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Effectiveness of tele-rehabilitation programs in the follow-up of adult patients diagnosed with heart failure: a systematic review and meta-analysis

Efetividade dos Programas de tele-reabilitação no seguimento de adultos diagnosticados com Insuficiência Cardíaca: revisão sistemática e meta-análise

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Efetividade dos Programas de tele-reabilitação no seguimento de adultos diagnosticados com Insuficiência Cardíaca: revisão sistemática e meta-análise

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Dedicatória

“Quando as raízes são profundas, não há razão para temer o vento.”

À minha família pelo apoio incondicional ao longo de todo este percurso.

Effectiveness of tele-rehabilitation programs in the follow-up of adult patients diagnosed with heart failure: a systematic review and meta-analysis

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ABSTRACT

Aims: To implement a systematic review focused on telerehabilitation (TR) programs in heart failure (HF) patients in order to characterize practices and understand their impact and safety.

Methods and Results: Four databases (PubMed/Medline, CENTRAL, SCOPUS and ISI Web of Science) were searched without language or date restriction for randomized controlled trials that explored potential benefits of TR programs in HF patients compared to Usual Care (with or without cardiac rehabilitation). Risk of bias, quality of evidence, and the strength of the recommendation about TR were assessed according to the Cochrane Collaboration and GRADE recommendations. Our primary outcome was CV Death or Heart failure-related hospitalizations but only two studies reported the number of hospitalizations (total: TR – 36; Control – 67). We also analyzed functional capacity and quality of life. In general, both groups showed improvements in functional capacity between baseline and end of the trial, with significantly better results in TR groups for 6MWT but not for pVO2 (6MWT- Mean Difference 27.1; CI 95% [5.5;48.6]; I^2= 75%); pVO2 - Mean Difference 2.0; CI 95% [-0.1;4.1); I^2=94%). We found a statistically significant better score in MLHFQ in TR group (Mean Difference -8.0; CI 95% [-12.2;-3.7]; I^2=59%). In general all studies considered to have high adherence rates. No major adverse events were reported during TR exercise. Only two studies made a cost-analysis showing possible savings with TR programs.

Conclusion: This systematic review and meta-analysis suggests that Tele-Rehabilitation is non-inferior to Usual Care and might be non-inferior to standard CR. If supported by future and better designed studies, TR may become an attractive alternative to standard center-based CR, allowing to fulfill the class I recommendation of rehabilitation to these patients. Future trials shall use more standardized protocols in order to attain a more systematic analysis of the effectiveness of these programs, as well as their safety and cost-effectiveness.

Key-words (4): Tele-rehabilitation; Heart Failure; Functional capacity; Quality of Life;

INTRODUCTION

Heart Failure (**HF**) is a complex clinical syndrome in which an increase in left ventricular diastolic pressure with or without a decrease in cardiac output may cause a set of signs and symptoms, such as dyspnea, fatigue, edema and rales.

Globally, this problem affects 2% of the adult population and it increases with age (affecting 6-10% of adults over 65 years old). The lifetime risk of HF at age 55 years is 33% for men and 28% for women (1).

The etiology of HF is diverse, but in developed countries it is accepted that ischemic cardiopathy is the leading cause. Hypertension is a relevant cause mainly in patients with Heart Failure preserved Ejection Fraction (HFpEF). Valvular heart disease remains a relevant etiology in developing countries.

In what concerns HF prognosis, the functional status New York Heart Association Classification (NYHA) is an important factor. Patients at NYHA I have no limitation of physical activity, NYHA II are comfortable at rest but ordinary physical activity results in symptoms. In more advanced stages, patients at NYHA III have marked limitation of physical exercise, while NYHA IV are symptomatic even at rest. NYHA IV show a one-year mortality rate of 30 to 70%, while patients with NYHA II have 10% of mortality rate within a 5-year period (2).

Acute exacerbations of HF symptoms with severe clinical characteristics (e.g., pulmonary congestion, hemodynamic collapse), often demand patients' hospitalization. These cases are associated with high in-hospital mortality rates, as well as a prolonged length of stay, which causes a strong socioeconomic and societal impact (2).

HF treatment involves a multidisciplinary approach that includes pharmacological treatment, device and surgical treatment. Non-pharmacological treatment is key and

includes modification of lifestyle through dietary interventions and regular aerobic exercise. There is evidence that this combined approach can improve quality of life, reduce hospital admissions and mortality in HFrEF, while in HFpFE no evidence of reduction in mortality is available, although certain forms of therapy might reduce hospitalizations.

Cardiac Rehabilitation (**CR**) is a part of HF non-pharmacological therapy. It has a class I recommendation and a level of evidence A for patient with stable and symptomatic Heart Failure (1). CR refers to a combination of different core components such as physical activity, behavioural change, risk factor modification, nutritional counselling and psychosocial wellbeing (1). Recent systematic reviews and meta-analyses showed positive effect of exercise-based cardiac rehabilitation with a significant reduction of the risk of hospital admissions and improvement of health-related quality of life (**HRQoL**) (3, 4).

There is considerable heterogeneity in CR programs concerning setting, components and duration. CR setting ranges from hospital-based medically supervised and closely monitored programs, usually for higher risk patients, non-hospital center-based CR (CR clinics) to home-based or community-based programs (coronary support groups, local gyms). Most programs are hospital-based and comprise 30-45minute of medically supervised sessions, 2-3 times per week for up to 6 months. Additionally, nutritional counselling and psycho-behavioral interventions are used. These programs should be adapted to patient's comorbidities and personal and social context (1).

Accessibility is a limiting factor. While indicated, most patients are not enrolled in CR programs. This may be due to personal economical constrains and/or lack of availability of CR programs (5). Other barriers include patients and doctor's unawareness of the impact of such programs (6). All the above limits compliance with guidelines,

introducing inequities in access to CR and significantly impact in HF prognosis. In fact, considering that there are 15million HF patients in Europe it's not conceivable a scenario where all could do hospital-based rehabilitation. In practice, nowadays, this class A indication guideline is impossible to implement in real life.

Recent technology advances allowed new forms of patient monitoring and care delivering. Among them, telemonitoring is increasingly raising interest from scientific community. Telemonitoring involves a loop including patients' biological variables assessment, data transmission to the medical team and backward medical response in order to correct possible clinical parameters deviations. Invasive and non-invasive telemonitoring showed a dramatic impact in reducing hospitalizations in these patients, as well as improvements in HRQoL.(7-9).

Recently reports focusing on non-invasive telemonitoring as a basis to facilitate TR, demonstrate that, additionally to regular patient's monitoring, TR introduces regular physical exercises at patient's home. Patient specific information (physical activity, blood pressure, ECG-recordings, heart rate variability, oxygen saturation, etc.) can be monitored and wirelessly transmitted to the medical team. The latter can then provide weekly feedback to the patient in order to adequate exercise program to the patient's status (10).

The biggest advantage of TR is that it overcomes the problem of accessibility to CR centers reducing inequities. In addition, the possibility of doing rehabilitation exercises at home, may help improve adherence and modifications in life style.

While the concept is appealing, TR is in its early days and there is a lack of information on its impact. There are less than 30 published trials on this subject. Most have not reported any major adverse events, such as arrhythmias or death (8). Preliminary

evidence shows potential for cost savings and reduction in health-care facilities utilization (11).

The paucity of information on remote TR drives also from major heterogeneity among studies regarding study populations, duration of interventions, type of home-care devices, and communication with the patient (including intensity and frequency) (12).

Bearing this in mind, we implemented a systematic review focused on the effectiveness of TR programs in HF patients to help characterize practices in TR programs, and understand their advantages, impact and safety in HF patients.

METHODS

The methods of the systematic review and meta-analysis were specified in advance. Details of the protocol were registered on PROSPERO and can be accessed at http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019119409.

Eligibility criteria

Study designs

This systematic review included only randomized controlled trials (RCT) exploring the potential effectiveness of TR programs compared to the standard care for the management of chronic heart failure (usual care with or without exercise prescription). We excluded reviews, preclinical studies, in vitro studies, editorial or opinion articles and conference papers. Nevertheless, previous reviews and meta-analysis were assessed as guide and reference lists were searched to identify additional RCTs.

Participants

This review involved studies including HF patients either if with reduced or preserved ejection fraction. Studies were included either if they had stable chronic patients or those after recent discharge from a heart failure hospitalization.

Interventions

We defined TR as an intervention including physical exercise prescription by CR specialist that must be performed outside the hospital or the CR center (done at home or community). Additionally, some form of interaction between patients and CR team had to be established in order to adjust patient's exercise program and therapy.

Comparators

"Usual care" was defined as the standard multidisciplinary management programs proposed by the 2016 ESC Guidelines. This consisted in regular follow-up consultations (usual care with or without exercise prescription) to ensure the safety and optimal dosing of medicines and detect the development of complications or disease progression that may require a change in management.

Outcome

Endpoints related to evaluation of HF progression were of primary interest and they were collected as reported.

Primary endpoints

- CV Death or Heart failure-related hospitalizations

Secondary endpoints

- Functional capacity and exercise tolerance – Six-minute walk test (6MWT), peak oxygen uptake (pV02)
- General and disease specific quality of life – Minnesota Living Heart Failure Questionnaire (MLHFQ), Short Form Health Survey (SF36), EQ5D
- Psychosocial wellbeing – Hospital Anxiety Depression Score (HADS)
- Healthcare costs and cost effectiveness
- Cardiovascular safety
- Self-care and therapeutic adherence
- Cognitive function
- Frailty (time up-and-go, Fried)
- Intervention group complications with technology

Search strategy. Four databases (PubMed/Medline, Cochrane Central Register of Controlled Trials, SCOPUS and Science Citation Index Expanded - Web of Science) were systematically searched for relevant studies that reported some form of TR in HF patients. To search for those articles different combinations of Medical Subject Headings (MeSH) terms were used, such as tele-rehabilitation, telecardiology, telecare, remote rehabilitation, virtual rehabilitation. We also performed manual searching through grey literature across clinicaltrials.gov in order to retain efficacy in the identification of additional published, unpublished or ongoing trials. No limitation concerning date or language of publication was applied.

Study Selection. Two reviewers independently screened and selected the studies. After elimination of duplicated references, initial selection of eligible manuscripts was based

on the information in their titles and abstracts. During the second step, relevant full-text articles were obtained. We analyzed only randomized controlled trials that included HF patients and reported some form of cardiac TR. Inter-reviewer disagreements were solved by discussion and consensus. When a full-text was not available, authors were contacted via email. In the end only one reference could not be found. (13)

Data extraction. Included papers were analyzed and information about the design of the study, characteristics of participants, type of intervention and all reported outcomes were collected using Excel. Our primary outcome was "CV Death or Heart failure-related hospitalizations". As secondary outcomes, we analyzed changes in "Functional capacity and exercise tolerance", "General and disease specific quality of life", "Psychosocial wellbeing" and "Adherence and safety of intervention". When articles did not have all information available, or if we had some doubts about data, authors were contacted via email.

Statistical analysis. Statistical analysis was performed using Review Manager 5.3. To assess the possible risk of bias (RoB) for each study, we collected information using the Cochrane Collaboration RoB tool. Each study was classified as "high risk", "low risk" or "unclear risk" of bias. We computed graphic representations of potential bias within and across studies using the same software. Assessments of quality of evidence were performed using the GRADE approach for every outcome (14).

A meta-analysis regarding Functional Capacity (6MWT, PVO2) and Quality of life (MLHFQ and SF-36) was performed using a random effects model with the DerSimonian & Laird method, taking into account the high heterogeneity observed. Data for each outcome was combined and calculated using the RevMan 5.3 software. To overcome the limitations associated with some missing values for important data we strictly followed Cochrane recommendations. To calculate the standard deviation (**SD**) of

the change between baseline and post-test assessments we used the mean correlation coefficient and SD values of baseline and post-trial measures. Three studies did not report the SD from baseline and post-trial measures. For that reason, we assumed the mean value of SD across the studies analyzed.

A qualitative description was performed for other outcomes that could not be included in meta-analysis. Heterogeneity was analyzed by Chi-square2 test and I-square2 statistic (I^2). Moderate or severe heterogeneity was considered if I^2>40% and I^2>90%, respectively.

To assess potential moderators of heterogeneity, the following subgroup analysis were performed:

1. HF Classification
    a. HFrEF (<40%)
    b. HFrEF + HFpEF
2. Presence of telemonitoring
    a. With telemonitoring
    b. Without telemonitoring
3. Bias assessment
    a. Low or Unclear risk of bias
    b. High risk of bias
4. Follow-up intensity
    a. Regular Follow-up
    b. Intense Follow-up

Sensitivity analysis was performed with a classic take-one-out approach.

RESULTS

Study Selection

Out of the 3902 studies initially identified, 15 studies were included in the meta-analyses. Figure 1 shows the selection process and the reasons for exclusion for each study during the full-text assessment.

Bias Assessment

Overall bias classification was “high risk”. In the total of fifteen studies, four were classified as “low risk”, two as “unclear risk” and nine as “high risk” (Figure 2).

Selection bias related to random sequence used was “low risk” in almost all trials. Two studies reported significant differences in baseline characteristics of control and intervention groups.

Allocation Concealment was low risk in seven trials. Other seven did not have a detailed description of this procedure neither their authors could clarify this topic, so they were classified as “unclear”. One trial was classified as “high risk” because patients’ assignment was based on their acceptance of the intervention. (15)

All studies were classified as high risk for performance bias because all were non-blinded due to the nature of interventions.

Considering detection bias, the most frequent classification was “unclear”. Seven studies didn’t clarify that point (15-21), two studies did not blind outcome assessors (22, 23) and six studies performed a blind assessment.

Regarding attrition and reporting bias, the majority was “low risk”. Only one study did not report all pre-specified outcomes in the protocol (19).

We analyzed the risk of intensive monitoring and feedback influence adherence to the intervention. For that topic, eight studies were considered to have low risk, two were unclear and five had high risk (16, 19, 20, 24, 25). These last group reported intensive contacts (daily or weekly) to assess compliance with the program and showed high adherence rates.

Adherence

Adherence to the program had different definitions across studies making impossible to perform a meta-analysis. In six studies, defining adherence as "attending all sessions" and rates ranged from 70% to 100% in the intervention groups. In four studies in which adherence was defined as attendance to more than 80% of sessions and rates ranged from 71% to 95% in experimental group.

Efficacy Outcomes

Our primary outcome was CV Death or Heart failure-related hospitalizations but only two studies reported the number of hospitalizations that occurred during the trial or during the long-term follow-up. Lang et al. followed patients for three months after the end of the trial and registered 4 hospital admissions in the intervention group and 7 hospital admissions in the control group. Frederix et al. revaluated patients 2 years later and reported 32 cardiovascular admissions in the intervention group and 60 in the control group. Due to lack of analysis of hospital admissions in all trials we could not perform a statistical analysis of these data.

Functional capacity (FC) was assessed by 6MWT at baseline and at the end of trial in nine studies (Figure 3). The majority of controls group were submitted to usual care without exercise prescription but in four studies, controls were submitted to standard CR. In general, patients in TR group had a significant better improvement (Mean

Difference (MD) 27.05; CI95% [5.48;48.63]; participants= 664). Moderate heterogeneity was found (I^2=75%). GRADE assessment considered evidence as Moderate quality (Supplementary files).

Peak VO2 (pVO2) was measured in seven studies at baseline and at the end of trial (Figure 4). In four studies controls were submitted to standard CR and three were under usual care without exercise prescription. In general, patients in the TR group had a better improvement on pVO2 (MD 2.00; CI95% [-0.12;4.12]; participants = 564) but the pooled estimate was not statistically significant. Severe heterogeneity was found (I^2=94%). GRADE assessment considered evidence as Very Low quality (Supplementary files).

Quality of life (QoL) was evaluated by MLHFQ in eight studies at baseline and at the end of trial (Figure 5). Only in one study, control group was submitted to standard CR. We found a statistical significant better score in intervention group (Mean Difference -7.95; CI95% [-12.21;-3.70]; participants=441). Moderate heterogeneity was found (I^2=59%). GRADE assessment considered evidence as High quality (Supplementary files). Two studies using EQ5D to evaluate QoL did not find differences between groups (26, 27).

In five studies, authors used SF-36 to assess patient's quality of life, but only results from four studies were included due to lack of information (17, 19, 20, 28). Considering Physical score, no statistically significant differences were found (Mean Difference 0.24; CI95% [-5.79;6.26]; participants=256) but controls had an increased score in three studies while TR had higher scores only in two studies. Considerable heterogeneity was found (I^2=80%). GRADE assessment considered evidence as Very Low quality (Supplementary files). Considering Mental score of SF-36, no statistically significant differences were found (MD 0.38; CI95% [-4.93;5.70]; participants=256) but

controls had an increased score in three studies while TR had lower scores in three studies. Significant heterogeneity was found (I^2=81%). GRADE assessment considered evidence as Very Low quality (Supplementary files).

Considering psychological wellbeing, two other studies used the Hospital Anxiety and Depression Symptoms (HADS) to analyze the impact of TR on the presence of anxiety and depressive symptoms. Peng et al. found a positive impact of TR on anxiety and depression reduction in both standards (p=0,030 for anxiety; p=0,032 for depression) (29), while Keast et al. reported a significant reduction only in the depression score (p=0,014) (22).

Safety evaluation varied widely among trials. The majority only reported clinical adverse events and in six studies, they were classified as major or minor. In spite of this heterogeneity, all of them reported the TR interventions as safe and no major adverse events were reported.

Two studies made a cost-analysis about TR program. Frederix et al. calculated a cost per patient in intervention group of 3252€ and 4140€ in control group. Lang et al. reported a cost of 326,61£ (370,59€) per patient.

Considering long-term feasibility, five trials extended the follow-up period beyond the duration of the training program – minimum two months and maximum of two years. Three of them found sustained benefits in FC and QoL in TR group (29, 30), although in one study, authors observed a partial decline (31). The other two only found a sustained benefit in QoL assessment (26, 27).

Others secondary outcomes were not analyzed because they were not reported in any of the trials.

Subgroup analysis

A set of prespecified subgroup analysis of the potential moderators of heterogeneity in TR were conducted. We found better improvements for TR groups in all outcomes after subgroup division (Supplementary files).

Sensitivity analysis

We identified a decrease in heterogeneity of pVo2 (94 to 78%) and QoL (59 tp 17%) after leaving out of the analysis the study by Servantes et al. In 6MWT, TR showed non-inferior effect after removing Bernocchi et al. and Piotrowicz et al.,2015 (Supplementary files).

DISCUSSION

We performed a systematic review and meta-analysis that included 15 studies assessing the effectiveness of telerehabilitation programs in HF patients (Table 1), which globally revealed a paucity of effective programs and a huge heterogeneity in terms of settings, forms of intervention and monitoring.

Our primary outcome was the evaluation of the impact of such programs on the occurrence of CV Death/Heart failure hospitalizations amongst these patients, however only two studies reported on this kind of events. We hypothesize that this may be due to the short period of intervention and follow-up of most studies. None lasted for more than 4 months and most did not include a post-trial evaluation at 6 months. Furthermore, the low number of reported hospitalizations may also be related to the fact that few patients were included in the post-discharge vulnerable phase. Additionally, most were stable and under optimal medical therapy.

