vasive hTMS A. Cardiac Implantable Electronic Devices A charanso 2011 (REDUCEhf) = Böhma 2016 (MORE-CARE) = Domenichini 2015 (LIMIT-CHF) = Hindricks 2021 (IN-TIME) = Treskes 2021 - Yan Veldhuisen 2011 (DOT-HF) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01) Test for overall effect: Z = $-0.18$ (P = 0.86) B. Invasive Hemodynamic Monitoring A Abraham 2016 (CHAMPION) - Angernann 2020 (MEMS-HF) - Cowie 2022 (COAST) - Lindenfeld 2021 (GUIDE-HF)** - Sharid 2022 (GRONA2) - Shariel 2020 (CardioMEMS PAS) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.08, df = 1 (P = 0.15), Test for overall effect: Z = $-2.96$ (P = 0.003)	); l <sup>2</sup> = 70% 72 220 111 44 7 60 ); l <sup>2</sup> = 67% 182 363 27 185 11 628 1396	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4 1107 <b>2306.8</b>	78 218 103 6 47 27 36 515 279 225	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3 452.7 <b>863.0</b>	4.6% 5.9% 1.2% 3.7% 1.5% 3.7% 25.7% 5.9% 5.8%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat Not estimat 0.75 [0.61, 0.
total events terogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001) ti for overall effect: Z = $-2.43$ (P = 0.02) vasive hTMS A. Cardiac Implantable Electronic Devices - Adamson 2011 (REDUCEhf) = Böhm 2016 = Böhm 2016 = Böhm 2016 (MORE-CARE) = Domenichini 2015 (LIMIT-CHF) = Hindricks 2014 (IN-TIME) - Treskes 2021 - Van Veldhuisen 2011 (DOT-HF) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01) Test for overall effect: Z = $-0.18$ (P = 0.86) B. Invasive Hemodynamic Monitoring - Abraham 2016 (CHAMPION) - Angermann 2020 (MEMS-HF) - Gowie 2022 (COAST) - Lindenfeld 2021 (GUIDE-HF)** - Shavell 2020 (CardioMEMS PAS) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.08, df = 1 (P = 0.15); Test for overall effect: Z = $-2.96$ (P = 0.003) btotal Invasive hTMS (95% CI)	72 220 111 11 44 7 60 ); I <sup>2</sup> = 525 60 ); I <sup>2</sup> = 67% 182 363 27 185 11 628 ; I <sup>2</sup> = 52%	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4 1107	78 218 103 6 47 36 515 279 225 504	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3	4.6% 5.9% 5.1% 1.2% 3.7% 25.7% 5.9%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat Not estimat 0.75 [0.61, 0.
total events terogeneity: Tau <sup>2</sup> = 0.06: Chi <sup>2</sup> = 59.98, df = 18 (P < 0.001); ti for overall effect: Z = $-2.43$ (P = 0.02) vasive hTMS A. Cardiac Implantable Electronic Devices - Adamson 2011 (REDUCEhf) = Böhm 2016 = Böhm 2016 (MORE-CARE) = Domenichini 2015 (LIMIT-CHF) = Hindricks 2014 (IN-TIME) = Treskes 2021 - Van Veldhuisen 2011 (DOT-HF) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 18.21, df = 6 (P = 0.01) Test for overall effect: Z = $-0.18$ (P = 0.86) B. Invasive Hemodynamic Monitoring - Abraham 2016 (CHAMPION) - Angermann 2020 (MEMS-HF) - Cowie 2022 (COAST) - Lindenfield 2021 (GUIDE-HF)** - Shaveli 2020 (Cardio/MEMS PAS) Subtotal events Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.08, df = 1 (P = 0.15). Test for overall effect: Z = $-2.96$ (P = 0.003) btotal Invasive HTMS (95% CI) xotal events terogeneity: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 29.35, df = 8 (P < 0.001);	);   <sup>2</sup> = 70% 72 220 111 11 44 7 60 );   <sup>2</sup> = 525 182 363 27 185 11 628 ;   <sup>2</sup> = 52%	195.3 993.2 874 42 305.2 68 208.6 <b>2686.3</b> 395.7 218.5 100 451.2 34.4 1107 <b>2306.8</b>	78 218 103 6 47 27 36 515 279 225	191.4 923.6 856 40 295.1 68 207.4 <b>2581.5</b> 410.3 452.7 <b>863.0</b>	4.6% 5.9% 1.2% 3.7% 1.5% 3.7% 25.7% 5.9% 5.8%		0.90 [0.66, 1. 0.94 [0.78, 1. 1.06 [0.81, 1. 0.26 [0.11, 0. 1.66 [1.10, 2. 0.98 [0.76, 1. 0.98 [0.76, 1. 0.68 [0.56, 0. Not estimat 0.82 [0.68, 1. Not estimat Not estimat 0.75 [0.61, 0.
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**Figure 4** Forest plot total hospitalizations. TM, telemonitoring; STS, structured telephone support; complex TM, complex telemonitoring; hTMS, home telemonitoring systems; CIED, cardiac implantable electronic devices; IHM, invasive haemodynamic monitoring. \*The studies of Mortara et *al.*<sup>71</sup> have multiple intervention arms. Therefore, those articles are presented more than once in the forest plot. In the subtotal non-invasive home telemonitoring systems and the total pooled analysis, event rates of each study arm are added together. \*\*From the article of Lindenfeld et *al.*, the post-COVID analysis was used, to avoid bias in observed outcomes due to the COVID pandemic.

