

# OUTCOMES OF DIETARY INTERVENTIONS IN HFPEF

Living Review, version 1, 30 April 2022



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### 1.0 Search dates

Conducted: August 2019 and April 2021

# **1.2 Search Strategies**

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R)

1 (chf or hfpef or "preserved ejection fraction" or ((cardia\* or myocardial or heart) adj (failure or insufficienc\*)) or ((heart or cardia\* or myocardial) adj5 diastolic failure) or (decompensat\* adj2 (heart\* or cardia\*))).mp. or exp heart failure/

2 (Morbid\* or comorbid\* or co-morbid\* or mortality or symptom\* or "quality of life" or weight or "body composition" or "muscle strength" or "lean mass" or overweight\* or thin\* or "multiple chronic conditions" or obes\* or adipos\*).mp. or exp weight loss/ or exp morbidity/ or exp multiple chronic conditions/ or exp mortality/ or exp mortality, premature/ or exp quality of life/ or exp body weight/ or exp body weight changes/ or exp weight gain/ or exp weight loss/ or exp overweight/ or exp thinness/ or exp body composition/ or exp muscle strength/ or exp obesity/

3 (Nutrition\* or nutrient\* or diet\* or micronutrient\* or macronutrient\* or eat or eating or feed\* or drink\* or beverage\* or beet\* or "beta vulgaris" or (nitrous adj oxide) or salt or (sodium adj chloride) or dash or meal or meals or calori\* or high-calori\* or low-calori\*).mp. or exp Sodium, Dietary/ or exp diet/ or exp healthy diet/ or exp "diet, food, and nutrition"/ or exp micronutrients/ or exp beta vulgaris/ or exp dietary supplements/ or exp feeding behavior/ or exp meals/ or exp drinking behavior/ or exp nitrous oxide/ or dh.fs.

4 ((pre adj3 post) or trial\* or placebo\* or control\* or random\* or review\* or (systematic\* adj3 search\*)).mp. or exp "Systematic Review"/ or exp "Review"/ or exp Randomized Controlled Trial/ or exp Clinical Trial/ or exp Meta-Analysis/

5 1 and 2 and 3 and 4

6 animals/ not humans/

7 5 not 6

8 limit 7 to yr="2001 -Current"

# Embase 1974 to 2019 August 02

1 (chf or hfpef or "preserved ejection fraction" or ((cardia\* or myocardial or heart) adj (failure or insufficienc\*)) or ((heart or cardia\* or myocardial) adj5 diastolic failure) or (decompensat\* adj2 (heart\* or cardia\*))).ti,ab. or exp \*heart failure with preserved ejection fraction/ or exp \*heart ejection fraction/ or exp \*heart failure/

2 (Morbid\* or comorbid\* or co-morbid\* or mortality or symptom\* or "quality of life" or weight or "body composition" or "muscle strength" or "lean mass" or overweight\* or thin\* or "multiple chronic conditions" or obes\*).mp. or exp \*body weight loss/ or exp \*morbidity/ or exp \*comorbidity/ or exp \*multiple chronic conditions/ or exp \*mortality/ or exp \*premature mortality/ or exp \*"quality of life"/ or exp \*body weight/ or exp \*body weight change/ or exp \*body weight gain/ or exp \*weight loss/ or exp \*lean body weight/ or exp \*obesity/ or exp \*underweight/ or exp \*body composition/ or exp \*muscle strength/ or exp \*obesity/

3 (Nutrition\* or nutrient\* or diet\* or micronutrient\* or macronutrient\* or eat or eating or feed\* or drink\* or beverage\* or beet\* or "beta vulgaris" or (nitrous adj oxide) or salt or (sodium adj chloride) or dash or meal or meals or calori\* or high-calori\* or low-calori\*).ti,ab. or exp \*sodium intake/ or exp \*diet/ or exp \*salt intake/ or exp \*healthy diet/ or exp \*trace elements/ or exp \*beetroot/ or exp \*dietary supplement/ or exp \*feeding behavior/ or exp \*eating habit/ or exp \*drinking behavior/ or exp \*nitrous oxide/ or exp \*sodium chloride/ or exp \*meal/