Patients submitted to TR showed better results than those submitted to usual care (without exercise prescription), as reflected by 6MWT and pVo2. In three of the studies where controls were submitted to standard CR, these showed better improvements than TR but not statistically significant. Nevertheless, it is relevant to note that patients under TR showed a performance improvement in both tests at end of study, comparing to baseline, which highlights TR validity even if less performant than standard center-based CR.

Patients assigned to TR showed a consistent improvement in QoL compared to usual care, when evaluated with MLHFQ. This probably is due to the fact that TR is performed at home, with family support, less time constrains and easier logistics and it is an opportunity to the patient feel more useful and involved in management of his condition.

Contrary to MLHFQ, SF-36 showed no statistical differences between both groups which may be explainable by the higher specificity of MLHFQ in assessing Health related QoL in HF patients.

Studies included in this meta-analysis were extremely heterogenous regarding adherence evaluation, allowing no definite conclusion. This highlights the need to create a globally acceptable definition of patient adherence in this setting, that could be uniformly used in future trials. We suggest that TR sessions adherence ≥80% could be a reasonable definition of TR adherence in this setting. A standard definition should be established and used consistently in all future trials.

TR cost-effectiveness evaluation was not feasible since only two trials presented some results regarding costs, but no formal cost-effectiveness analysis We strongly suggest that this should be considered in future studies, in order to evaluate the feasibility and the potential value of the generalization of such programs.

In alignment with this, the above-mentioned evidence showing that TR can improve patients' functional capacity, autonomy and psychological well-being, being superior to usual care. Nevertheless, the paucity of studies available and their high heterogeneity calls for prudence in the interpretation of data.

We suggest that future studies protocols should include:

- Standard cardiac rehabilitation as control group.
- Performance of an ECG before the training sessions.
- Telemonitoring surveillance of exercise sessions (ideally with pulse oximeter).
- Intervention Standardization: 3 sessions/week, aerobic exercise with increasing load
- Programed contacts with the rehabilitation team 1-2 x/week, in order to review patient's clinical status and physical exercise program.
- Longer follow-up periods and post-end-of-trial evaluation, at 6 months after the end of intervention

Strengths and Limitations

This systematic review was performed according to recommended guidelines, with rigorous data selection and analysis. However, it may have some limitations derived from the big heterogeneity amongst trials. Nine studies were classified as presenting a "high risk of bias" and all were non-blinded. In some we had to input missing values, due to the lack of information and poor reporting. These reasons hampered the comparison.

CONCLUSION

Despite being a class I recommendation for patients suffering from heart failure, center-based CR is presently neither feasible nor accessible to most of the patients, due to manifest logistic limitations. Considering the high prevalence of HF there simply are not enough centers to perform cardiac rehabilitation to all patient to which it is indicated.

This systematic review and meta-analysis suggests that Tele-Rehabilitation is non-inferior to Usual Care and might be non-inferior to standard CR. If supported by future and better designed studies, TR may become an attractive alternative to standard center-based CR, allowing to fulfill the class I recommendation of rehabilitation to these patients.

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FIGURE LEGENDS

Figure 1. Flow Chart of included studies

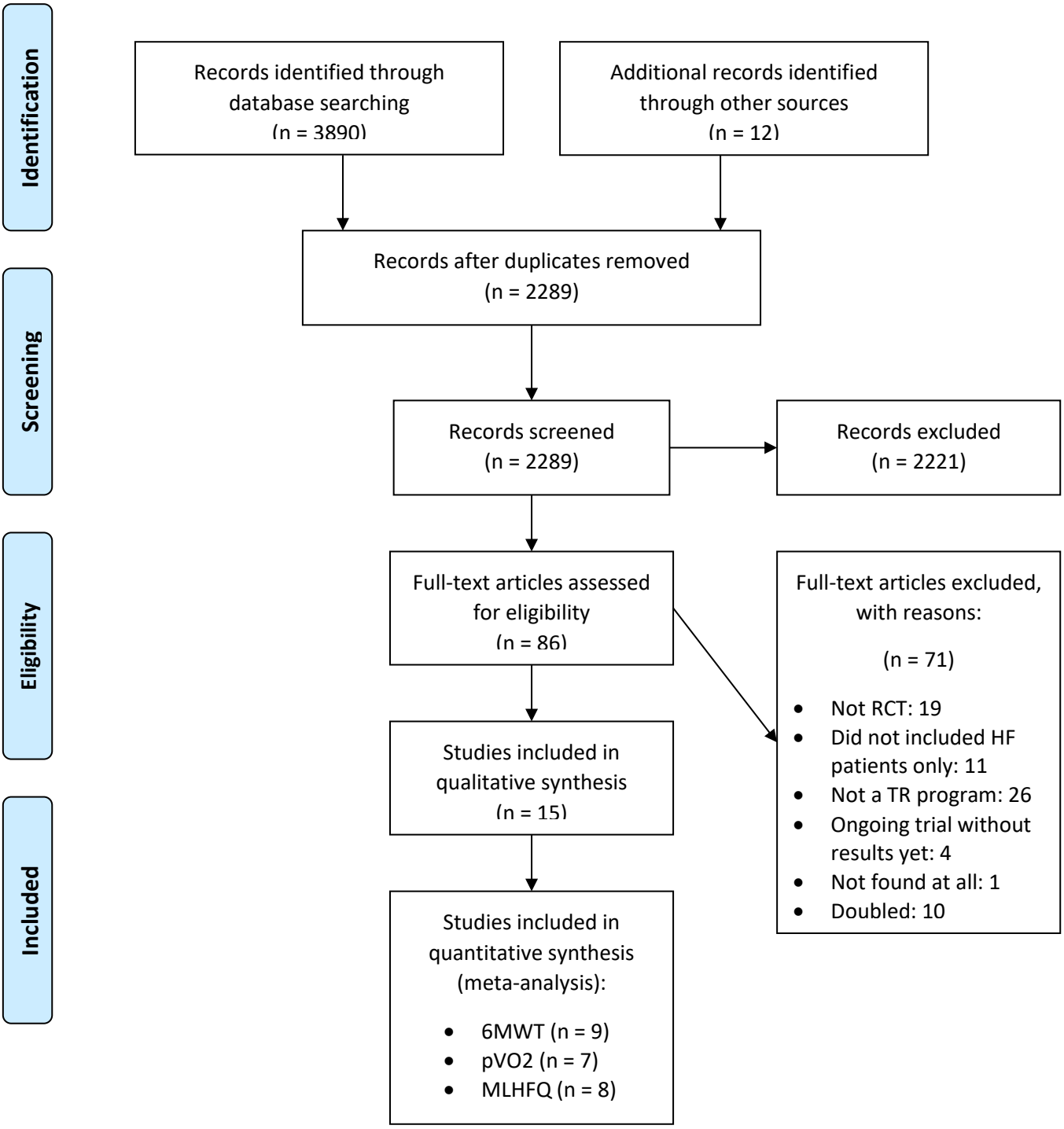


Figure 2: Risk of Bias across studies.

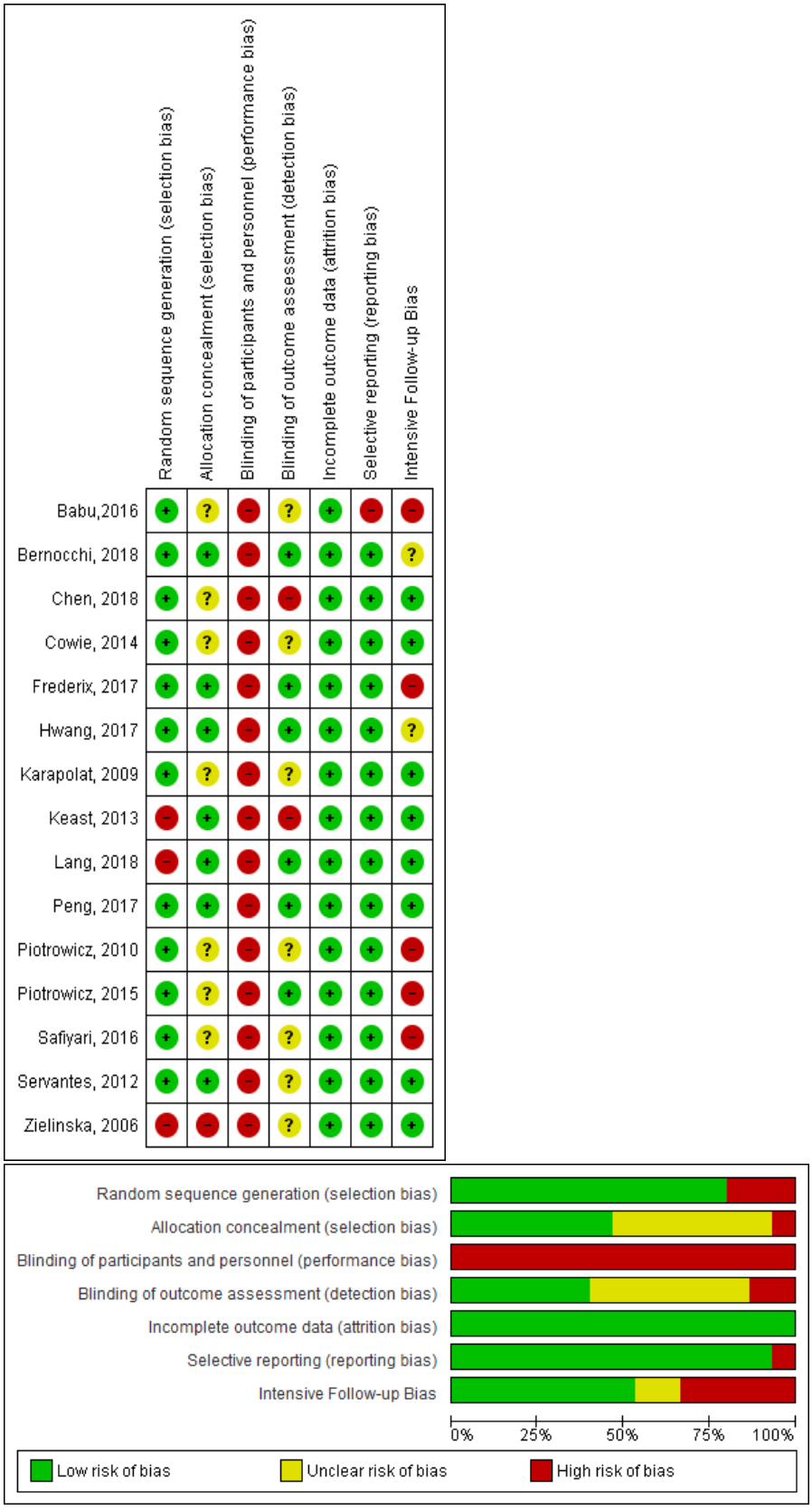


Figure 3. Analysis of 6MWT Outcome

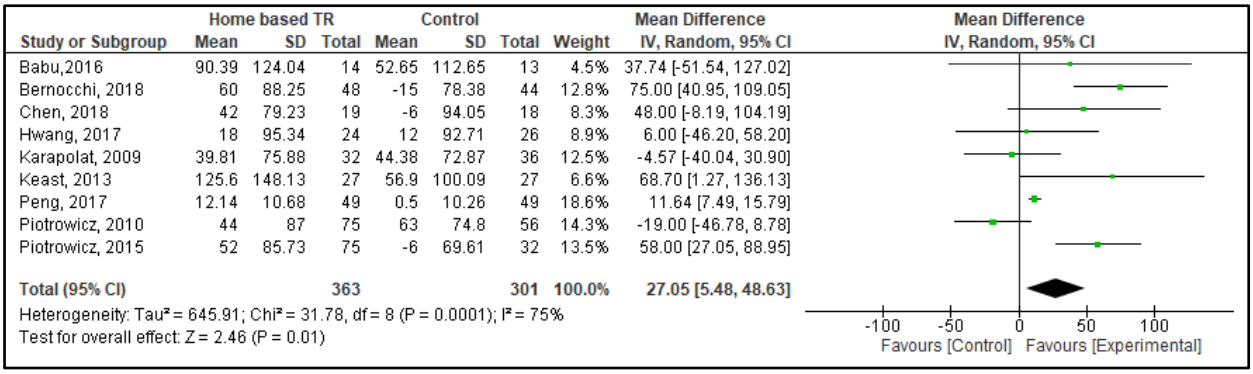


Figure 4. Analysis of Peak VO2 Outcome

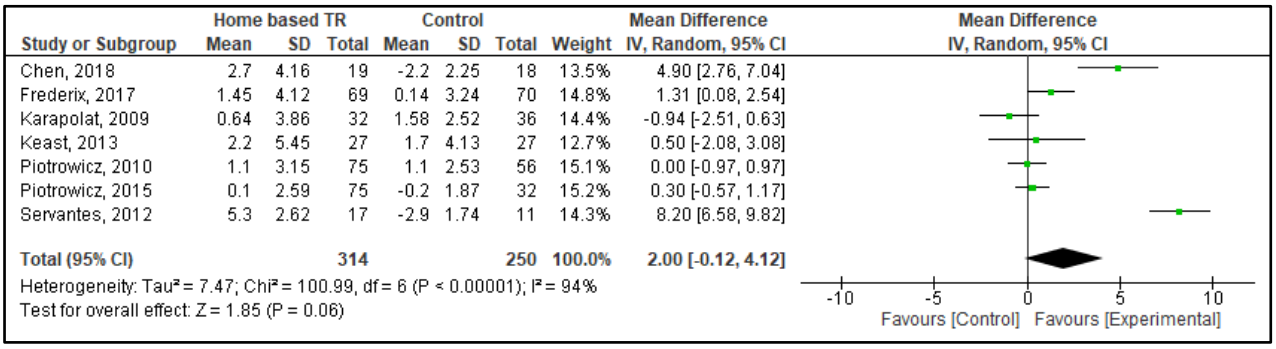


Figure 5. Analysis of QoL (MLHFQ) Outcome

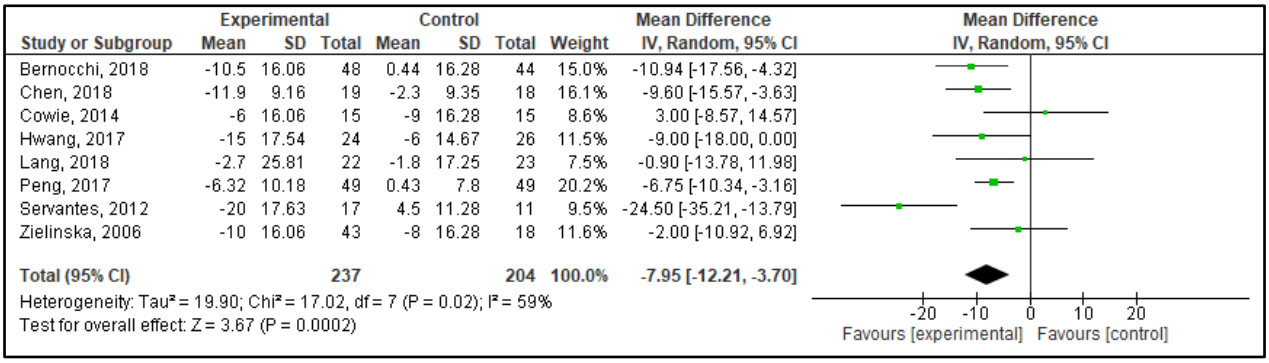


Table 1: Randomized clinical trials of Tele-rehabilitation in HF patients.
General characteristics of the studies and patients.

1st Author Year Country	HF Population	Recruitment setting	Intervention during session	Monitoring during exercise	Feedback	Comparasion	1ry Outcome	Enrolled Patients (retention,%)	Duration of trial / Follow-up
Babu 2011,India	CHF NYHA II-IV	University teaching hospital	Walking	No	Weekly calls	Usual Care	6MWT	30 (90)	8w / 8w
Bernocchi 2018,Italy	NYHA II-IV With COPD	3 rehabilitation centers	Cycling and strength	ECG, Pulse oximeter	Weekly calls	Usual Care	6MWT	112 (71.4)	4M / 6M
Chen 2018,Taiwan	HFrEF NYHA <IV	Outpatient, general ward and intensive care unit	Aerobic exercise	No	Calls every 2w	Usual Care	VO2 p, QoL 6MWT	75 (49.3)	3M / 3M
Cowie 2014,Scotland	HFrEF NYHA II-III	National Health Service Scotland	Interval aerobic training	No	Calls every 2w	Hospital CR OR Usual Care	ISWT, QoL	60 (76.7)	8w / 8w
Hwang 2017,Australia	NYHA<IV recent hospitalized	Cardiology and general medical ward	Aerobic and strength exercises	ECG, Pulse oximeter	During the session	Outpatient CR	6MWT	53 (92.4)	12w / 24w
Lang 2018,Scotland	HFpEF NYHA< IV	Single center (Tayside, Scotland)	Walking or chair-based exercises	No	As needed	Usual Care	ISWT, QoL, Hospitalization	50 (90)	12w / 6M
Servantes 2012, Brazil	HFrEF 30-70yo NYHA II-III	Medical center from São Paulo Federal University	Walking and strength exercises	No	Weekly calls	Usual Care	VO2p, QoL Strength Endurance	50 (90)	3M / 3M
Karapolat 2009,Turkey	HFrEF NYHA II-III	Ege University Hospital's Cardiac Rehabilitation	Walking with strength exercises	No	Weekly calls	Hospital based CR	VO2 peak 6MWT QoL	74 (91,9)	8w / 8w
Keast 2013,Canada	EF 20-35% NYHA II-III	Tertiary cardiac care center, Otawa	Nordic Walk	online supervision	During the session	Outpatient CR	6MWT	54 (79,6)	12w / 12w
Piotrowicz 2010, Poland	HFrEF NYHA II-III	Institute of Cardiology,Warsaw	Walking	ECG, Vitals	Daily calls	Outpatient CR	VO2p, QoL 6MWT	152 (86,2)	8w / 8w
Piotrowicz 2015, Poland	HFrEF NYHA II-III	Institute of Cardiology,Warsaw	Nordic walk	ECG, Vitals	Daily calls	Usual Care	VO2p	111 (96,4)	8w / 8w
SafiyariHafiz 2016,Canada	HFrEF NYHA<IV	Not reported	HIIT (walking) and resistance training	HR and Pedometer	Calls 2-3x/w	Usual Care	6MWT VO2p, QoL	40 (72.5)	12w / 12w
Frederix 2017,Belgium	HFpEF, HFrEF NYHA<IV	Multi-center trial	Walking	accelerometer	Weekly calls or sms	Outpatient CR	VO2 p	140 (85)	12w /2y
Peng 2018, China	HFrEF NYHA I-III	Teaching hospital in Chengdu	Aerobic and strength	online supervision	At session, weekly calls	Usual Care	QoL, 6MWT, HADS	98 (84.7)	2M / 6M
Zielinska 2006, Poland	HFrEF NYHA II-III	3 clinics and 1 hospital in Poland	3w OutpatientCR 9w home exercise	ECG, HR	No regular feedback	Usual Care	QoL, Duration of Stress Test	61 (100)	12w / 12w