Furthermore, there is not only a variation in the identification of distinct pathological parameters between IHM and CIED, but the method of monitoring is often different as well. Pulmonary artery pressures are frequently measured daily to weekly with the use of IHM, and treatment is changed accordingly, while CIED are frequently operated on an alarm basis rather than frequent data monitoring. In addition, alarms are frequently based on less intuitive measurements, such as impendence or algorithms, compared to clinically relevant pressure data. The IHM was not able to show a benefit on short-term mortality. This is most likely caused by the low power considering the small number of studies and events with a higher level of uncertainty of our data as well as the relative short follow-up time. The type of patients selected is generally sicker or has more advanced HF with NYHA class III and a previous HF hospitalization, with a reduced life expectancy. Several recent drug and device trials could not show a benefit of treatment on mortality in advanced stages of HF and/or against high levels of background therapies. The IHM studies primarily target congestion with modifications in diuretic dosages to prevent decompensation, which potentiates primarily the effects on recurrent HFH. It is unknown whether this translates to indirect benefits on mortality at long term. In the future, the long-term data on IHM will be expanded e.g. with the MONITOR-HF trial.<sup>65,107</sup>

#### **Clinical impact and future perspective**

This meta-analysis provides support for telemonitoring to be incorporated in HF care. A tailored approach seems necessary in order to lead to a maximal benefit of hTMS with various determinants such as the type of healthcare system, funding, and also characteristics of the patients such as disease severity and symptoms. Patients with more advanced HF (NYHA class III) appear to benefit of a more intensive form of (invasive) monitoring, which could be achieved through IHM with main effects on recurrent HF hospitalizations (targeting congestion), while a patient with a more 'stable' HF (NYHA classes I-II) would suffice with the use of non-invasive hTMS, which is simpler and less costly, also considering the enormous patient volumes. This clearly makes sense from a cost-effectiveness perspective, where the most costly method is reserved for the sickest patients who have most to profit from it. In addition, such systems ideally should be adaptable over time, i.e. to intensify when the patient is in a more unstable phase and taper off when the patient is stable. The latter will most likely lead to a higher adherence during prolonged follow-up. Future research should focus on defining these subgroups of patients (based on age, gender, LVEF, NYHA class, stable/unstable aetiology, or other factors) and the effect of the different hTMS modalities on these subgroups. Moreover, the approach will also largely depend on the compatibility with the healthcare system that is already in place. It may also be important to not only focus on detecting HF deterioration, but also to implement a health maintenance strategy.<sup>108</sup>

The evidence provided by this meta-analysis supports non-invasive hTMS and invasive hTMS using IHM (but not CIED). Considering IHM, as the CIs of treatment effects are quite wide, more evidence is needed before widespread use of IHM is to be broadly advocated in specific target populations. Still, there is an urge of wider implementation of remote monitoring strategies within clinical practice and healthcare systems. This requires facilities and personnel, which needs to be funded by the healthcare insurances, and also significant advances in IT development and support in hospitals to reduce workload (e.g. with digital technology and artificial intelligence). Many hTMS studies are on top of care, and the field must also work on replacing standard care components by hTMS, self-management at home, and further reduce face-to-face contacts, such as shown by the EVITA-HF study.<sup>99</sup> To effectuate this, wider implementation needs to be facilitated by the international HF community and guidelines that speak out about their position on hTMS modalities, with the increasing number of studies and data now provided. Also, we need to study and invest in patients, e.g. self-management and involvement in their disease and remote monitoring strategies, which can help in diet,

lifestyle, and treatment adherence and close the loop between hospital and patient.