4 ((pre adj3 post) or trial\* or placebo\* or control\* or random\* or review\* or (systematic\* adj3 search\*)).ti,ab. or exp "Systematic Review"/ or exp "Review"/ or exp Randomized Controlled Trial/ or exp "Clinical Trial"/ or exp Meta Analysis/

- 5 1 and 2 and 3 and 4
- 6 animals/ not humans/
- 7 5 not 6
- 8 limit 7 to yr="2001 -Current"

\*\*\*\*\*

#### CINAHL

#	Query	Limiters/Expanders
S18	s13 not s16	Limiters - Published Date: 20010101-20211231 Search modes - Boolean/Phrase
S17	s13 not s16	Search modes - Boolean/Phrase
S16	s14 not s15	Search modes - Boolean/Phrase
S15	(MH "Human")	Search modes - Boolean/Phrase

S14	(MH "Animals+")	Search modes - Boolean/Phrase
S13	S3 AND S6 AND S9 AND S12	Search modes - Boolean/Phrase
S12	S10 OR S11	Search modes - Boolean/Phrase
S11	(MH "Literature Review+") OR (MH "Scoping Review") OR (MH "Systematic Review") OR (MH "Meta Analysis") OR (MH "Randomized Controlled Trials+") OR (MH "Clinical Trials+") OR (MH "Therapeutic Trials")	Search modes - Boolean/Phrase
S10	((pre n3 post) or trial* or placebo* or control* or random* or review* or (systematic* n3 search*))	Search modes - Boolean/Phrase
S9	S7 OR S8	Search modes - Boolean/Phrase
58	(MH "Nutrition+") OR (MH "Nutrients+") OR (MH "Diet+") OR (MH "Micronutrients") OR (MH "Macronutrients") OR (MH "Eating") OR (MH "Eating Behavior+") OR (MH "Food Habits") OR (MH "Drinking Behavior+") OR (MH "Beverages+") OR (MH "Beet") OR (MH "Nitrous Oxide") OR (MH "Beet") OR (MH "Nitrous Oxide") OR (MH "Sodium Chloride, Dietary") OR (MH "Sodium Chloride+") OR (MH "DASH Diet") OR (MH "Meals+") OR (MH "Energy Intake") OR (MH "Food Intake+") OR (MH "Dietary Supplements+") OR (MH "Dietary Supplementation")	Search modes - Boolean/Phrase
S7	(Nutrition* or nutrient* or diet* or micronutrient* or macronutrient* or eat or eating or feed* or drink* or beverage* or	Search modes - Boolean/Phrase

beet\* or "beta vulgaris" or ("nitrous oxide") or salt or ("sodium chloride") or dash or meal or meals or calori\* or high-calori\* or low-calori\*)

S6

S4 OR S5

Search modes - Boolean/Phrase

S5	(MH "Morbidity+") OR (MH "Comorbidity") OR (MH "Mortality+") OR (MH "Symptoms+") OR (MH "Quality of Life+") OR (MH "Body Composition+") OR (MH "Body Weight Changes+") OR (MH "Muscle Strength+") OR (MH "Fat Free Mass") OR (MH "Obesity+") OR (MH "Adipose Tissue+") OR (MH "Weight Loss+") OR (MH "Weight Gain+") OR (MH "Thinness")	Search modes - Boolean/Phrase
S4	(Morbid* or comorbid* or co-morbid* or mortality or symptom* or "quality of life" or weight or "body composition" or "muscle strength" or "lean mass" or overweight* or thin* or "multiple chronic conditions" or obes*)	Search modes - Boolean/Phrase
S3	S1 OR S2	Search modes - Boolean/Phrase
S2	(MH "Heart Failure+")	Search modes - Boolean/Phrase
S1	(chf or hfpef or "preserved ejection fraction" or ((cardia* or myocardial or heart) n (failure or insufficienc*)) or ((heart or cardia* or myocardial) n5 diastolic failure) or (decompensat* n2 (heart* or cardia*)))	Search modes - Boolean/Phrase