APPENDICES

Table 1.1 Description of trial and patients' characteristics of all included studies

Author Year Country	Study Population	Specific characteristics of experimental group	Specific characteristics of control group	Exclusion criteria	Comorbidities / Medication (exp/cont)	Sample size	Enrolled patients (n)	Intervention	Duration of the rehabilitation program	Follow-up visits and total period	Adherence rate/ Satisfaction	Outcomes
Babu 2011 India	Congestive HF NYHA II-IV Tertiary care, university teaching hospital	Mean age: 56.87+-10.45 Sex(M/F): 13:3 EF: 30+-8.8 Length of stay: 5.46 +-0.91 Length of stay UCI:1 +-0.92 SF36: 33.8	Mean age: 58.73+-10.81 Sex(M/F): 10:5 EF: 31+-12.5 Length of stay: 6.8 +-3.7 Length of stay UCI: 1.13 +-1.6 SF36: 32.3	AMI, Uncontrolled arrhythmias, valvular disease, severe orthopedic and neurological problems	Not described Diuretics: all Digoxin: 9/8 ACE-I: 12/12	Calculated: 15 for each group (considered 20% drop-out rate)	30 CONt: 15 EXP: 15 Final: 27 CONt: 13 EXP: 14	Home based CR vs standard care without exercise program	8w	8w Assessment: **-6MWT**: Baseline and at 8w **-QoL**: Baseline, Discharge and at 8w	72,6% (defined as exercise >80% days)	6MWT QoL (SF36)
Bernocchi 2018 Italy	HF patients undergoing in-hosp rehab (3	Mean age: 71+-9	Mean age: 70+-9.5	Physical activity limitations due to non-cardiac/ pulmonary	Not reported	Calculated: at least 44	112 CONt: 56	Home based CR vs Standar	4M	6M Assessment of	65% performed 3-5d/w	6MWT QoL (MLHFQ) BARTHEL

	rehabilitation centers) NYHA II-IV Diagnosis of COPD (B,C,D) for >12M	Sex: 88% male Mean BMI: 28,5 EF%: 44.5 +- 12.4 FEV1/FVC: 60+- 10.2	Sex: 75% male Mean BMI: 27,7 EF%: 43.3 +- 13.2 FEV1/FVC: 62+- 8.9	conditions; life expectancy<6M; severe cognitive impaiments; did not return home after hospitalization	SABA/LAMA/ICS: 56/56 Digitalis: 4/11 BB: 37/30 ACE-I: 25/28 Diuretics: 42/47 Aldosterone antag: 27/32	(20-25% drop-out rate)	EXP: 56 Final: 80 CONt: 45 EXP: 35	d Medical Care without exercise program		satisfaction, 6MWT, QoL, BARTHEL: -Baseline -4M -6M	16% >5d/w 19%<3d/w High satisfaction	CAT Dyspnoea PASE
Chen 2018 Taiwan	HF patients from outpatient, general ward, intensive care unit HFrEF NYHA <IV	Mean age: 61+-11 Sex (M/F): 17/2 BMI: 24.9 +- 2.6 Mean EF: 36+- 9 Mean Pvo2: 18.2 +- 4.1 CABG:2	Mean age: 60+-16 Sex (M/F): 14/4 BMI: 25.2 +- 5.7 Mean EF: 32+- 11 Mean Pvo2: 18.9 +- 4.1 CABG: 0	LVEF>50% NYHA IV High bedridden status Musculoskeletal system problems or other contraindications for exercise	Not described	Not mentioned	75 CONt: 40 EXP: 35 Final: 37 CONt: 18 EXP: 19	Home based CR vs standard medical care without exercise program	3M	3M Assessment of physical parameters (CPET, 6MWT): Baseline End of the trial	11 losses in control, 16 in intervention No specific measure about adherence.	Pvo2 6MWT Anaerobic threshold QoL

Cowie 2014 Scotland	HF patients selected at NHSS Stable for 1M With OMT With EF reduced NYHA II-III	Mean age: 65.5 Sex (M/F): 18/2 BMI: 26.6 NYHA II/III: 12/8 Severe LV Impairment: 15	**HOSPITAL**Mean age: 71.2 Sex (M/F): 16/4 BMI: 27.3 NYHA II/III: 12/8 Severe LV Impairment: 10 **CONTROL** Mean age: 61.4 Sex (M/F): 17/3 BMI: 27.1 NYHA II/III: 13/7 Severe LV Impairment: 10	Not reported at the article	DM, COPD, HT, CVA, PVD, Anemia, Renal failure, Osteoporosis No information about medications	Not reported at the article	60 HOME: 20 HOSP: 20 CONt: 20 Final: 46 HOME: 15 HOSP: 15 CONt: 16	Home based CR vs Hospital CR vs usual care	8w	8w Assessment -Baseline -End of the trial	HOME: 77% HOSP: 86% (defined as completion of total of exercise sessions)	ISWT QoL
Hwang 2017 Australia	HF patients from cardiology and general medical ward, with recent hospital	Mean Age: 68 Sex (M/F): 19/5 Mean LVEF: 36%	Mean Age: 67 Sex (M/F): 21/6 Mean LVEF: 35%	Symptomatic severe aortic stenosis, significant ischemia at low exercise intensity; lived in an	DM, Chronic respiratory conditions, Depressio	Calculated: 48 (drop-out rate of 10%; power 80%)	53 CONt 29 EXP: 24 Final: 49	Home based CR vs Outpatient CR	12w	24w Assessment of walking, balance, strength,	EXP: 71% CONt:30 % (adherent: >80%	6MWT TUGT 10min walk test Strength grip QoL RUIS

	admission and referred to HF service >18yo NYHA<IV	HFpEF: 3 NYHA: I – 3 II – 9 III – 12 Atrial Arrythmia: 9	HFpEF: 2 NYHA: I – 2 II – 21 III – 6 Atrial Arrythmia: 12	institution; lived more than 1h driving distance from the treating hospital; no support person at home	n, Stroke, Arthritis Medications: ACE-I: 23/25 BB:22/23 Diuretics: 21/26 Home O2: 3/0		CONt 26 EXP: 23			incontinence, QoL: Baseline End 3M after the end of trial	sessions)	BOOMER EQ-5D Adherence Satisfaction
Lang 2018 Scotland	HFpEF EF>45% NYHA< IV Single center (Tayside, Scotland)	Mean Age: 71.8 Sex (M/F): 9/16 BMI: 32.1 HF ischemic: 8 NYHA: I- 1; II-15; III- 9	Mean Age: 76 Sex (M/F): 14/11 BMI: 32.2 HF ischemic: 16 NYHA: I- 1; II-16; III-8	Patients who have undertaken (CR) within the last 6 months; with severe chronic pulmonary disease, requiring home oxygen or hospitalization for exacerbation within 12 months; any of the following contraindications to exercise	HTA, DM, Renal impairment, AF (6/13), previous AMI (4/5) Medication: BB: 18/13 ACE-I: 11/14 Angiotensin antag: 7/7	Planned to recruit 50 patients based on "estimations"	50 EXP: 25 CONt :25 Final: 45 EXP: 22 CONt :23	Home based CR vs Usual Care	12w	6M Assessment of: HRQoL, clinical events, ISWT, EQ-5D, SCHFI at baseline, 4M and 6M	Minimum adherence: 92% (attend to 1st and 2 other contacts) High level of satisfaction (qualitative analysis)	ISWT QoL Clinical events SCHFI Safety Acceptability

				testing or exercise training documented: Early phase after ACS; Untreated life-threatening arrhythmias; Acute heart failure; Uncontrolled hypertension; Advanced AV block; Acute myocarditis and pericarditis; Symptomatic aortic stenosis; Severe hypertrophic obstructive cardiomyopathy; Acute systemic illness; Intracardiac thrombus; Progressive worsening of exercise tolerance or							

				dyspnoea at rest over previous 3–5 days, Significant ischaemia during low-intensity exercise, Recent embolism, Thrombophlebitis,Recent-onset atrial fibrillation /atrial flutter (in the last 4 weeks); unable to understand the study information or to complete study procedures; in a long-term care establishment or who are unwilling or unable to travel to research assessments;							

Servantes 2012 Brazil	HF patient followed at HF medical center (São Paulo Federal University) EF<40% Pvo2<20 w/ OMT stable for 3M age 30-70y NYHA II-III	**EXP1**: Mean Age: 51.76 +- 9.83 Sex (M/F): 47/53 % BMI: 26.87+- 4.69 Mean EF: 29.59+- 6.61 NYHA: II-82.4%; III-17.6% **EXP2**: Mean Age: 50.82 +- 9.45 Sex (M/F): 47/53 % BMI: 27.98 +- 4.42	Mean Age: 53 +- 8.19 Sex (M/F): 45.5/54.5% BMI: 27.73 +- 3.66 Mean EF: 31.55+- 5.77 NYHA: II-72.7%; III-27.3%	NYHA IV; MI or revascularization in past 4M; unstable angina, complex or symptomatic ventricular arrythmias, obstructive aortic or mitral valvular disease, hypertrophic cardiomyopathy, abnormal exercise testing, hypotension, pulmonary arterial pressure >50mmHg, chronic obstructive pulmonary disease, leg claudication, musculoskeletal disorders or	All with sleep apnea and sedentary behaviour. HTA, Overweight DM, Dyslipidemia Medication: BB: all ACE-I: all Aldosterone antag: >90% Diuretics: 17/14/10 Anticoagulant: 7/7/4 Glycemic control: 5/7/4 Digitalis: 2/1/3 CCB: 1/0/0	Not mentioned	50 EXP1:18 EXP2:18 Cont: 14 Final: 45 EXP1:17 EXP2:17 Cont: 11	Home based CR – aerobic exercise w/ or without strength training – vs No training	3M	3M Assessment of CPET, Isokinet strength, QoL, Polysomnography at baseline, 1M, 2M and end of the trial (3M)	Adherence was assessed by nº sessions completed EXP1: 98.5+- 13.7% EXP2: 100+- 11.2% CONT: not reported	CET Muscle Strength Endurance QoL Polysomnography

		Mean EF: 31 +-5.02 NYHA: II-82.4%; III-17.6%		psychiatric disease								
Karapolat 2009 Turkey	HF as result of ischemic or cardiomyopathy Clinical stability for at least 3M HFrEF NYHA II-III Under OMT Stable during exercise tests Patients from Ege University Hospital's Cardiac Rehabilitation	Mean Age 45.16+-13.58 Sex(M/F) 21/11 BMI 25.19+-4.20 Dilated HF 59.4% NYHA II- 17; III- 15 FEV1: 78.78+-13.06	Mean Age 44.05+-11.49 Sex (M/F) 22/14 BMI 27.09+-3.83 Dilated HF 44.4% NYHA II-26; III-10 FEV1: 76.86+-16.86	neurological, orthopedic, peripheral vascular, or severe pulmonary disease; NYHA class IV; unstable angina pectoris; poorly controlled or exercise-induced cardiac arrhythmias; recent ACS or revascularization (<3M); significant valvular heart disease; AF; uncontrolled HT; performing exercise training at	DM, HT, Hyperlipidemia Medication: Digoxin 46.9/63.9 % BB (alfa+beta) 84.4/76.7 % ACE-I 87.5/77.8 % AT1-I 12.5/5.6% Diuretics Spiro 81.3/83.3 %	Not mentioned	74 EXP: 37 Cont: 37 Final: 68 EXP: 36 Cont: 32	Home based CR vs Hospital based CR	8w	8w Assessment of: CPET, 6MWT, HR-QoL, Psychological symptoms, Hemodynamic parameters At baseline and End of the trial	Interv: 87,5% Control: 90% (defined as "mean attendance")	CPET 6MWT QoL (SF36) Psychological symp: BDI, STAI Echocardiographic measures

				regular intervals during the previous 6w	Furo 37.5/32.3 % AAS 68.8/66.7 %							
Keast 2013 Canada	HF patients referral to CR program (Tertiary cardiac care center, Otawa) EF 20-35% NYHA II-III Clinical stable >40y	Mean Age 62.1 Sex(M/F) 22/5 Ischemic HF: 19 Mean EF%: 27.6 NYHA II- 6 III- 21 ICD: 10 Previous IM: 17	Mean Age 62.8 Sex(M/F) 22/5 Ischemic HF: 22 Mean EF%:26.3 NYHA II- 0; III- 27 ICD:7 Previous IM:23	Psychiatric disorder; inability to understand English	Previous IM, ICD, Pacemaker, Revascularization and others comorbilities not specified Medication ACE-I 25/21 BB 25/24 ARA 4/4 Diuretic 16/15 Digoxin 2/4	With total of 54 participants, the study has 80% power	54 EXP: 27 CON: 27 Final: 43 EXP: 22 CON: 21	Home based Nordic walk vs Outpatient CR	12w	12w Assessment: clinical history, BP, BW, Waist, HR, Anxiety, depression and leisure-time activity questionnaire, CPET at Baseline and End of the trial	EXP: 69,3% Control: 66,9% (defined as “attendance to supervised exercise sessions”)	6MWT CEPT Strength Anthropometric measures HADS

Piotrowicz 2010 Poland	HF diagnosis for >3M with HFrEF NYHA II-III Clinical stable and on OMT for 4w Able to exercise Patients with ICD were included; from Institute of Cardiology, Warsaw	Mean Age 60.5+-8.8 Sex (M/F) 53/3 BMI 26.5+-3.8 Ischemic HF 85.7% NYHA II- 31; III- 25 Previous IM 78.6%	Mean Age 56.4+-10.9 Sex (M/F) 64/11 BMI 27,7+-4.3 Ischemic HF 73.7% NYHA II- 37; III- 38 Previous IM 64%	NYHA class I or IV; unstable angina; (iii) a history ACS <1M, CAB<2M, initiation of CRT<1y, symptomatic and/or exercise-induced cardiac arrhythmia or conduction disturbances; valvular or congenital heart disease requiring surgical treatment; HCM; severe pulmonary hypertension or other severe pulmonary disease; uncontrolled HT; anemia, acute and/or decompensated non-cardiac	DM, Stroke, Hyperlipidemia, Angioplasty, CABG Medication BB- all ACE-I: 51/69 AR-b: 5/11 Digoxin 8/17 Diuretics 40/58 Spiro 51/72 AAS 48/55 Anticoagulation 16/28 Statins 52/67 ICD 13/24	For power= 0,8 and difference of this parameter over 8w= 20%, sample size= 47 is satisfied. For drop out rate of 25%, sample size= 63 patients is enough for each group	152 EXP: 77 Cont: 75 Final: 131 EXP: 75 Cont: 56	Home walking vs Outpatient CR	8w	8w Assessment of clinical status, 3D-echo, 6MWT, HRQoL, CPET at baseline and end of the trial	All patients in intervention group completed the program.	VO2 peak HRQoL 6MWT Safety Adherence

				disease; physical disability related to severe musculoskeletal or neurological problems; acute or chronic inflammatory disease; cancer; severe psychiatric disorder								
Piotrowicz 2015 Poland	HF diagnosis for >3M with HFrEF NYHA II-III Clinical stable and on OMT for 4w Able to exercise at home. Patients with ICD were included;	Mean Age 54.4+-10.9 Sex (M/F) 64/11 BMI 28+-3 Mean LVEF 30+-8 Ischemic HF 66.7% NYHA	Mean Age 62.1+-12.5 Sex (M/F) 31/1 BMI 28+-3 Mean LVEF 34+-6 Ischemic HF 84.4% NYHA	unstable angina; a history of an acute coronary syndrome within the last month, coronary artery bypass grafting within the last two months, or initiation of CRT-P or CRT-D <6M, or implantation of a pacemaker	DM, Stroke, Hyperlipidemia, Angioplasty, CABG Medication BB- all ACE-I: 61/27 AR-b: 12/4 Diuretics 37/13	Estimation was made, for 80% power and drop out rate of 15% - "sample size=32 is satisfied"	111 EXP: 77 Cont: 34 Final: 107 EXP: 75 Cont: 32	Home walking vs Usual Care without any formal exercise plan	8w	8w Assessment of clinical status, 3D-echo, 6MWT, HRQoL, CPET at baseline and end of the trial	94,7% were adherent (attended to at least 80% of sessions)	6MWT CPET QoL – SF36 Acceptance and Adherence

	from Institute of Cardiology, Warsaw	II- 51; III- 24 Previous IM 62.7%	II- 23;III- 9 Previous IM 81.3%	and/or ICD <6w; symptomatic and/or exercise induced cardiac arrhythmia or conduction disturbance; valvular or congenital heart disease requiring surgical treatment; HCM; severe pulmonary hypertension or other severe pulmonary disease; uncontrolled HT; anaemia; acute and/or decompensated noncardiac disease; physical disability related to severe musculoskeletal	Spiro/eplerr 24/9 AAS 54/24 Anticoagul 25/10 Statins 60/28 ICD 56/16							

				or neurological problems; acute or chronic inflammatory disease; severe psychiatric disorder								
Safiyari-Hafizi 2016 Canada	HF with HFrEF NYHA<IV VO2p<69% predicted for age 45-75y OMT	Mean Age 57.8+-8.1 Sex (M/F) 15/5 BMI 30.3 +-4.4 NYHA: I- 3 II- 14 III-3 Initial Pvo2 46.7 +-10.2 EF 27.8 +-8.8	Mean Age 58.9+-6.9 Sex (M/F) 14/6 BMI 28.9 +-4.9 NYHA: I- 3 II- 14 III- 3 Initial Pvo2 47.6 +-10.8 EF 26+-8.3	Musculoskeletal limitations; Pulmonary disorders that limit exercise; Contraindications to training; Patients already involved in an exercise program Medications: Diuretics 14/10 ACE-I 13/13 AR-B 9/9 Nitrates 19/20 BB 18/18 Digitalis 3/6 Antiarryth 1/5 CCB 16/15 Anticoag 10/12	Not reported	Not reported	40 EXP: 20 CONt: 20 Final: 29 EXP: 14 CONt: 15	Home based-interval training vs UC without any formal exercise prescription	12w	12w Assessment of 6MWT, QoL, VO2p at baseline and end of the trial	EXP: 77+/-20% “adherence to the exercise prescription was high in intervention group”	6MWT pVo2 QoL Adverse events