#### Strengths and limitations

This meta-analysis has several major strengths. The current meta-analysis is the most comprehensive, contemporary, and largest overview of hTMS (with all available modalities) in chronic HF to date including both clinical trial and real-world observational data. To the best of our knowledge, this is the first systematic review and meta-analysis that focuses on both non-invasive and invasive hTMS in contrast to the Cochrane review of 2015,<sup>5</sup> which only described non-invasive solutions. While we were unable to directly compare non-invasive with invasive hTMS, this study does offer insights into the effectiveness of both modalities. Furthermore, in this meta-analysis, opposed to earlier meta-analyses, we now also differentiated between first HFH and the total HFHs. In our opinion, this manner of analysing the hTMS data is crucial, since both outcomes have different implications and economic impacts.

Several limitations should be mentioned. Firstly, there was still some heterogeneity across studies. Albeit the heterogeneity is decreasing as compared with previous studies, we can specifically observe heterogeneity in the results on the total number of HFHs. The  $l^2$ -index as a relative measure of heterogeneity, which is not to be considered as an absolute number but as relative categories ranging from <25%, might not be important and >75% considerable heterogeneity. Possible explanations for this degree of heterogeneity are the large variety of hTMS, patient characteristics, and the large variety of HF management between studies. For IHM, the number of studies and events was low, which relates to the  $l^2$ -index. Attempts were made to minimize this heterogeneity and investigate the effects of the major categories distinguishing between non-invasive and invasive hTMS. The treatment algorithm used in TM strategies could differ across studies, which may have led to the effects demonstrated. As standard care is the comparator, we should acknowledge that the level of standard care varies between studies and in time-period with expanding GDMT. Compared with the Inglis analysis, we observe a decline in heterogeneity of included studies especially in the last 5 years, with many new structured telemonitoring projects.<sup>5</sup> Secondly, the follow-up times used in the meta-analysis of the total number of HFH were limitedly available across studies. These were calculated, as stated in the methods, which may introduce some bias. Thirdly, distortion of results may be present due to publication bias. However, based on our funnel plots, we assume the risk of publication bias to be low for the majority of the analyses.

## Conclusions

Our meta-analysis revealed that overall hTMS are effective in reducing HFH and improve survival. Non-invasive hTMS reduce all endpoints, whereas in invasive hTMS, only IHM reduces recurrent HFHs significantly. Therefore, telemonitoring should be strongly considered and may be integrated in current HF healthcare systems worldwide. For optimal impact, the implementation of hTMS should ultimately be tailored to the individual HF patient and based on compatibility with current healthcare systems.

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## Supplementary data

Supplementary data is available at European Heart Journal online.

## Data availability

The data underlying this article can be shared on reasonable request to the corresponding author.

## **Conflict of interest**

D.T. received research grants from Boston Scientific and Biotronik. O.M. received consulting fees from Abbott, AstraZeneca, and Boehringer-Ingelheim. R.d.B. has received research grants and/or fees from AstraZeneca, Abbott, Boehringer-Ingelheim, Cardior Pharmaceuticals GmbH, Ionis Pharmaceuticals, Inc., Novo Nordisk, and Roche; and has had speaker engagements with Abbott, AstraZeneca, Bayer, Bristol Myers Squibb, Novartis, and Roche. R.v.d.B. received an independent research grant and speaker fee from Abbott. J.B. received independent research grant from Abbott for ISS and has had speaker engagement or advisory boards in the past 5 years with Astra Zeneca, Abbott, Boehringer-Ingelheim, Bayer, Daiichi Sankyo, Novartis and Vifor. All other authors declared to have no conflict of interest.

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