#### Emcare

#### **Ovid Emcare**

(chf or hfpef or "preserved ejection fraction" or ((cardia\* or myocardial or heart) adj (failure or insufficienc\*)) or ((heart or cardia\* or myocardial) adj5 diastolic failure) or (decompensat\* adj2 (heart\* or cardia\*))).mp. or exp heart failure/

- (Morbid\* or comorbid\* or co-morbid\* or mortality or symptom\* or "quality of life" or weight or "body composition" or "muscle strength" or "lean mass" or overweight\* or thin\* or "multiple chronic conditions").mp. or exp morbidity/ or exp comorbidity/ or exp mortality/ or exp symptom/ or exp "quality of life"/ or exp body weight/ or exp obesity/ or exp underweight/ or exp body fat/ or exp body composition/ or exp lean body weight/ or exp muscle strength/ or exp weight reduction/ or exp weight gain/
- 2. (Nutrition\* or nutrient\* or diet\* or micronutrient\* or macronutrient\* or eat or eating or feed\* or drink\* or beverage\* or beet\* or "beta vulgaris" or (nitrous adj oxide) or salt or (sodium adj chloride) or dash or meal or meals or calori\* or high-calori\* or low-calori\*).mp. or exp nutrition/ or exp nutrient/ or exp diet/ or exp trace element/ or exp macronutrient/ or exp eating/ or exp eating habit/ or exp feeding/ or exp feeding behavior/ or exp drinking behavior/ or exp drinking/ or exp beverage/ or exp beet/ or exp nitrous oxide/ or exp sodium chloride/ or exp meal/ or exp calorie/ or exp caloric intake/ or exp dietary intake/
- 3. ((pre adj3 post) or trial\* or placebo\* or control\* or random\* or review\* or (systematic\* adj3 search\*)).mp. or exp "systematic review"/ or exp "review"/ or exp clinical trial/ or exp controlled clinical trial/ or exp randomized controlled trial/ or exp meta analysis/
- 4. (exp animal/ or exp animal experiment/ or exp animal model/) not exp human/
- 5. 1 and 2 and 3 and 4
- 6. 6 not 5
- 7. Limit 7 to yr="2001-Current"

#### Cochrane

Search Name: sandra mulrennan #3

Date Run: 05/08/2019 21:20:26

Comment:

ID Search Hits

#1 (chf or hfpef or "preserved ejection fraction" or ((cardia\* or myocardial or heart) next (failure or insufficienc\*)) or ((heart or cardia\* or myocardial) near/5 diastolic failure) or (decompensat\* near/2 (heart\* or cardia\*)))
 29053

#2 MeSH descriptor: [Heart Failure] explode all trees 8315

#### #3 #1 or #2 29067

#4 (Morbid\* or comorbid\* or co-morbid\* or mortality or symptom\* or "quality of life" or weight or "body composition" or "muscle strength" or "lean mass" or overweight\* or thin\* or "multiple chronic condition\*" or obes\* or adipos\*)
 447868

- #5 MeSH descriptor: [Weight Loss] explode all trees 5664
- #6 MeSH descriptor: [Morbidity] explode all trees 14601
- #7 MeSH descriptor: [Multiple Chronic Conditions] explode all trees16
- #8 MeSH descriptor: [Mortality] explode all trees 12756
- #9 MeSH descriptor: [Mortality, Premature] explode all trees 3
- #10 MeSH descriptor: [Quality of Life] explode all trees 21832
- #11 MeSH descriptor: [Body Weight] explode all trees 25151
- #12 MeSH descriptor: [Body Weight Changes] explode all trees 7804
- #13 MeSH descriptor: [Weight Gain] explode all trees 2340
- #14 MeSH descriptor: [Weight Loss] explode all trees 5664
- #15 MeSH descriptor: [Overweight] explode all trees14372
- #16 MeSH descriptor: [Thinness] explode all trees 275
- #17 MeSH descriptor: [Body Composition] explode all trees 4746
- #18 MeSH descriptor: [Obesity] explode all trees 12309
- #19 #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 457473