Frederix 2017 Belgium	Patients were on current active rehabilitation a center; HFrEF or HFpEF, or CAD treated conservatively, with PCI or CABG; NYHA<IV OMT and stable for >4w 18-80y. Patients were recruited from different centers.	Mean Age 61 Sex (M/F) 59/10 BMI 28 HFrEF 2 HFpEF 2 CAD 65 EF>50%: 52 NYHA I- 54 II- 12 III- 3	Mean Age 61 Sex (M/F) 55/15 BMI 28 HFrEF 4 HFpEF 1 CAD 65 EF>50%: 50 NYHA I- 61 II- 4 III- 5	Non-CV condition that limits ability to exercise; terminal disease, dementia, cognitive impairment; simultaneous participation on another trial; history of VF exertional sustained VT/SVT within previous 6M	AF, DM, HT, PAD, Hyperlipidemia, Overweight, PCI, CABG Medication BB 53/57 ACE-I 44/48 Statin 66/64 Antiplatet Dual 37/40 Mono 29/27 Diuretics 12/14 Oral Antidiabetic 10/10 Insulin 7/5 Anticoagulation 4/5 Antiarrhythmics 4/3	For 95% power and account a dropout rate of 30%, a sample of 140 patients should be obtained	140 EXP: 70 Cont: 70 Final: 119 EXP: 60 CON: 59	Center based CR followed by Home based CR Vs Center CR only	12w	2y Assessment: Assessment of clinical status, echoTTE, CPET, MET, HRQoL, IPAQ, EQ-5D at Baseline, end of study and 2y later	“TR was associated with sign lower lack of adherence (OR 0,56, CI 0.45-0.69)”	pVo2 CV risk control, HR-QoL, IPAQ physical activity, EQ-5D CV readmission rate Costs analysis

Peng 2018 China	HF patients from a Teaching hospital in Chengdu, discharge to home. >18yo HFrEF NYHA I-III Stable condition and medication for >4w	Age: ≤60: 14 >60: 35 Sex (M/F) 28/21 Duration of HF: ≤1y: 16 >1y: 33 NYHA: I-11 II-18 III-20 Ischemic HF: 61,2% (30)	Age: ≤60: 16 >60: 33 Sex (M/F) 30/19 Duration of HF: ≤1y: 14 >1y: 35 NYHA: I-3 II-18 III-18 Ischemic HF: 59,2% (29)	MI<1M; unstable angina, uncontrolled HT, severe respiratory diseases, decompensated non-cardiac disease, malignancy, physical disability, mental disease; previous participation in exercise cardiac rehabilitation programs.	Comorbidities median: EXP – 1.0 CONT – 1.0	For 80% power, 52 patients were needed. To allow withdrawals, 98 patients were included.	98 EXP: 49 CONt: 49 Final: 83 EXP: 42 CONt: 41	TR program home-based vs usual care (without any exercise prescription)	2M	6M Assessment of MLHFQ, 6MWT, NYHA, resting HR, HADS anxiety and depression at baseline, end of trial and 4M later	Attrition: EXP: 14,3% CONt: 16,3%	QoL (MLHFQ), 6MWT, HADS, Heart Rate, LVEF, Changes in NYHA Classification
Zielinska 2006 Poland	HF patients referred to different clinics and hospitals in Poland. HFrEF NYHA II-III Clinical stable and stable doses of	Mean Age: 62+-7 BMI: 28,6 +-5,3 HF etiology: CAD: 36 DCM: 7 Mean LVEF:	Mean Age: 56,2+-13,5 BMI: 25,7 +-3,3 HF etiology: CAD: 14 DCM:4	MI, coronaroplasty or heart surgery <3M; disorders of musculoskeletal system, positive initial stress test; mental disorders; resting HR>110 bpm	Medication: ACE in BB Spiro Furosemid Statin	Not mentioned	61 EXP: 43 CON: 18 FINAL: 61 EXP: 43 CON: 18	3w of Outpatient CR followed by 9w home based exercise training	12w	Assessment of MLHFQ Stress Test HR, BP at baseline, 3w and 12w (end of the trial)	All patients completed the program	QoL (MLHFQ) Duration of Stress Test HR, BP

	drugs for >4w	33,3+-8,1	Mean LVEF: 31,2 +-7,1									

Table 1.2 Description of TR intervention in all included studies

Study	Exercise modality	Session duration/ intensity/ frequency	Supplemental exercise	Monitoring during the session	Feedback (type, frequency)	Educational sessions / Previous inpatient CR	Control group	Management of HF condition
Babu 2011 India	Walking + exercises	1st week: Walking: 5-10min, RPE 4-6 Exercises: 5reps x 2sets 2-4w: walking 10-15min; exercises 5reps x 4sets 4-6w: walking 20-30min; exercises 5reps x 6sets 6-8w: walking 30-40min; exercises 5reps x 8sets	Not reported	No telemonitoring during exercise session.	Weekly calls by therapist to assess patient's status and to adjust exercise level.	1w of supervised exercises and walking for 1h, 3x/day. Prescription was based RPE between 3-4/10, individualized for each patient. The progression was made when the patient was comfortable at that level.	physician directed advice on staying active	According to American Heart Association Guidelines

Bernocchi 2018 Italy	Exercise program with mini-ergometer and pedometer	Depended on patient's status: Basic level: 15-25min mini-ergometer + 30min callisthenic exercises for 3x/w High level: 30-45min mini-ergometer (0-60W) + 30-40min muscle reinforcement (0.5kg) for 3-7d/w	Basic level: free walking 2x/w High level: pedometer-based walking	Yes - pulse oximeter and ECG monitors.	Weekly structured calls from: -NT to assess patients' status and give healthy style advices. -**PT** to assess dyspnea, muscle fatigue (Borg scale) and adjust training plan.	Educational intervention from NT and PT for 4M	Standard care program with medication and oxygen, visits from the general practitioner and in-hospital check-ups. At enrollment received educational session and were invited to practice daily physical activity	Not mentioned
Chen 2018 Taiwan	Aerobic exercise based on patient's preference – walking (47%) jogging (5.4%), stationary cycling (47%)	At least 30min for at least 3x/w Exercise at 60-80% of peak HR	Not reported	No telemonitoring during exercise session.	Telephone interviews every 2w only to monitor patient's status. No changes to exercise plan were done.	Educational support during admission. 1w of outpatient CR at the hospital	Standard health care, with previous activity levels. No formal exercise prescription.	Medications were not changed in any patient during the study
Cowie 2014 Scotland	Aerobic exercise,	2x/w, at 40-60% HR reserve, 12-13 Borg RPE	Not reported	No telemonitoring	Telephone interviews by PT every 2w to	No previous CR. Support for home exercise	- Standard health care, no training	Not reported

	interval training	1h session: 15min warm-up, 30min aerobic overload, 15min cool-down HIIT: 90second functional aerobic exercise stations per circuit, 2 rounds.		during exercise session.	assess patient's status. Registry of exercise session parameters in a dairy	by a DVD and booklet.	-Hospital CR: similar to home program	
Hwang 2017 Australia	Aerobic and strength training	Synchronous videoconferencing for PT guidance 60min, 2x/w 10min warm-up, 40min aerobic and strength exercises, 10min cool down. Intensity gradually progressed; prescription was tailored.	Additional home exercises to undertake 3x/w at similar intensity.	Real Time monitoring before and during each session – pulse oximeter and HR monitor.	RT feedback during each session. Telephone contacts in case patient needed additional support.	Session for experimental group to familiarization with videoconference software. Educational sessions for both groups (face-to-face or by electronic slides).	Outpatient CR 2x/w, similar program as experimental group. They also had home exercises to undertake 3x/w at similar intensity.	Not mentioned
Lang 2018 Scotland	Walking or chair-based exercises	Progressive exercise training, tailored, based on walking or chair-based exercise DVD, or combination of two.	Not reported	Not specific reported but no indications of telemonitoring during exercise session.	Support by cardiac nurses as need by telephone contacts	No prior CR. REACH Manual also provided information about HF, medication, symptom	Usual Care without any formal exercise program	According to Guidelines

		2-3x/w Also includes a CD for relaxation and breathing control exercises				monitoring and how to manage stress/anxiety.		
Servantes 2012 Brazil	Walking only (EXP1) or with strength exercises (EXP2)	1-2M: 3x/w Session: 10min warm-up, 30min walking, 10min cool-down. 3rdM: 4x/w Session: 10min warm-up, 45min walking, 10min cool-down. Intensity established by VO2 AT.	EXP2 did additional strength exercises for upper and lower limbs with graduated free weights (1M: 12rep; 2M:14rep; 3M:16rep)	No telemonitoring during exercise session	Weekly calls to assess patient's status, adherence and give support. Reviewed monthly by physiotherapist and cardiologist to adjust exercise intensity.	3 sessions of supervised exercise to plan training program. Educational session about CVRF. Home group had manual with information about exercise.	No training at all Evaluated weekly	Not mentioned
Karapolat 2009 Turkey	Aerobic exercise (walking), strength and flexibility exercises	45-60min session, 3x/w; 5min warm-up, 30min of aerobic exercise, 5min cool-down at 60-70% pVO2, 13-15 Borg scale, 60-70% HRR specific program for each patient	Not mentioned	No telemonitoring during exercise session	Weekly calls to assess patient's status and exercise motivation	Educational session by physiotherapist and a manual with instructions.	Outpatient CR (exercise program similar to intervention, done at rehabilitation unit)	During the trial, patient's drug therapy remained unchanged

Keast 2013 Canada	Nordic Walk (NW) – walking with poles	2x/w, 1h session: 15min warm up, 10-15min NW (progression to 30min), 15min stretching Intensity: at 60-75% HRR, Borg scale 3-5	Additional walking to accumulate 200-400 min/week	Supervised online sessions. Patients self-monitored their HR at rest and immediately after workout.	RT-feedback during online sessions	Initial session for learning the Nordic Walking technique	2x/w supervised exercise sessions for 1h: 15min warm up, 10-15min walking (progression to 30min), 15min stretching. Additional walk and strength training at home, to accumulate 200-400min/wk. Intensity: at 60-75% HRR, Borg scale 3-5	During the trial, patient's drug therapy was modified as needed.
Piotrowicz 2010 Poland	Walking on level ground	2x/day, 3x/w 5-10min warm up Gradually increase time of continuous walking (10min 2x/d – 15min 2x/d – 20min/d) 5min cool-down	Not mentioned	Telemonitoring of clinical status, vital signs and ECG before each session. If no contraindications, patients received permission from monitoring	Daily telephone contacts to assess patient's status and give psychological support. Based on monitoring	3-6 monitored educational sessions	Supervised Interval training on cycle ergometer (gradually increase: 10/15min/d with 1-3min of exercise followed by 1-	Not reported

		Intensity: 40-70% of HR reserve (11 at Borg scale)		center to start training. Patients transmitted ECG immediately after the end of every session.	before and after each session, consultants were able to adjust training protocol.		2min of active recovery –-> 30min/d 4min of exercise followed by 2min of active recovery), 3x/w During the session, ECG, HR and BP were monitored.	
Piotrowicz 2015 Poland	Nordic walk (NW)	5x/w; tailored sessions for each patient 5-10min warm-up; 15-45min of NW 5min cool-down At 40-70% of HRR, Incremental over time: Pvo2<14: 10min NW; Pvo2 14-20: 15min NW; Pvo2>20: 20min NW. Final goal was to perform 45-60min session	Not reported	Telemonitoring of clinical status, vital signs and ECG before each session. If no contraindications, patients received permission from monitoring center to start training. Patients transmitted ECG immediately after the end of every session. Patients were advised to be	Daily telephone contacts to assess patient's status and to give psychological support. Based on monitoring before and after each session, consultants were able to adjust training protocol.	3-6 monitored educational sessions	Usual Care according to guidelines, without any formal exercise training and did not perform supervised rehabilitation	Not reported

				accompanied during training.				
Safiyari-Hafizi 2016 Canada	HIIT (walking) + resistance training supervised	Period of high intensity work (80-85% pVO2) followed by periods of active recovery (40-50% pVO2). Duration of each interval was individualized FC<3METs started short daily walks of 5-10min; (2-3min fast, 1min rest). Week12 walks of 45-60min w/ 7-8min fats and 1-2min slow FC 3-5METs started walks of 15min, 1-2x/d; Progression was the same as for group with FC>5METs. FC>5METs started sessions of 20-30min 3-5x/w (1min fast, 3min slow); Week 12	Not reported	Telemonitoring by HR monitor and pedometer, to track work out. Program was adjust based on changes in HR responses to exercise	Contacts to ensure compliance: 1st M: 3x/w; 2nd M: 2x/w; 3rd M: 1x/w	No previous CR. No mention to educational sessions	No formal exercise training – standard health care with encouragement to exercise moderately on a regular basis	Not reported

		walks of 55-60min w/ 7-8min fast and 1min slow, for 6-7x/week. Resistance: 10 exercises with bands 15reps; same number of reps but resistance increased (over 12w, resistance increase 30%)						
Frederix 2017 Belgium	Aerobic exercise: walking	If Pvo2>80%: 30min sessions, 3x/w If Pvo2<80%: patient chose the intensity of exercise session. Instructed to wear the accelerometer during entire study period. Volume of steps was based on BMI (10000-12000 if BMI>30, 8000-10000 if BMI<30)	Not reported	Telemonitoring by accelerometer, data was transmitted automatically. Patients uploaded data at least every 2w.	Weekly tele feedback through SMS or email with intention to encourage patients to achieve the goals.	6w of center-based CR and 7day training led by nurse after randomization. Weekly advice on healthy life-style (dietary, smoking cessation, etc)	24w center-based CR: 2-3x/w, 45-60min sessions of walking/ running/ cycling. Patients were instructed to wear the accelerometer 3times (start, after 6w, end) They did not receive advices on healthy life-	Not reported

							style or telecoaching	
Peng 2018 China	Aerobic exercise with strength exercises	Stage 1(w1-w4): 3x/w – 3-5min warm-up; 10-14min of walking/jogging at 40-70%HRR, 3-5min cool-down. Stage 2(w5-w8): 3x/w – 3-5min warm-up; 20-24min of walking/jogging and muscular strength exercises, at 40-70%HRR, 3-5min cool-down	Not reported	Supervised sessions by physiotherapists (via online webcam) with real-time adjustments to the training session and protocol.	Weekly telephone contacts to assess patient's status. Consultation at any time (call or message).	One Education lecture at discharge and brochure.	Usual care with simple discharge education and regular follow-up visits at the clinic. They were not instructed to perform any type of exercise	According to guidelines.
Zielinska 2006 Poland	Aerobic exercise – cycling (in outpatient) ; walking, swimming or cycling at home	3w CR outpatient: 30min of cycling with 5cycles of 4min work with load and 2min unloaded; 30min general exercises (breathing, coordination, relaxation) 9w CR Home:	Not mentioned	Outpatient CR sessions were supervised and monitored by constant ECG and 6min measures of BP. Home program included measures of BP and HR	Assessments at baseline, 3w and 12w. No other follow-up or regular feedback during the trial was mentioned.	Educational program: lectures, 1x/w Sessions of psychotherapy about philosophy of life, emotional support, relaxation techniques	Usual care with education about physical exercise principles at discharge, regular follow-up visits according to guidelines. They didn't perform any	Not specified

		At least 4x/w 15min morning gymnastics, physical recreation (walking, swimming, cycling) and general exercises		performed by the patient			specific exercise program.	

Usual Care – cardiac rehabilitation program done at the hospital in outpatient setting; CONt – control group; EXP – experimental group; HFrEF – heart failure with reduced ejection fraction; HFpEF – heart failure with preserved ejection fraction; BMI – body mass index
NHSS – National Health Service of Scotland; HCM - hypertrophic cardiomyopathy; RPE: modified Borg's rating of perceived exertion
CAT – COPD Assessment Test; PASE – physical activity profile; BDI – Beck Depression Inventory; RPE – modified Borg's rating of perceived exertion
NT – nurse tutor; PT – Physiotherapist Tutor; FC – functional capacity; MET – metabolic equivalent task; IPAQ – international physical activity questionnaire
ISWT – incremental shuttle walking test; SCHFI – Self-care of HF Index Questionnaire; echoTTE – echocardiographic trans-esophageal
ACE-I - angiotensin-converting-enzyme inhibitor; AR-b – angiotensin receptor blocker; BB- Beta blocker; ICS – inhaled corticosteroid; SABA – short acting bronchodilator; LAMA - long acting bronchodilator; CCB – calcium channel blocker; AAS – acetylsalicylic acid; Spiro – spironolactone; OMT – optimal medical therapy; CRT - cardiac resynchronization therapy; ICD – implantable cardioverter defibrillator; CABG - Coronary artery bypass surgery.

Table 2.1. Outcomes measures of all Included studies

Study	Outcome	Definition	Time	Intervention group			Control group			
				Sample size	Mean change	Mean Standard deviation	Sample size	Mean/ mean change	Mean Standard deviation	P value
Babu 2011 India	Functional capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test	T0: Baseline T1: 8w (end of trial)	14	T0: 429.33 m T1: 514.53 m T1-T0: 90.39 m	T0: 125.15 m T1: 135.12 m T1-T0: 124.04	13	T0: 310.23 m T1: 357.15 m T1-T0: 52.65 m	T0: 121.11 m T1: 147.95 m T1-T0: 112.65 m	<0.05
	Quality of Life	SF-36: 36 short form survey for patient self-reporting of quality of life	T0: Baseline T1: 8w (end of trial)	14	PCS – T1-T0: 14.19 MCS – T1-T0: 14.59	PCS – T1-T0: 7.76 MCS –	13	PCS – T1-T0: 5.42 MCS – T1-T0: 5,03	PCS – T1-T0: 5.31 MCS – T1-T0: 7.97	PCS – 0,002 MCS – 0.003

						T1-T0: 7.18				
Bernocchi 2018 Italy	Functional Capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test	T0: Baseline T1: 4M (end of trial) T2: 6M	T0 and T1: 48 T2: 45	T1-T0: 60m (22.2;97.8) T2-T1: 7m (-11.6;25.7)	Not reported. Calculated T1-T0: 88.25	T1:44 T2:35	T1-T0: -15m (-40.3;9.8) T2-T1:-43m (-63.5;-22.2)	Not reported. Calculated T1-T0: 78.38	P btw groups T1-T0: 0.0040 T2-T1: 0.0040
	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental	T0: Baseline T1: 4M (end of trial) T2: 6M	T1: 48 T2: 45	T1-T0: -10,5 (-14.2;-6.8) T2-T1: -1,6 (-3.6;0.4)	Not reported. Calculated T1-T0: 16.06	T1:44 T2:35	T1-T0: -0,44 (-4.9;4.0) T2-T1: -0,15 (-2.9;2.6)	Not reported. Calculated T1-T0: 16.28	p btw groups T1-T0: 0,0007 T2-T1: 0,4091

		dimensions of QoL								
	Time-to-event	Event: hospitalization for any reason or death	Entire period of the study – 4M	T1: 48 T2: 45	113,4 days	Not reported	T1:44 T2:35	104,7days	Not reported	P=0,0484
Chen 2018 Taiwan	Functional Capacity	6MWT – not specified	T0: Baseline T1: 3M (end of the trial)	19	T0: 421 m T1: 462 m T1-T0: 42m	T0: 90 T1: 74 T1-T0: 79.23	18	T0: 350 m T1: 344 m T1-T0:-6 m	T0: 107 T1: 121 T1-T0: 94.05	p(exp)= 0.03 p(cont)= 0.43
	VO2 peak	Measure by CPET		19	T0: 18.2 T1: 20.9 T1-T0:+2,7	T0: 4.1 T1: 6.6 T1-T0: 4.16	18	T0: 18.7 T1: 16.5 T1-T0:-2,2	T0: 4.2 T1: 3.7 T1-T0: 2.25	p (exp)= 0,02 p (cont)< 0,01
	QoL	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental dimensions of QoL		19	T0: 32.1 T1: 20.2 m T1-T0:-11,9	T0: 18.2 m T1: 20.9 m T1-T0: 9.16	18	T0: 44.4 T1: 42.1 T1-T0:-2,3	T0: 15.3 T1: 14.0 T1-T0: 9.35	p (exp)< 0,01 p (cont)< 0,33
Cowie 2014 Scotland	ISWT	Symptom limited maximal test of functional	T0: Baseline T1: 8w (end of the trial)	T0:20 T1:15	T0:270 m T1: 318 m T1-T0: 118m	T0:142 m T1: 153 m	T0:20 T1:16	Control: T0: 233 m T1: 241 m T1-T0: 8 m	Control: T0: 132 m T1: 143 m	p within group

		capacity that relates strongly to VO2max during cardio-pulmonary exercise testing on a treadmill					T0:20 T1:15	Hospital: T0: 227 m T1: 312 m T1-T0: 85	Hospital: T0: 207 m T1: 155m	p(exp)= 0.02 p(cont)= 0.42 p(hosp)= 0.01
	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental dimensions of QoL	T0: Baseline T1: 8w (end of the trial)	T0:20 T1:15	T0: 43 T1: 37 T1-T0: -6	Not reported. Calculated T1-T0: 16.06	T0:20 T1:16 T0:20 T1:15	Control: T0: 59 T1: 50 T1-T0:-9 Hospital: T0: 41 T1: 32 T1-T0:-9	Not reported. Calculated T1-T0: 16.28	p within group p(exp)= 0.65 p(cont)= 0.37 p(hosp)= 0.5
		SF36: 36 short form survey for patient self-reporting of quality of life	T0: Baseline T1: 8w (end of the trial)	T0:20 T1:15	PCS: T0: 35.29 T1: 34.01 T1-T0: -1,28 MCS: T1-T0: -0,74	PCS: T0: 10.31 T1: 11.04 T1-T0: 6.48 MCS: T0: 45.18 T1: 44.44 T1-T0: 5.55	T0:20 T1:16 T0:20 T1:15	PCS: <u>Control</u> T0: 32.69 T1: 32.08 T1-T0: -0.61 **Hospital**: T0: 31.33 T1: 33.83 T1-T0: 9.62 MCS:	PCS: <u>Control</u> T0: 7.54 T1: 7.05 T1-T0: not calculated **Hospital** T0: T1: T1-T0: 2,50 MCS:	p within group PCS p(exp)= 0.34 p(cont)= 0.51 p(hosp)= 0.38 MCS

								<u>Control</u> T0: 39.6 T1: 37.44 T1-T0:-2,16 **Hospital**: T0: 46.17 T1: 48.25 T1-T0: 2,08	<u>Control</u> T0: 13.55 T1: 10.89 T1-T0: not calculated **Hospital**: T0: 12.05 T1: 11.21 T1-T0: 8.31	p(exp)= 0.71 p(cont)= 0.73 p(hosp)= 0.81
Hwang 2017 Australia	Functional Capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test. The test was performed twice as recommended	T0: Baseline T1: 12 (end of the trial) T2: 24 w	T0: 24 T1: 24 T2:23	T0: 346m T1: 364m T0-T1: 18m T2: 374 m	T0: 104 m T1: 96 m T1-T0: 95.34 m T2: 89 m	T0:29 T1:26 T2:26	T0: 382 m T1: 394 m T1-T0: 12m T2: 410 m	T0: 106 m T1: 119 m T1-T0:92.71m T2: 103 m	Not reported

	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental dimensions of QoL	T0: Baseline T1: 12 (end of the trial) T2: 24 w	T0: 24 T1: 24 T2:23	T0: 47 T1: 32 T1-T0: -15 T2: 34	T0: 19 T1: 19 T1-T0: 17.54 T2: 23	T0:29 T1:26 T2:26	T0: 41 T1: 35 T1-T0: -6 T2: 33	T0: T1: T1-T0: 14.67 T2: 21	Not reported
		EQ-5D – self measures health status from 0-100	T0: Baseline T1: 12 (end of the trial) T2: 24 w	T0: 24 T1: 24 T2:23	T0: 62 T1: 70 T2: 69	T0: 19 T1: 17 T2: 17	T0:29 T1:26 T2:26	T0: 69 T1: 70 T2: 75	T0: 18 T1: 18 T2: 14	Not reported
	Adverse events	Major:Death, cardiac arrest, syncope Minor: angina, diaphoresis, palpitations, falls	T0: Baseline T1: 12 (end of the trial) T2: 24 w	T0: 24 T1: 24 T2:23	Total: 6 Major: 0 Minor: 6	---	T0:29 T1:26 T2:26	Total: 2 Major: 0 Minor: 2	---	Not reported
Lang 2018 Scotland	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional,	T0: Baseline T1: 4M (end of trial) T2:6M	T0: 25 T1: 22 T2: 22	T0: 38.2 T1: 35.5 T1-T0: -2.7 T2: 29.2	T0: 27.6 T1: 28.3 T1-T0: 25.81 T2: 25.8	T0: 25 T1: 23 T2: 23	T0: 36.0 T1: 37.8 T1-T0: -1.8 T2: 38.7	T0: 26.5 T1: 27.9 T1-T0: 17.25 T2: 30.1	Not reported

		social and mental dimensions of QoL								
		Heart-QoL - health-related quality of life questionnaire	T0: Baseline T1: 4M (end of trial) T2:6M	T0: 25 T1: 22 T2: 22	T0: 1.4 T1: 1.5 T2: 1.8	T0: 0.8 T1: 1.0 T2: 0.8	T0: 25 T1: 23 T2: 23	T0: 1.6 T1: 1.4 T2: 1.4	T0: 0.9 T1: 1.0 T2: 0.8	Not reported
		EQ-5D - self measures health status from 0-100	T0: Baseline T1: 4M (end of trial) T2:6M	T0: 25 T1: 22 T2: 22	T0: 0.57 T1: 0.60 T2: 0.65 T1-T0: +0.3	T0: 0.29 T1: 0.28 T2: 0.31	T0: 25 T1: 23 T2: 23	T0: 0.58 T1: 0.52 T2: 0.55 T1-T0: +0.6	T0: 0.31 T1: 0.34 T2: 0.29	Not reported
	Clinical events	All cause mortality, hospital admission	During 6M	25	4 hospital admissions	---	23	7 hospital admissions - 4 HF related	---	Not reported
	Functional Capacity	ISWT - Symptom limited maximal test of functional capacity that relates strongly to VO2max during cardio-pulmonary exercise testing on a treadmill		T0: 25 T1: 18 T2: 17	T0: 183,6 T1: 218,9 T2: 224,7	T0: 174,2 T1: 185,5 T2: 161,4	T0: 23 T1: 17 T2: 16	T0: 157,6 T1: 178,2 T2: 183,8	T0: 117,8 T1: 115,0 T2: 98,1	Not reported
	Cost analyses	Unit costs per item		Estimated total delivery cost 362,61 £ per patient						

Servantes 2012 Brazil	Functional Capacity	Peak VO2 - measured by CPET	T0: Baseline T1: 3M	Group1: 17 **Group2:** 17	G1 – T0: 15.4 T1: 20.6 T1-T0: 5.2 **G2** – T0: 15.6 T1: 20.9 T1-T0: 5.3	G1 – T0: 2.7 T1: 4.4 T1-T0: not calculated **G2** – T0: 2.7 T1: 4.4 T1-T0: 2.62	11	T0: 15.7 T1: 12.8 T1-T0: -2.9	T0: 3.0 T1: 3.2 T1-T0: 1.74	p btw groups: p(T0)= 0.951 p(T1)<0.001
	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental dimensions of QoL	T0: Baseline T1: 3M	Group1: 17 **Group2**: 17	G1 – T0: 40.4 T1: 20.7 **G2** – T0: 45.1 T1: 25.1 T1-T0: -20	G1 – T0: 17.9 T1: 16.3 **G2**- T0: 20.8 T1: 16.5 T1-T0: 17.63	11	T0: 46.5 T1: 51.0 T1-T0: 4.5	T0: 18.5 T1: 16.8 T1-T0: 11.28	p btw groups: p(T0)= 0.671 p(T1)<0.001
Karapolat 2009 Turkey	Functional Capacity	Peak VO2 - measured by CPET	T0:Baseline T1: 8w (end of trial)	T0: 37 T1: 32	T0: 17.48 T1: 18.12 T1-T0: 0.64	T0:6.09 T1: 6.00 T1-T0: 3.86	T0: 37 T1: 36	T0: 17.85 T1: 19.43 T1-T0: 1.58	T0: 4.44 T1: 4.59 T1-T0: 2.52	P btw T1 and T0 for both groups <0.05
		6MWT – walking up and down 20m	T0:Baseline T1: 8w (end of trial)	T0: 37 T1: 32	T0: 383.97 T1: 423.78	T0: 82.39 T1:76.89	T0: 37 T1: 36	T0: 374.34 T1: 418.72	T0: 79.06 T1: 50.43	P btw T1 and T0 for both groups <0.05

		hallway for 6min at their own pace. They were allowed to stop and rest when they needed and they were instructed to continue walking as soon as they felt able to do so.			T1-T0: 39,81	T1-T0: 75.88		T1-T0: 44,38	T1-T0: 72.87	
	Quality of Life	SF36: 36 short form survey for patient self-reporting of quality of life	T0:Baseline T1: 8w (end of trial)	T0: 37 T1: 32	PCS T0: 54.64 T1:59.39 T1-T0:4.75 MCS T0: 67.67 T1:64.67 T1-T0: -3	PCS: T0: 27.43 T1: 25.35 T1-T0: 16.04 MCS: T0: 20.36 T1: 19.04 T1-T0: 9.03	T0: 37 T1: 36	PCS T0: 57.50 T1: 69.57 T1-T0:12.07 MCS T0: 67.70 T1:70.52 T1-T0: 2.82	PCS: T0: 23.98 T1: 20.94 T1-T0: 23.80 MCS: T0: 19.63 T1: 20.37 T1-T0: 14.24	PCS: p btw T1 and T0 for both groups <0.05 MCS: p not inferior to 0.05
Keast 2013 Canada	Functional capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The	T0:Baseline T1: 12w (end of the trial)	27	T0: 429.9 T1: 555.5 T1-T0: 125.6	T0: 137.3 T1: 168.8 T1-T0: 148.13	27	T0: 502.6 T1: 559.5 T1-T0: 56.9	T0: 106.2 T1: 131.9 T1-T0: 100.09	P<0.001

		distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test. The test was performed twice as recommended								
		Peak VO2 - measured by CPET	T0:Baseline T1: 12w (end of the trial)	27	T0: 19.3 T1: 21.5 T1-T0: 2.2	T0: 7.1 T1: 9.0 T1-T0: 5.45	27	T0: 20.1 T1: 21.8 T1-T0: 1.7	T0: 6.2 T1: 7.7 T1-T0: 4.13	p=0.623
	Psychological symptoms	HADS score - depression	T0:Baseline T1: 12w (end of the trial)	27	T0: 4.6 T1: 2.4 T1-T0: -2.2	T0: 2.8 T1: 3.0 T1-T0: 2.57	27	T0: 4.6 T1: 4.4 T1-T0: -0.2	T0: 3.7 T1: 2.9 T1-T0: 0.95	p=0.014
		HADS score - anxiety		27	T0: 4.9 T1: 4.1 T1-T0: -0.8	T0: 3.6 T1: 2.7 T1-T0: 4.15	27	T0: 6.8 T1: 5.3 T1-T0: -1.5	T0: 3.9 T1: 3.3 T1-T0: 3.67	p=0.862
Piotrowicz 2010 Poland	Functional Capacity	Peak VO2 - measured by CPET	T0:Baseline T1: 8w (end of the trial)	T0:77 T1:75	T0: 17.8 T1:19.7 T1-T0: 1.1	T0: 4.1 T1: 5.2	T0:75 T1:56	T0:17.9 T1:19.0 T1-T0: 1.1	T0: 4.4 T1: 4.6	p=0.0001

						T1-T0: 3.15			T1-T0: 2.53	
	Functional capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test. The test was performed twice as recommended	T0:Baseline T1: 8w (end of the trial)	T0:77 T1:75	T0: 418 T1: 462 T1-T0: 44	T0: 92 T1: 91 T1-T0: 87.00	T0:75 T1:56	T0: 399 T1: 462 T1-T0: 63	T0: 91 T1: 92 T1-T0: 74.80	p=0.0469
		Change in NYHA Class	T0:Baseline T1: 8w (end of the trial)	T0:77 T1:75	T0: 2.5 T1: 2.1	T0: 0.5 T1: 0.5	T0:75 T1:56	T0: 2.5 T1: 2.3	T0: 0.5 T1: 0.5	p=0.0070
	Quality of Life	SF36: 36 short form survey for patient self-	T0:Baseline T1: 8w (end of the trial)	T0:77 T1:75	PCS T0: 23.3 T1:21.60 T1-T0: -1.7	PCS: T0: 11.32 T1: 9.65	T0:75 T1:56	PCS T0: 25.39 T1:23.20 T1-T0:-2.19	PCS: T0: 10.89 T1: 10.71	PCS P=0.0490

		reporting of quality of life			MCS T0: 25.11 T1:21.68 T1-T0:-3.43	T1-T0: 6.52 MCS: T0: 12.01 T1: 12.46 T1-T0: 5.57		MCS T0: 22.78 T1:18.56 T1-T0:-4.22	T1-T0: 11.38 MCS: T0: 13.22 T1: 9.18 T1-T0: 8.82	MCS: P=0.0052
	Safety	Clinical events during training ou routine daily activities	Entire period of the study	T0:77 T1:75	3 episodes of paroxysmal Atrial Fibrillation		T0:75 T1:56	1 episode of paroxysmal Atrial Fibrillation		
Piotrowicz 2015 Poland	Functional capacity	Peak VO2 - measured by CPET (ml/kg/min)	T0:Baseline: T1:8w (end of the trial)	T0: 77 T1: 75	T0: 16.1 T1: 18.4 T1-T0: 0.1	T0: 4.0 T1: 4.1 T1-T0: 2.59	T0: 34 T1: 32	T0: 17.4 T1: 17.2 T1-T0: -0.2	T0: 3.3 T1: 3.4 T1-T0: 1.87	p(exp)= 0.0001 p(cont)= 0.0004
		6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and	T0:Baseline: T1:8w (end of the trial)	T0: 77 T1: 75	T0: 428 m T1: 480 m T1-T0: 52m	T0: 93m T1: 87m T1-T0: 85.73	T0: 34 T1: 32	T0: 439m T1: 465m T1-T0:26m	T0: 76 T1: 91 T1-T0: 69.61	p(exp)= 0.0001 p(cont)= 0.0483

		encouragement were commonly given during the test. The test was performed twice as recommended								
	Quality of Life	SF36: 36 short form survey for patient self-reporting of quality of life	T0:Baseline: T1:8w (end of the trial)	T0: 77 T1: 75	T0: 79.0 T1: 70.8 T1-T0: -8.2	T0: 31.3 T1: 30.3 T1-T0: not calculated	T0: 34 T1: 32	T0: 73.6 T1: 67.4 T1-T0: -6.2	T0: 25.6 T1: 25.9 T1-T0: not calculated	p not stastically significant
Safiyari-Hafizi 2016 Canada	Functional capacity	Peak VO2 measured by CPET (mL/kg/min)	T0: Baseline T1: 12w (end of the trial)	T0: 20 T1: 14	No values available	No values available	T0: 20 T1: 15	No values available	No values available	No Significant improvement
		6MWT – without verbal encourgement	T0: Baseline T1: 12w (end of the trial)	T0: 20 T1: 14	No values available	No values available		No values available	No values available	Significant improvement
	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and	T0: Baseline T1: 12w (end of the trial)	T0: 20 T1: 14	No values available	No values available		No values available	No values available	Significant improvement

		mental dimensions of QoL								
Frederix 2017 Belgium	Functional capacity	Peak VO2 measured by CPET (mL/kg/min)	T0:Baseline T1: 6w T2: 24w	T0:69 T1:69 T2:60	T0: 22,46 T1: 23,91 T2: 24,46 T1-T0: 1,45	T1-T0: 4.12	T0:70 T1:70 T2:59	T0: 22,72 T1: 22,86 T2: 22,15 T1-T0: 0,14	T1-T0: 3.24	P<0,001 (overall)
	Quality of Life	14 item HeartQoL questionnaire - Global score	T0:Baseline T1: 6w T2: 24w	T0:69 T1:69 T2:60	T0: 2,27 T1: 2,46 T2: 2,53	T0: 0,63 T1: 0,51 T2: 0,44	T0:70 T1:70 T2:59	T0: 2,31 T1: 2,40 T2: 2,32	T0:0,59 T1:0,51 T2:0,58	P=0,01 (overall)
	Safety	CV readmission rate Days to 1st eadmission Days lost	Entire period of study	Initial: 69 End:60	-32 readmissions -1014days to 1st readm -1,20 days lost	---	Initial: 70 End:59	-60 readmissions -894days to 1st readm -1,89 days lost	---	P=0.110 P=0.155 P=0.142
	Cost effectiveness	Total Average cost per patient			3262€	339€		4140€	513€	TR was cost-saving
Peng 2018 China	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental	T0: Baseline T1:2M (end of the trial) T2: 6M	T0: 49 T1: 49 T2: 42	T0: 49.43 T1: 43.11 T1-T0: -6.32 T2: 42.32	T0: 12.25 T1: 8.76 T1-T0: 10.18 T2: 8.83	T0: 49 T1: 49 T2: 41	T0: 48.77 T1: 49.20 T1-T0: 0.43 T2: 49.63	T0:12.21 T1: 12.44 T1-T0: 7.80 T2: 12.39	Btw groups: p=0,072

		dimensions of QoL								
	Functional Capacity	6MWT: Patients were asked to walk as far as possible in 6 min along a flat corridor. The distance in meters was recorded. Standardised instructions and encouragement were commonly given during the test. The test was performed twice as recommended	T0: Baseline T1:2M (end of the trial) T2: 6M	T0: 49 T1: 49 T2: 42	T0: 407.09 T1: 419.23 T1-T0: 12.14 T2: 418.25	T0: 12.27 T1: 9.67 T1-T0: 10.68 T2: 9.68	T0: 49 T1: 49 T2: 41	T0: 406.05 T1: 406.55 T1-T0: 0.50 T2: 406.38	T0: 12.35 T1: 12.54 T1-T0: 10.26 T2: 12.57	Btw groups: p=0,171
	Psychological Symptoms	HADS score - depression	T0: Baseline T1:2M (end of the trial) T2: 6M	T0: 49 T1: 49 T2: 42	T0: 6.69 T1: 6.64 T2: 6.58	T0: 0.959 T1: 0.973 T2: 0.979	T0: 49 T1: 49 T2: 41	T0: 6.65 T1: 6.70 T2: 6.58	T0: 0.954 T1: 0.924 T2: 0.856	Btw groups: p=0.030
		HADS score - anxiety			T0: 6.77 T1: 6.56 T2: 6.53	T0: 0.911 T1: 0.965 T2: 0.927		T0: 6.73 T1: 6.77 T2: 6.82	T0: 0.876 T1: 0.743 T2: 0,727	Btw groups: p=0.032