#20 (Nutrition\* or nutrient\* or diet\* or micronutrient\* or macronutrient\* or eat or eating or feed\* or drink\* or beverage\* or beet\* or "beta vulgaris" or (nitrous oxide) or salt or (sodium chloride) or dash or meal or meals or calori\* or high-calori\* or low-calori\*) 184578

- #21 MeSH descriptor: [Sodium, Dietary] explode all trees 648
- #22 MeSH descriptor: [Diet, Food, and Nutrition] explode all trees 49673
- #23 MeSH descriptor: [Micronutrients] explode all trees 3321
- #24 MeSH descriptor: [Beta vulgaris] explode all trees 121

- #25 MeSH descriptor: [Dietary Supplements] explode all trees 11287
- #26 MeSH descriptor: [Feeding Behavior] explode all trees 8313
- #27 MeSH descriptor: [Meals] explode all trees 1151
- #28 MeSH descriptor: [Drinking Behavior] explode all trees 3681
- #29 MeSH descriptor: [Nitrous Oxide] explode all trees 1417
- #30 #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 192240
- #31 #3 and #19 and #30 with Publication Year from 2001 to 2019, with Cochrane Library publication date from Jan 2001 to Dec 2019, in Trials1193

# 1.2 Summary of Studies

Type	Author & Year, Study Acronym,	Populat	ion	Intervention & Control	(cł	nange between base	Outcomes line and follow-up u	nless otherwise state	ed)
Ţ	Design	Populat			Haemodynamic	Function	Anthropometric	HF Status	Quality of Life
		п	66	Intervention: 28 days of prepared food					
	Hummel <i>et al.</i> 2018 (33)	HFpEF (%)	24	matching the DASH eating pattern nutritional content (carbohydrate: 55%,					
		Other key inclusion criteria	Hypertension	protein: 20%, fat: 30%) with daily sodium intake of 50 mmol (1150				BNP (log	KCCQ Summary
	GOURMET HFpEF	Age years (mean SD)	71±8	mg)/2100 kcal	Systolic BP (mmHg) Intervention: -5; Control: 0; p=0.46	-	-	transformed) Intervention: +56; Control: +82;	Score (points) Intervention: +13; Control: +10;
		Female (%)	30					p=0.59	p=0.46
	Randomised controlled, parallel group trial	NYHA II (%)	NR	Control: usual care					
DASH	8 <b>P</b>	NYHA III (%)	NR						
DA		п	48						
	Rifai <i>et al.</i> 2015 (34)	HFpEF (%)	44	Intervention: 91 days of personalised DASH eating plan and shopping list					
		Other key inclusion criteria	None	augmented by in-person and/or bi- weekly phone counselling from dietitian		6MWD (meters)		BNP (pg/ml)	MLWHFQ (points)
	NA	Age years (mean SD)	62±11*		-	Intervention: +38; Control: -5;	-	Intervention: -8; Control: +61;	Intervention: -8; Control: +1;
		Female (%)	39			p=0.018		p=0.081	p=0.006
	Randomised controlled, parallel	NYHA II (%)	23	Control: usual care					
	group trial	NYHA III (%)	52						
		п	65						
NOIL	Colin-Ramirez <i>et al.</i> 2004 (35)	HFpEF (%)	37	<b>Dose</b> : 182 days of individualised diets (carbohydrate: 50-55%, protein: 15- 20%, fat: 25-35%) with salt restricted to		BMI (kg/m²)	Weight (kg)	NYHA I/ II/III (n)	Bespoke HF
SALT REDUCTION		Other key inclusion criteria	None	20%, fat. 25-35%) with sait restricted to 2.0-2.4 grams/day and fluid restricted to 1.5L/day	-	Intervention: -0.4; Control: -0.1;	Intervention: -0.5; Control: -0.1,	Intervention: +15/- 4/-15.1; Control: -	questionnaire Intervention: +19.3%, Control:
SALT	NA	Age years (mean SD)	62±16*			p=not significant	p=not significant.	+7.8/-10.6/+2.8	+3.2%; p=0.02
		NA Female (%) 64 Control: usual care	Control: usual care						