Zielinska 2006 Poland	Quality of Life	MLHFQ – disease specific questionnaire with 21 questions determining key physical, emotional, social and mental dimensions of QoL	T0: Baseline T1:3w T2:12w	T0: 43 T1: 43 T2: 43	T0: 46.3 T2: 36 T2-T0: -10	T0 and T1 not reported Calculated T0-T1: 16.06	T0: 18 T1: 18 T2: 18	T0: 62.7 T2: 55 T2-T0: -8	T0 and T1 not reported Calculated T0-T1: 16.28	No comparision btw groups
	Functional Capacity	Changes in duration of stress test: at cycloergometer with ECG; test with increasing load at constant speed of 70/min, starting with 25W load increasing it every 3min. performed until symptoms indicating for interruption (17 on Borg scale)	T0: Baseline T1:3w T2:12w	T0: 43 T1: 43 T2: 43	T0: 521 T1: 657 T2: 688	T0: 189 T1: 209 T2: 231	T0: 18 T1: 18 T2: 18	T0: 385 T1: 420 T2: 428	T0: 205 T1: 216 T2: 235	P(exp)<0.05 P(cont) not statistically significant

Figure 2.2. Other outcomes reported and limitations of included studies

Study	Other Outcomes	Limitations
Babu 2011 India	Not reported	Barriers to the program - fear, lack of motivation; Better assessment of adherence is required Small sample size and short follow-up period
Bernocchi 2018 Italy	CAT – COPD Assessment Test; Dyspnoea by MRC PASE – physical activity profile; BARTHEL – disability	Trial wasn't blind. It is more a program of physical maintenance than a specific program for exercise training.
Chen 2018 Taiwan	Parameters of heart function measured by noninvasive cardiac output monitor	Small sample size and short period of study.
Cowie 2014 Scotland	Not reported	Subjective measures of training intensity at home. Small sample size.
Hwang 2017 Australia	TUGT – time Up and Go Test; 10min walk test; Strengh grip RUIS – Revised Urinary Incontinence Scale BOOMER – balance outcome measure for elder rehabilitation EQ-5D; Adherence; Satisfaction – CSQ8	Low training volume and not objectively measured. Recruitment bias – results might not be generalizable.
Lang 2018 Scotland	Healthcare utilization SCHFI – self-care of HF Index Questionnaire Acceptability of program	Trial wasn't blind; imbalance between control and intervention group. Recruitment bias – results might not be generalizable. Open label can cause improvements in patient-reported outcomes.
Servantes 2012 Brazil	Muscle Strength – isokinetic test Polysomnography	Not possible to totally ensure that patients completed their exercise program. Results might not be generalizable.
Karapolat 2009 Turkey	Psychological symptoms: BDI – beck depression inventory, STAI – spielberg's state-trait anxiety inventory Echocardiographic measures of heart function	Short rehabilitation time, no long-term follow-up. Lack of control group.
Keast 2013 Canada	Strength and Anthropometric measures	Lack of blinding. Sample was composed by mostly men.

Piotrowicz 2010 Poland	Not reported	Small sample size. Short duration of program. No long term follow-up. Difficult to determine if the improvement in QoL was exercise related or caused by overall psychosocial support.
Piotrowicz 2015 Poland	Acceptance of TR program Safety (number of adverse events)	Single center trial, not blinded, short duration, small sample size. Few women were recruited – can't be generalized to female population. No comparison with other training modalities.
Safiyari-Hafizi 2016 Canada	Safety (number of adverse events)	Small sample size; High percentage of male patients; Patients were younger than 75yo.
Frederix 2017 Belgium	CPET – cardiopulmonary exercise test CV risk control, IPAQ physical activity, CV readmission rate	low generalizability because: sample had a minority of HF patients, lack of women and black patients, reflects a Belgium situation
Peng 2018 China	LVEF and HR; Changes in NYHA Classification HADS Anxiety and Depression	Limited representativeness and generalizability of the sample (all from the same hospital). Simple randomization was used. Short period of intervention and follow-up.
Zielinska 2006 Poland	Changes in NYHA, BP and HR at rest	Short intervention and follow-up period. Not properly randomized.

Figure 2.3. Adverse events reported in all included studies

Study	Total of adverse events	AV during exercise	AE outside of exercise period	Type of Adverse events
Babu, 2011, India	0	0	0	Not specified
Bernocchi, 2018, Italy	Hospitalizations: 58	No major side effects INT: 21 (11 CV, 6Resp, 5 others)	No major side effects CONT: 37 (25 CV, 11 Resp, 5 others)	Not specified
Chen, 2018, Taiwan	0	0	0	Not specified
Cowie, 2014, Scotland	9 withdrawals	4 withdrawals: -worsening of HF:2 worsening co-morbiditites: 2	HOSP: 3 withdrawals: -worsening of HF:2 -worsening of co-morbiditites: CONT: 2 withdrawals: -worsening of HF:1 -worsening comorbiditites: 1	Worsening of HF or co-morbidities
Hwang, 2017, Australia	0 major adverse events 8 minor adverse events: 3 angina, 3 diaphoresis, 2 palpitations	6 minor adverse events: 3 angina, 1 diaphoresis, 2 palpitations	2 minor adverse events: 2 diaphoresis	major adverse events: death, cardiac arrest, syncope, fall minor adverse events: angina, diaphoresis, palpitations
Lang, 2018, Scotland	11 hospitalizations	4 hospitalizations related to HF but considered unrelated to the study	7 hospitalizations 1 died related to HF shortly after 6M period follow-up	hospitalizations
Servantes, 2012, Brazil	0 major adverse events	0	0	Traumatic, orthopedic or cardiovascular events
Karapolat, 2009, Turkey	0 major adverse events	0	0	Not specified

Keast, 2013, Canada	6 adverse events reported by the patient	EXP: ankle pain:1; foot ulcer:1; increase in CHF symptoms:1 CONT: foot ulcer:1; pericarditis:1; increase in CHF symptoms:1		Adverse events reported by the patient
Piotrowicz, 2010, Poland	0 deaths or hospitalizations	No worrying symptoms	EXP: 3 paroxysmal AF CONT: 1 paroxysmal AF	Death, hospitalizations, changes in ECG
Piotrowicz, 2015, Poland	0 major events	Minor skin reactions due to electrodes	during unsupervised activity: EXP- 2, CONT- 1	Death, hospitalizations, changes in ECG, musculoskeletal injuries, need to discontinue rehabilitation cycle, intervention from CIEDs
Safiyari-Hafizi, 2016, Canada	0 adverse events	0 adverse events	Not mentioned	Not specified
Frederix, 2017, Belgium	23 rehospitalizations 1y after study termination	7 rehospitalizations – reasons: In-stent restenosis:1 Atypical thoracic pain: 1 Arrythmia: 2 Pericarditis: 1 PAD: 1	16 rehospitalizations – reasons: In-stent restenosis:1 ACS: 2 Stable angina: 6 Atypical thoracic pain: 2 Arrythmia: 1 AF ablation: 1 Resynchronization ther :1 PAD: 1	Rehospitalizations
Peng, 2018, China	“No adverse events were reported”	---	---	Not specified
Zielinska, 2006, Poland	“There were no serious side effects”	---	---	Not specified

Table 3.1. GRADE Summary of Findings Table for Functional Capacity Outcome

Home TR compared to Control in Functional Capacity

Outcomes	Anticipated absolute effects* (95% CI)		Mean Difference (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Mean Difference with Control	Mean Difference with Home TR				
Six-minute walk test (6MWT)	The mean 6MWT was 28.83m more	The mean 6MWT was 53.77 m more	27,05 m (5,48 to 48,63)	664 (9 RCTs)	⊕⊕⊕◯ MODERATE [a,b]	Patients are asked to walk as far as possible in 6 min along a flat corridor. The distance in meters is recorded follow up: range 2 months to 24 months
Peak VO2 (pVO2)	The mean peak VO2 was 0.11 lower	The mean peak VO2 was1.93 higher	2 mL/(kg·min) (-0,12 to 4,12)	564 (7 RCTs)	⊕◯◯◯ VERY LOW [a,c]	Cardiopulmonary exercise test follow up: range 2 months to 24 months

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

EXPLANATIONS a. All studies were classified as high risk for performance bias because all were non-blinded due to the natures of trials. Considering detection bias almost half of the studies were clasified as "unclear risk" b. There is a important heterogeneity across studies (I2=75%) and one study wuth high weight showed results a lot different from the others. c. There is an important heterogeneity across studies (I2=94%)

Table 3.2. GRADE Summary of Findings Table for Quality of Life Outcome (MLHFQ)

Home TR compared to Control in Quality of Life (MLHFQ)

Outcome	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Mean Difference (95% CI)	Anticipated absolute effects		Comments
				Mean Difference with Control	Mean difference with Home TR	
Quality of Life (MLHFQ)	441 (8 RCTs)	⊕⊕⊕⊕ HIGH [a]	**- 7.95** (-12.21; -3.7)	The mean QoL was - 2.71	The mean QoL was - 10.30	Minnesota Living With Heart Failure Questionnaire follow up: range 2 months to 24 months

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. All studies were classified as high risk for performance bias because all were non-blinded due to the natures of trials. Considering detection bias, the most frequent classification was “unclear risk”.

Table 3.3. GRADE Summary of Findings Table for SF-36 Score

Home TR compared to Control in Quality of Life (SF-36)

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Mean Difference (95% CI)	Anticipated absolute effects		Comments
				Risk with Control	Risk difference with Home TR	
Quality of Life (SF 36 - PCS)	256 (4 RCTs)	⨁◯◯◯ VERY LOW [a,b,c]	**0.24** (-5.79; 6.26)	The mean QoL was 4.45	The mean QoL was 3.99	36-Item Short Form Survey follow up: range 2 months to 24 months
Quality of Life (SF-36 MCS)	256 (4 RCTs)	⨁◯◯◯ VERY LOW [a,b,d]	**0.38** (-4.93;5.7)	The mean QoL was 1.53	The mean QoL was 1.83	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. All studies were classified as high risk for performance bias because all were non-blinded due to the natures of trials. Considering detection bias, the most frequent classification was “unclear risk”.
b. 2 studies showed a small improvement in physical score but 1 showed an important decrease
c. The lack of effects on patients evaluation of his/hers physical function might be explain by the shorter period of follow-up because it takes some time for patient to note these changes
d. The lack of effects on patients evaluation of his/hers mental function might be explain by the shorter period of follow-up because it takes some time for patient to note these changes

Table 3.4. GRADE Summary of Findings Table for Cost-effectiveness Outcome

Home TR compared to Control for Cost-analysis

Outcome	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Impact
Cost-analysis assessed with: cost per patient follow up: range 2 months to 24 months	(2 RCTs)	⨁◯◯◯ VERY LOW [a,b]	One study calculated a cost per patient in intervention group of 3252€ and 4140€ in control group. The other reported a cost of 370,59€ per patient. No other trial asses the costs of intervention.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. studies showed very different values of cost per patient (one calculated a cost per patient 3252€ for intervention, and the other calculated a cost of 370,59€ per patient
b. Authors didn't clarify what topics were included in this analysis

Table 3.5. GRADE Summary of Findings Table for Adherence to the Intervention

Home TR compared to Control for Adherence

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Impact
Adherence to the intervention assessed with: attendance to sessions follow up: range 2 months to 24 months	(15 RCTs)	⊕⊕◯◯ LOW [a,b,c]	Different definitions were used across the studies making impossible to perform a statistical analysis. According to that, in studies where adherence was defined as "attending to all sessions", rates varied from 70% to 100% in the intervention groups. Studies where adherence was defined as attendance to more than 80% of sessions, rates varied from 71% to 95% in experimental group. . In all studies, authors considered that they obtained high rates of adherence.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. We also analyzed the risk of intensive monitoring and feedback influence adherence to the intervention. For that topic, 8 studies were considered to have low risk, 2 were unclear and 5 had high risk.
b. Some studies had a intense follow up with daily or weekly calls which might lead to higher adherence rates
c. Four studies defined adherent as a patient who attend to more than 80% of sessions, while six studies assumed an adherent patient attended to all sessions. The rest of the studies didn't used any specific measure

Table 3.6. GRADE Summary of Findings Table for Safett of TR Intervention

Home TR compared to Control for Safety

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Impact
Safety of TR Intervention assessed with: reported events follow up: range 2 months to 24 months	(13 RCTs)	⨁⨁⨁⨁ HIGH [a,b]	Any trial used a specific measure to evaluate the safety of training program (most of them only reported clinical adverse). In spite of this high imprecision, all authors concluded TR was safe because the majority of clinical events were minor and not exercise related.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations
a. All of the trials showed they were safe because the majority of clinical events were minor and not exercise related.
b. Considering safety outcomes, none trial used a specific measure to evaluate the safety of training program. Most of them only reported clinical adverse events but two didn't mention that topic.

Table 3.7. GRADE Summary of Findings Table for CV Death or Heart failure-related hospitalizations

Home TR compared to Control for CV Death or Heart failure-related hospitalizations

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Impact
CV Death or Heart failure-related hospitalizations assessed with: number of reported events follow up: range 2 months to 24 months	184 (2 RCTs)	⨁◯◯◯ VERY LOW a,b,c	Two studies reported the number of hospitalizations that occurred during the trial or during the long-term follow-up. One study registered 4 hospital admissions in intervention group and 7 hospital admissions in control group after 3 months. The other study revaluated patients 2 years later and reported 32 cardiovascular admissions in intervention group and 60 in control group.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. These 2 studies were classified as "high risk" because both had 2 high risk classifications at bias assessment.
b. One study registered 11 hospital admissions, while the other reported a total of 90 admissions.
c. Reasons for hospital admissions aren't specified and these 2 trials had different times of follow-up, which might explain the differences found.

Table 4.1. Sensitivity Analysis of heterogeneity for 6MWT Outcome

6MWT		
Studies included	**Mean Difference (95%IC)**	**I^2 (%)**
Without Babu	26.67 [4.18, 49.16]	78
Without Bernocchi	**18.61 [-0.95, 38.16]**	**63**
Without Chen	25.25 [2.40, 48.11]	77
Without Hwang	29.45 [5.94, 52.97]	78
Without Karapolat	32.00 [7.56, 56.43]	77
Without Keast	24.06 [1.95, 46.17]	76
Without Peng	31.59 [1.38, 61.80]	75
Without Piotrowicz 2010	34.93 [10.87, 58.99]	74
Without Piotrowicz 2015	**21.78 [-0.36, 43.91]**	**70**
All	27.05 [5.48; 48.63]	75

Table 4.2. Sensitivity Analysis of heterogeneity for Peak VO2 Outcome

Peak VO2		
Studies included	**Mean Difference (95%IC)**	**I^2 (%)**
Without Chen	1.55 [-0.68, 3.78]	94
Without Frederix	2.13 [-0.44, 4.70]	95
Without Karapolat	**2.50 [0.14, 4.86]**	**95**
Without Keast	2.22 [-0.11, 4.56]	95
Without Piotrowicz 2010	2.36 [-0.25, 4.97]	95
Without Piotrowicz 2015	2.31 [-0.39, 5.02]	95
Without Servantes	**0.85 [-0.33, 2.04]**	**78**
All	2.00 [-0.12, 4.12]	94

Table 4.3. Sensitivity Analysis of heterogeneity for QoL Outcome

QoL (MLHFQ)		
Studies included	**Mean Difference (95%IC)**	**I^2 (%)**
Without Bernocchi	-7.40 [-12.34, -2.47]	63
Without Chen	-7.61 [-12.73, -2.48]	64
Without Cowie	-8.95 [-13.12, -4.78]	56
Without Hwang	-7.79 [-12.61, -2.97]	65
Without Lang	-8.52 [-13.00, -4.05]	62
Without Peng	-8.14 [-13.68, -2.59]	63
Without Servantes	**-6.84 [-9.75, -3.93]**	**17**
Without Zielinska	-8.73 [-13.31, -4.15]	61
All	-7.95 [-12.21, -3.70]	59

Table 4.4. Sensitivity Analysis of heterogeneity for SF-36 Score

QoL (SF-36 PCS)		
Studies included	**Mean Difference (95%IC)**	**I^2 (%)**
Without Babu	**-2.05 [-6.23, 2.13]**	**40**
Without Cowie	1.49 [-6.02, 8.99]	83
Without Karapolat	1.90 [-4.57, 8.37]	83
Without Piotrowicz 2010	-0.30 [-10.41, 9.82]	86
All	0.24 [-5.79, 6.26]	80
QoL (SF-36 MCS)		
Studies included	**Mean Difference (95%IC)**	**I^2 (%)**
Without Babu	**-2.01 [-6.00, 1.98]**	**61**
Without Cowie	1.44 [-5.63, 8.52]	86
Without Karapolat	2.25 [-3.61, 8.11]	81
Without Piotrowicz 2010	0.26 [-8.66, 9.18]	88
All	0.38 [-4.93, 5.70]	81

Figure 1: **Draft MEDLINE search strategy**. This strategy was adapted to the syntax of the other databases.

Draft Medline Search

1. MeSH descriptor: [Heart Failure] explode all trees
2. ("heart failure" OR "cardiac failure" OR "myocardial failure" OR "myocardial insufficiency" OR "heart decompensation")
3. (#1 OR #2)
4. MeSH descriptor: [Telerehabilitation] explode all trees
5. MeSH descriptor: [Cardiac Rehabilitation] explode all trees
6. ("tele-rehabilitation" OR "telerehabilitation" OR "telecardiology" OR "tele-cardiology" OR "telecare" OR "Remote Rehabilitation" OR "Virtual Rehabilitation")
7. (#4 OR #5 OR #6)
8. (#3 AND #7)
9. randomized controlled trial [pt]
10. controlled clinical trial [pt]
11. randomized [tiab]
12. placebo [tiab]
13. drug therapy [sh]
14. randomly [tiab]
15. trial [tiab]
16. groups [tiab]
17. #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
18. animals [mh] NOT humans [mh]
19. #17 NOT #18
20. #8 AND #19

Figure 2.1. Analysis of SF-36 (PCS) Outcome

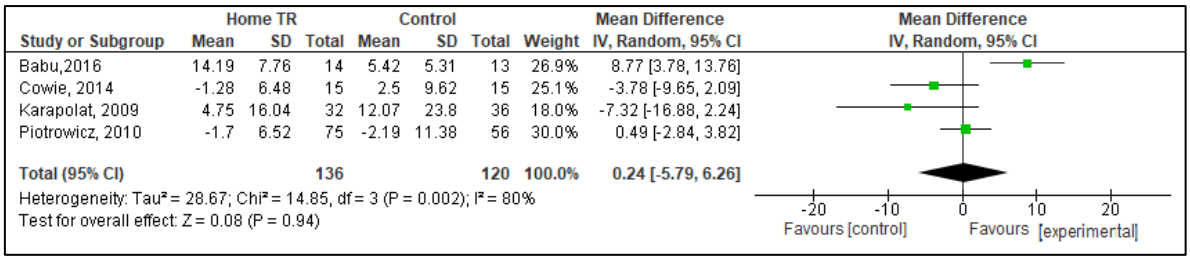


Figure 2.2. Analysis of SF-36 (MCS) Outcome

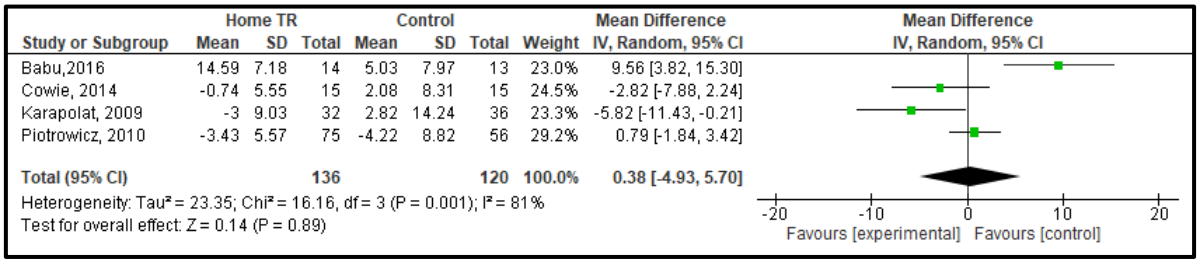


Figure 3.1. Subgroup analysis of heterogeneity for HF Classification considering 6MWT

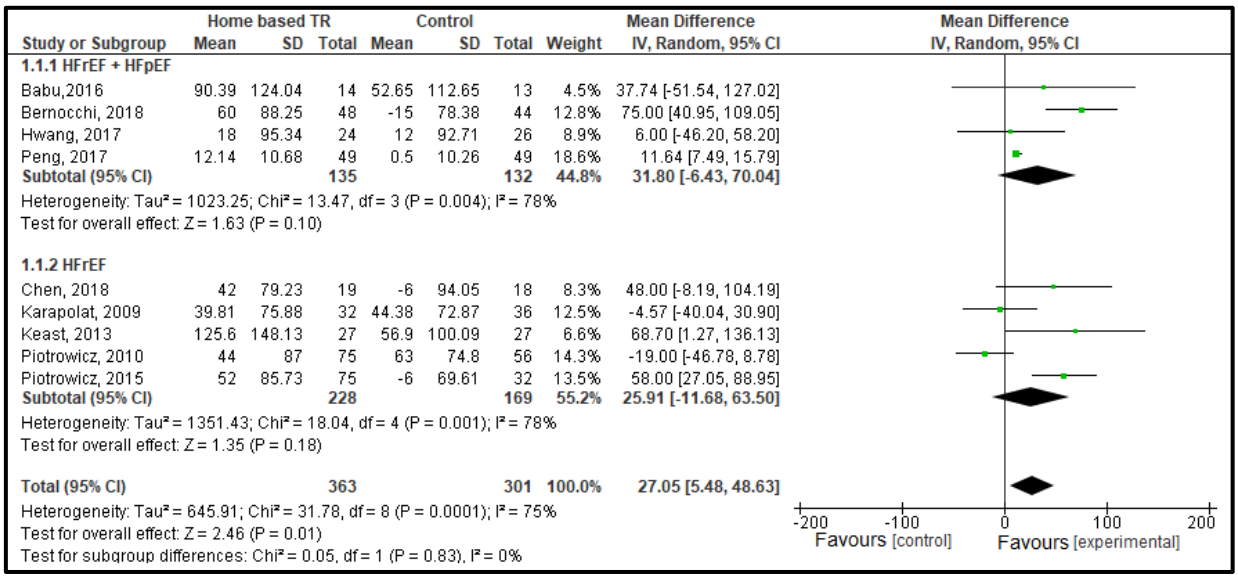


Figure 3.2. Subgroup analysis of heterogeneity for HF Classification considering QoL (MLHFQ)

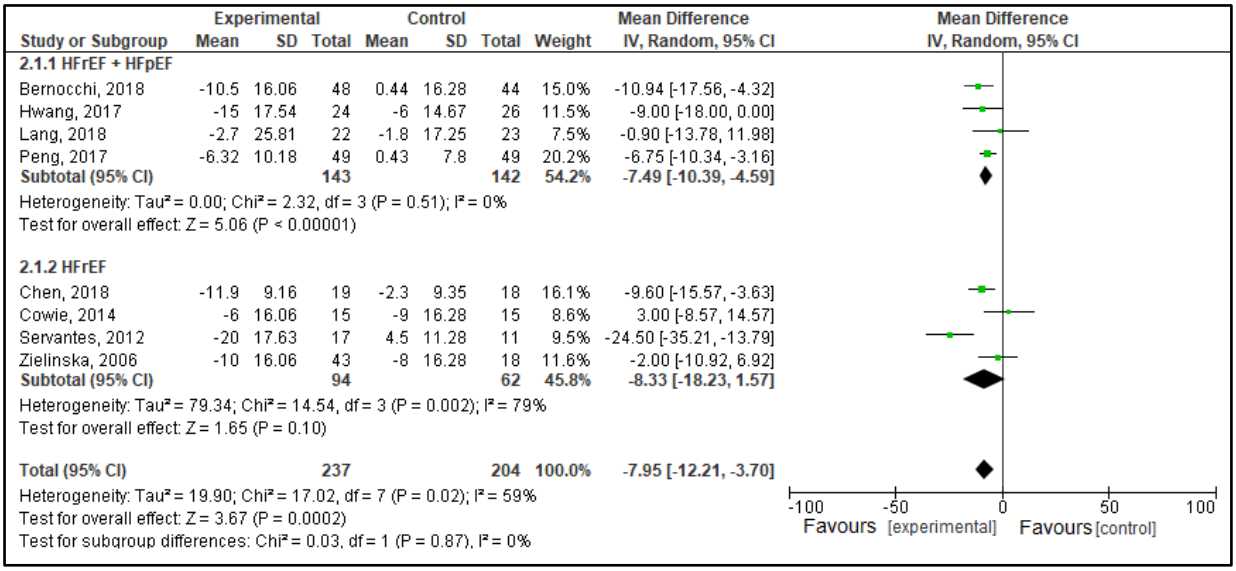


Figure 4.1. Subgroup analysis of heterogeneity for Bias Assessment considering 6MWT

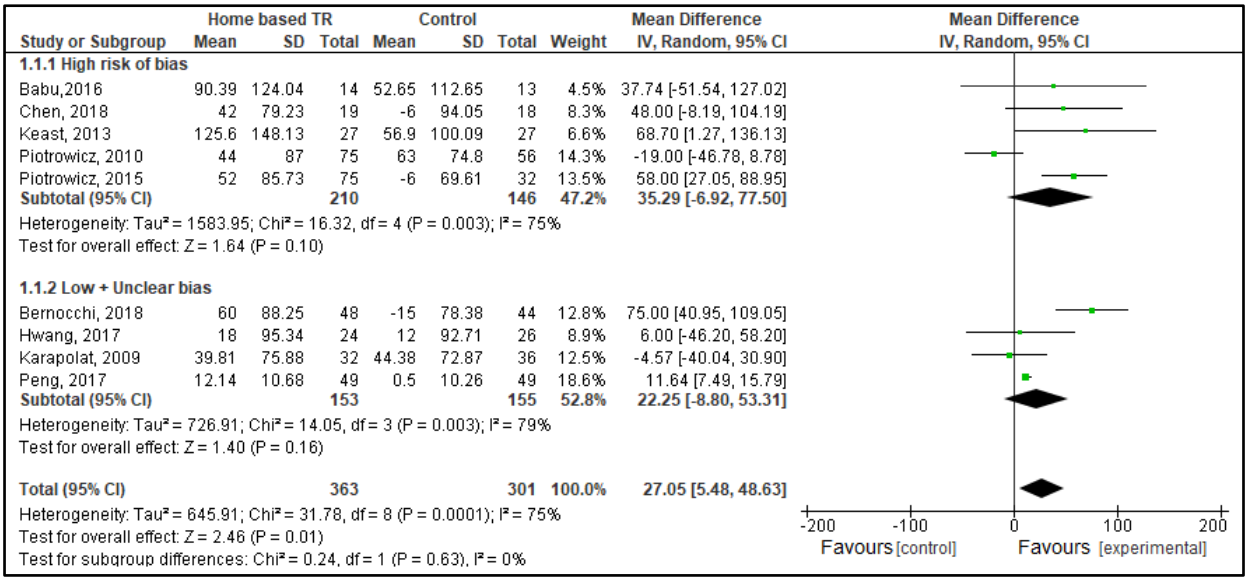


Figure 4.2. Subgroup analysis of heterogeneity for Bias Assessment considering Peak VO2

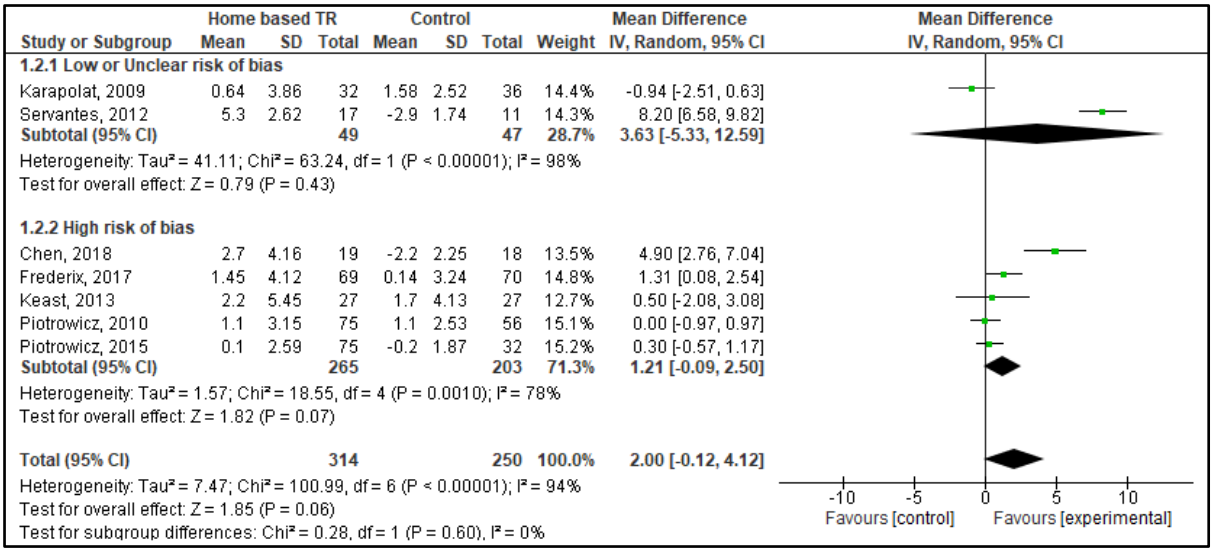


Figure 4.3. Subgroup analysis of heterogeneity for Bias Assessment considering QoL (MLHFQ)

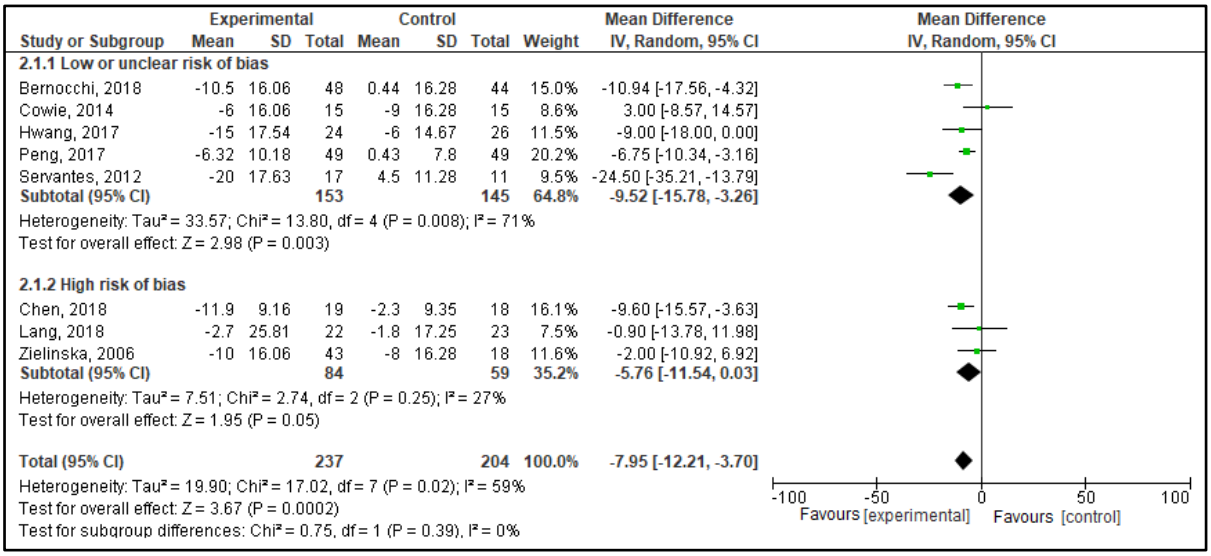


Figure 5.1. Subgroup analysis of heterogeneity for Presence of Telemonitoring considering 6MWT

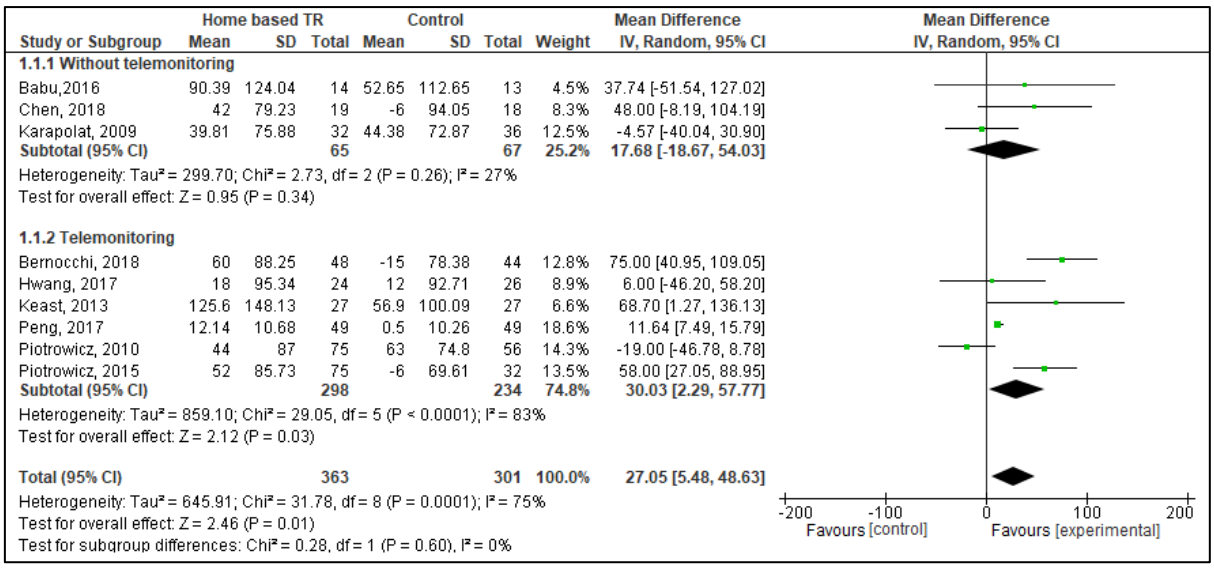


Figure 5.2. Subgroup analysis of heterogeneity for Presence of Telemonitoring considering Peak VO2

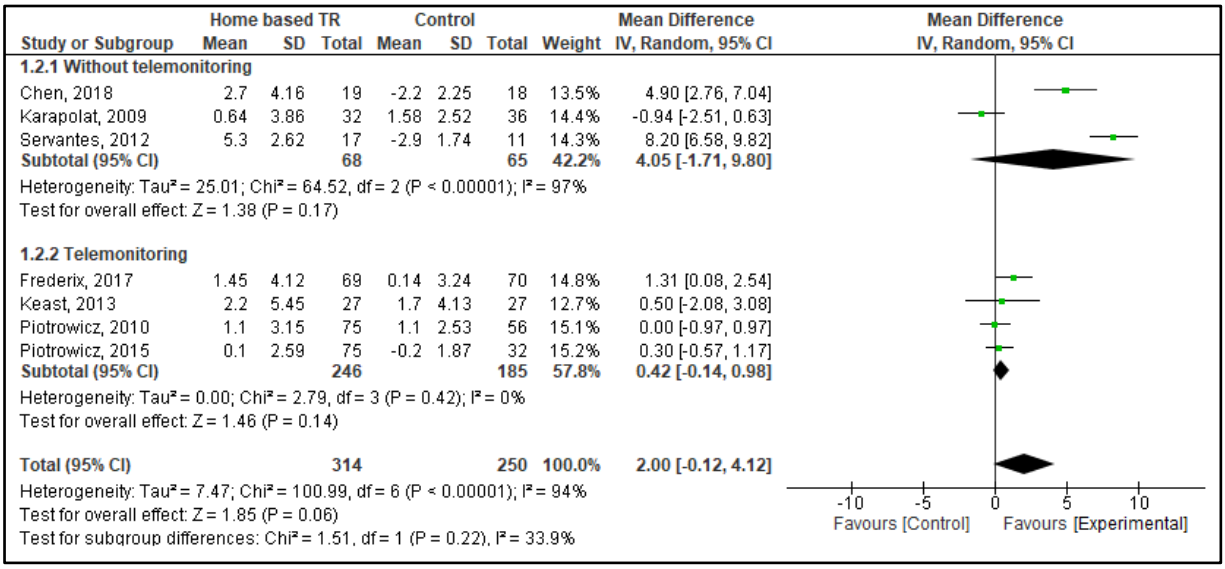


Figure 5.3. Subgroup analysis of heterogeneity for Presence of Telemonitoring considering QoL (MLHFQ)

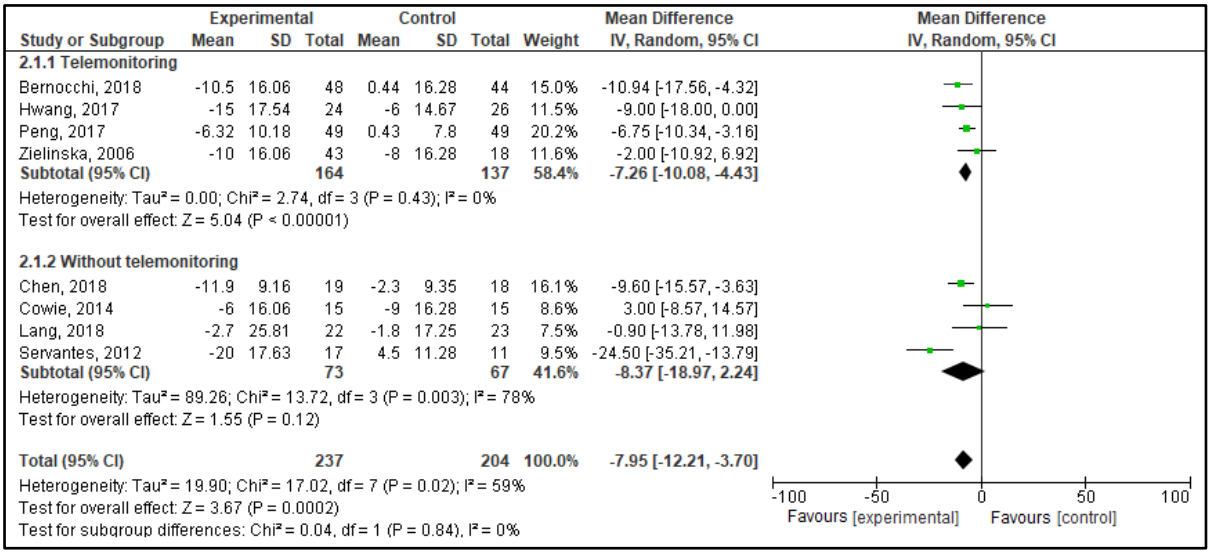


Figure 6.1. Subgroup analysis of heterogeneity for Follow-up Intensity considering 6MWT

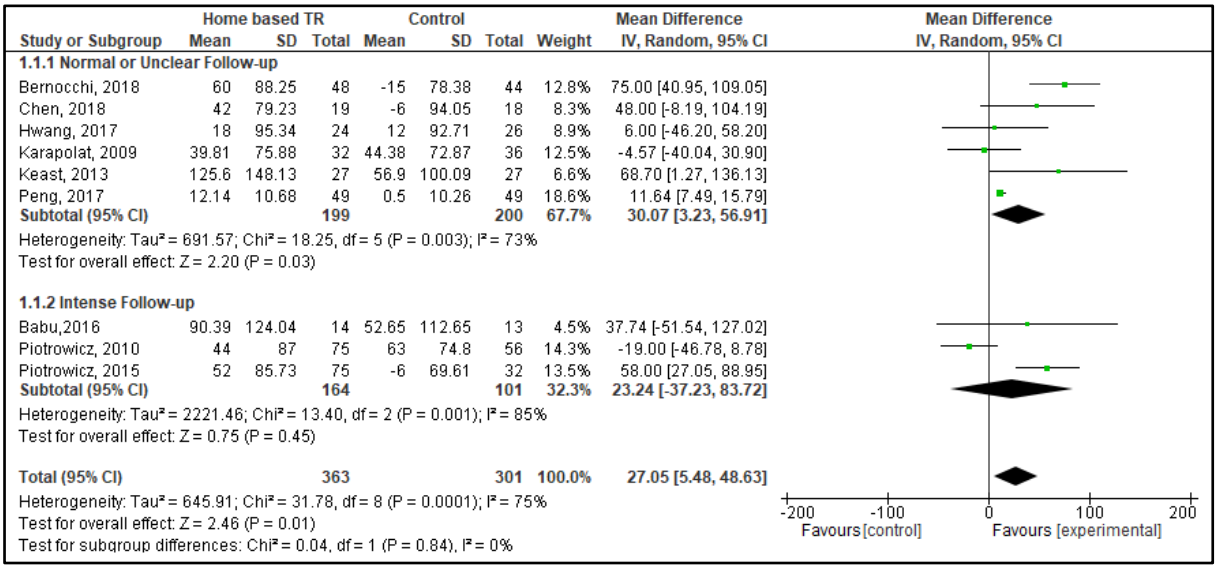
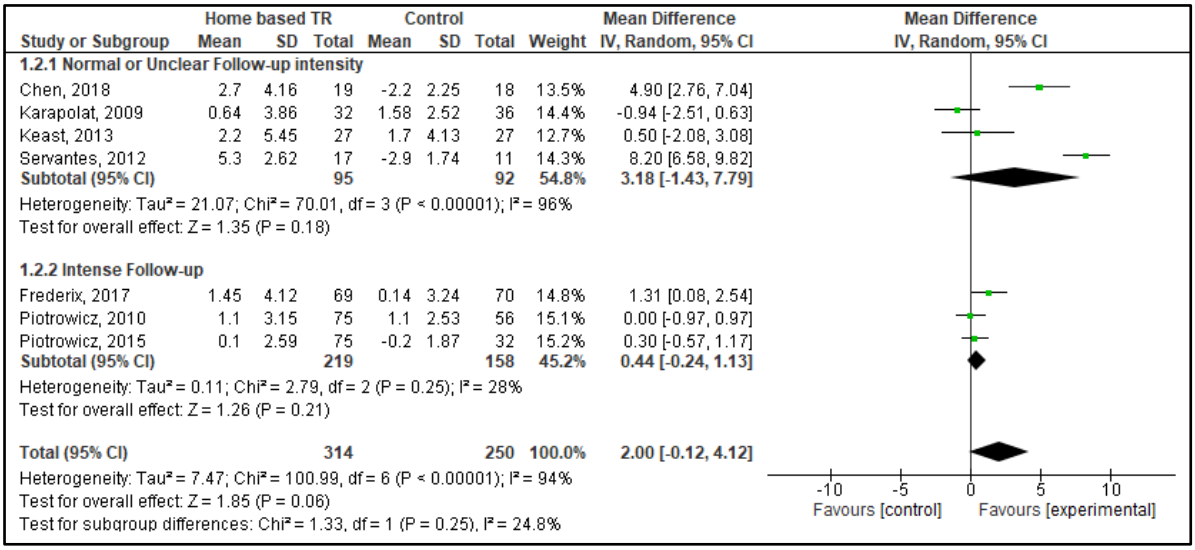


Figure 6.2. Subgroup analysis of heterogeneity for the Follow-up Intensity considering Peak VO2



ANEXOS

European Journal of Heart Failure

Author Guidelines

REQUIRED FORMS

European Journal of Heart Failure requests that all authors complete:
An ICMJE Conflicts of Interest disclosure form
Author Contribution form

Please note that these forms are here for reference, and authors will have the opportunity to complete versions of these forms in the online submissions system.

INTRODUCTION

Thank you for your interest in *European Journal of Heart Failure*. Please consult the following instructions for help in preparing your manuscript, and feel free to contact us with any questions. To ensure fast peer review and publication, manuscripts that do not adhere to the following instructions will be returned to the corresponding author for technical revision before undergoing peer review. We look forward to your submission.

AIMS AND SCOPE

The *European Journal of Heart Failure* is the international journal of the Heart Failure Association of the European Society of Cardiology dedicated to the advancement of knowledge in the field of heart failure. The journal publishes reviews and editorials in order to improve the understanding, prevention, investigation and treatment of heart failure. Molecular and cellular biology, pathology, physiology, electrophysiology, pharmacology, as well as the clinical, social and population sciences all form part of the discipline that is heart failure. Accordingly, submission of manuscripts on basic, clinical and population sciences is invited. Original contributions on nursing, care of the elderly, primary care, health economics and other specialist fields related to heart failure are also welcome.

HEART NETWORK

The *European Journal of Heart Failure* participates in the HEART Network which is a network of Editors from most cardiovascular journals. Information is exchanged between Editors on a regular basis. The network has recently approved a common ethics standard.

Its purpose is to ensure transparency and honesty in the scientific process that promotes ethical conduct in performance and publication of research.

The following will be considered as parts of this process:

a. Disclosure of potential conflicts of interest for all involved in the performance of research and in the evaluation and publication process of a manuscript. Relevant relationships with commercial interests should be disclosed according to the guidelines of the journal's sponsoring society, or, when no such guidelines exist, according to those of the AHA, ACC, or ESC.

b. Establish thorough review processes particularly alert to discovering scientific fraud and data falsification, redundant or duplicate publication, and plagiarism, and to adopt a uniform standard of dealing with authors guilty of fraudulent practices.

c. To maintain confidentiality and embargos where appropriate.

d. To create uniform criteria to establish authorship. To qualify for authorship, individuals must have made substantial contributions to the intellectual content of the paper in at least one of the following areas: conceived and designed the research, acquired the data, analysed and interpreted the data, performed statistical analysis, handled funding and supervision, drafted the manuscript, or made critical revision of the manuscript for important intellectual content. Authors must give final approval of the version to be submitted and any revised version to be published. For multi-centre trials, individuals who accept direct responsibility for the manuscript should fully meet the criteria for authorship defined above and contributors not meeting these criteria should be acknowledged.

e. Avoidance of false claims of ownership, priority, by attention to previous publications.

f. Avoidance of excessive claims of benefits of a product/technique, in the publication as well as with news media.

g. Noting compliance with institutional review board requirements and, when appropriate, approved laboratory procedures for animal research, and that the research conforms to the ethical standards of the *Declaration of Helsinki*, the *Geneva Declaration*, the *Belmont Report*, and *Good Clinical Practices* from the FDA, and the submission conforms to the *International Committee of Medical Journal Editors (ICMJE): Uniform Requirements for Manuscripts Submitted to Biomedical Journals: writing and editing for biomedical publication* (*Haematologica* 2005; **89:**264).

PRE-SUBMISSION

1. Editorial Review and Acceptance

The acceptance criteria for all papers are the quality and originality of the research and its significance to our readership. Except where otherwise stated, manuscripts are double-blind peer reviewed by at least two anonymous reviewers and the Editor. Final acceptance or rejection rests with the Editorial Board, who reserves the right to refuse any material for publication.

Manuscripts should be in a clear, concise and direct style. Where contributions are judged as acceptable for publication on the basis of content, the Editor and the Publisher reserve the right to modify typescripts to eliminate ambiguity and repetition and improve communication between author and reader. If extensive alterations are required, the manuscript will be returned to the author for revision.

2. Pre-submission Resources

2.1. Author Services

Prior to submission, we encourage you to browse **Wiley's Author Resources site**, which provides useful information on topics such as preparing your article and digital artwork; publishing ethics; copyright and open access; and how to promote your published work.

2.2. Pre-submission English-language Editing

Authors for whom English is a second language are advised to consider having their manuscript professionally edited before submission to improve the English, and to ensure the paper is clearly written in standard, scientific English language appropriate to the discipline. This can be undertaken by a service such as the Wiley English Language Editing Service, at **http://wileyeditingservices.com**. Please note that using the Wiley English Language Editing Service does not guarantee that your paper will be accepted by this journal, and all services are paid for and arranged by the author.

3. Manuscript Preparation

3.1. Manuscript Categories and Criteria

The *European Journal of Heart Failure* accepts the following categories of articles:

Research Articles

These should not exceed 3500 words (excluding references, tables and figures) and may include up to a maximum of 6 figures and/or tables and up to 30 references. Research articles should be divided into the following sections: (1) Title page, (2) Abstract and up to six Keywords, (3) Introduction, (4) Methods, (5) Results, (6) Discussion, (7) Acknowledgements, (8) Funding, (9) Conflict of interest, (10) References, (11) Figure legends, (12) Appendices, (13) Tables, (14) Figures. The Abstract should be divided into the following sections 'Aims', 'Methods and results' and 'Conclusion'; it should not exceed 250 words.

Reviews

The *European Journal of Heart Failure* publishes a limited number of scholarly, comprehensive review papers. Reviews should not exceed 3500 words. They should summarise and critically evaluate research in the subject area, and should discuss implications for the future. Reviews have unstructured abstracts with no headings, which should not exceed 250 words and may include up to 45–50 references. Please see below for systematic reviews.

Systematic Reviews

These reviews should follow the format of research articles (refer to the section, 'Research Articles'). These should be submitted as a research article during the submission process.

Editorials

All editorials should be limited to 1500 words (excluding references), with a maximum of 15 references. They do not require an abstract and may include one table and/or one figure. In particular, the addition of one figure would be welcome and could add to the understanding and attractiveness of the article. The following different categories of editorials may be considered:

- **Editorial comment.** Written upon invitation by the Editor, it is a comment to a research article and should discuss its results, compare them with the current literature and give a personal interpretation of the study.
- **Viewpoint.** This is a commentary on a topical item. It may be invited or not. When we receive more viewpoints regarding a similar topic they may be gathered under the category of "Different viewpoints" in the index page. However, their labelling will remain "viewpoint" in the title page so that they may be considered alone.
- **Opinion Piece.** This has to be written by one single author and have possibly controversial content and opinions.
- **In the News.** This is a single author comment on recent event or trial.
- **From opinion to evidence.** This is an expert opinion and can be written by multiple authors. It must be based on facts and be evidence based. Differently from the other categories of editorials, it may reach 2000 words and 30 references.

Short Reports

These reports should not exceed 1500 words and should comprise a Background section (≈100 words), Aims (≈50 words), Methods (≈300 words), Results (300 words) and Conclusion (250 words). The editorial team reserves the right to decide which of the tables/figures submitted are necessary. A structured abstract not exceeding 250 words is also required for Internet purposes.

Letters to the Editor

Letters to the Editor may regard comments to an article published in our journal in the previous months. These letters should have a maximum of 3 authors, should not exceed 400 words and have a maximum of 5 references, including one reference to the article that they are about. We may ask for a reply to the authors of the original article and the letter and its reply be published together.

Research Letters

Letters based on original research findings are also allowed. The letter may include up to 1000 words, including a maximum of 8 references, and one figure and/or Table. Research letters should have no abstract and no sub-headings. However, a short description of methods, results and conclusions is required.

Case Reports

These reports should not exceed 1200 words. Case reports should include an unstructured Abstract with no subheadings (not exceeding 100 words), an Introduction, a Description of the case(s) under the heading, 'Case Report' and a Discussion of the findings in the context of current practice.

Study Design

These should not exceed 3500 words (excluding references, tables, and figures) and may include up to a maximum of 6 figures and/or tables and up to 30 references. Study design papers should be divided into the following sections: (1) Title page, (2) Abstract and up to six Keywords, (3) Introduction, (4) Study Design, (5) Discussion, (6) Acknowledgements, (7) Funding, (8) Conflict of Interest, (9) References, (10) Figure legends, (11) Appendices, (12) Tables, (13) Figures. The Abstract should be divided into the following sections 'Aims', 'Methods', and 'Conclusion'; it should not exceed 250 words.

Book Reviews

Book reviews may include up to 800 words, including a maximum of 3 references. They should have no abstract and no sub-headings.

3.2. Manuscript Format and Structure

General Format

Prepare your manuscript text using a Word processing package (save in .doc or .rtf format). Submissions of text in the form of PDF files are not permitted. Manuscripts should be double-spaced, including text, tables, legends and references.

Number each page. Please avoid footnotes; use instead, and as sparingly as possible, notes within brackets. Enter text in the style and order of the journal. Type references in the correct order and style of the journal. Type unjustified, without hyphenation, except for compound words (where two words are joined to form a new word e.g. end-systolic, non-infarcted). Type headings in the style of the journal. Use the TAB key once for paragraph indents. Where possible use Times New Roman for the text font and Symbol for Greek and special characters. Use the word processing formatting features to indicate bold, italic, Greek, maths, superscript and subscript characters. Clearly identify unusual symbols and Greek letters. Differentiate between the letter O and zero; the letters I and l; and the number 1.

Add the word count of the abstract and of the text in the article's title page. The word count of the text includes just the text without the title page, tables, figure legends or references.

Check the final copy of your paper carefully, as any spelling mistakes and errors may be translated into the typeset version.

Style and Spelling

Oxford English spelling should be used. Authors whose first language is not English are requested to have their manuscripts checked carefully before submission. This will help expedite the review process and avoid confusion.

Abbreviations

Abbreviations of standard SI units of measurement only should be used.

Ethics

Declaration of Helsinki: The authors should state their study complies with the *Declaration of Helsinki*, that the locally appointed ethics committee has approved the research protocol and that informed consent has been obtained from the subjects (or their guardians).

ARRIVE Guidelines: The contribution of animal research in enabling better health for man and animals is incontrovertible and *EJHF* is committed to the publication of research studies which use animal models, but demands the same rigorous attention to detail as in clinical trials. Failure to describe research

methods and to report results appropriately has scientific and ethical implications for the entire research process and the reputation of those involved in it.

Experiments involving animals should be appropriately designed, correctly analysed and then transparently reported, to both increase the validity of the results, and maximise the scientific gain. A minimum amount of relevant information must be included in manuscripts published in this journal to ensure that the methods and results of a study can be reviewed, analysed and repeated. *EJHF* will therefore refer to the *ARRIVE (Animals in Research: Reporting In Vivo Experiments) Guidelines* as the basis for the process of reviewing manuscripts of research involving animals.

These guidelines were generated by The National Centre for the Replacement, Refinement and Reduction of Animals in Research, which is an independent scientific organisation, established by the UK Government, in consultation with scientists, statisticians, journal editors and research funders.

DNA Sequences and GenBank Accession Number

For each and every gene accession number cited in an article, authors should type the accession number in bold, underlined text. Letters in the accession number should always be capitalised. Example: (GenBank accession nos. **AI631510**, **AI631511**, **AI632198** and **BF223228**), a B-cell tumor from a chronic lymphatic leukemia (GenBank accession no. **BE675048**), and a T-cell lymphoma (GenBank accession no. **AA361117**).

3.3. Parts of the Manuscript

Title Page

Manuscripts should be preceded by a title page which includes a full list of authors and their affiliations, as well as the corresponding author's contact details. You may like to use **this template**. When entering the author names into Editorial Manager, the corresponding author will be asked to provide a CRediT contributor role to classify the role that each author played in creating the manuscript. Please see the Project CRediT website for a list of roles.

Add the word count of the abstract and of the text in the article's title page. The word count of the text includes just the text without the title page, tables, figure legends or references.

Abstract and Keywords

All abstracts may not contain more than 250 words and should be submitted as a separate file. The abstract should be formatted with the following heading: (1) Aims, (2) Methods and Results, (3) Conclusion.

A maximum of six keywords may be submitted.

Introduction

This section should provide a rationale for conducting the study within the context of previous work by other authors.

Methods

This section should be sufficiently detailed to enable repetition of the study by other investigators. If pertinent, the section may be divided into headed subsections. For animal studies, this section should contain a statement that, "The investigation conforms to the *Guide for the Care and Use of Laboratory Animals* published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1985)". Human studies should contain a statement that, "The investigation conforms with the principles outlined in the *Declaration of Helsinki*" (*Br Med J* 1964; **ii:** 177). In addition details of the ethics committee approval procedures and a statement that all subjects gave written informed consent to participate in the study should be included.

Results

If pertinent, the section may be divided into headed subsections. For presentation of data, figures are preferred to tables. Data should not be duplicated in both figures and tables. Extensive numerical data should be presented in legends to the figures rather than in the main body of text. SI units should be used throughout.

Discussion

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