Randomised controlled, parallel	NYHA II (%)	26						
group trial	NYHA III (%)	16						
	n	38						
Colin-Ramirez, McAlister <i>et al.</i> 2015 (36)	HFpEF (%)	Unclear	Intervention: 182 days prescribed diet targeted to reduce sodium to 1.5 grams/day (low); macronutrient				BNP (pg/ml) Intervention: -145;	
	Other key inclusion criteria	None	composition: carbohydrate: 50-55%, protein: 15-20%, fat: 25-35%.			Weight (kg)	Control: -17 NYHA I/ II/III (n)	KCCQ summary
NA	Age years (mean SD)	65 ±12		-	-	Intervention: -0.4; Control: -0.1;		score. Intervention: +5;
NA	Female (%)	52.6	<b>Control:</b> 182 days prescribed diet			p=not significant	Intervention: +16.7/-23.1/+6.4; Control: +22.2/-	Control: -2.0.
Randomised controlled, parallel	NYHA II (%)	89.5	targeted to reduce sodium to 2.3 grams/day (moderate); macronutrient composition: carbohydrate: 50-55%,				28/+5.8; p=0.08	
group trial	NYHA III (%)	10.5	protein: 15-20%, fat: 25-35%					
	n	30						
Philipson <i>et al.</i> 2010 (38)	HFpEF (%)	Unclear	Intervention: 84 days of restricted sodium intake to 2-3 grams/day for 12 weeks; composition of other micro/macronutrients unknown.	Systolic BP (mmHg) Intervention: -3; Control: +2.		Weight (kg) Intervention: -1; Control: -1. BMI (kg/m <sup>2</sup> ). Intervention: -1; Control: -1.		
	Other key inclusion criteria	None						Bespoke measure
NA	Age years (mean SD)	76±8			-		NTproBNP (pg/ml) Intervention: -149; Control: -33	(0=worst, 6=best) Intervention: 0;
NA	Female (%)	26						Control: +0.1
Randomised controlled, parallel	NYHA II (%)	10	Control: usual care					
group trial	NYHA III (%)	60						
	п	97					NYHA I/ II/III/IV (n)	
Philipson , Ekman <i>et al.</i> 2013 (37)	HFpEF (%)	23	Intervention: 84 days of restricted sodium intake to 2-3 grams/day for 12			Weight (kg) Intervention: -1;	Intervention: +1/+6/-7/0;	
	Other key inclusion criteria	none	weeks; composition of other micro/macronutrients unknown.			Control: 0; p=not significant.	Control: -1/- 6/+7/0; p=0.01	Bespoke measure (0=worst, 6=best)
NA	Age years (mean SD)	75±8			-	BMI (kg/m2)	NTproBNP (pg/ml)	Intervention: 0; Control: +0.2; p=0.11
NA	Female (%)	42				Intervention: 0; Control: -1; p=not significant	Intervention: +185; Control: +402;	
	NYHA II (%)	24	Control: usual care			o.p.mount	p=0.13.	

	Randomised controlled, parallel group trial	NYHA III (%)	73						
		n	76						
	Evangelista <i>et al.</i> 2021 (39)	HFpEF (%)	43	Intervention: 91 days of a high protein,					
		Other key inclusion criteria	High BMI, Type 2 Diabetes	hypocaloric diet (30% protein, 40% carbohydrates, 30% fat)	Systolic BP (mmHg)		BMI (kg/m²) Intervention: -1.5; Control: -1;		
	PRO-Heart	Age years (mean SD)	58 ± 10		Intervention: - 10.8; Control: +0.7;	-		-	-
	PRO-neart	Female (%)	27		p=0.001		p=0.067		
	Randomised controlled, parallel	NYHA II (%)	77.6	<b>Control:</b> 91 days of a standard protein hypocaloric diet (15% protein, 55% carbohydrates, 30% fat)					
	group trial	NYHA III (%)	22.4						
		n	66						
NC	Pineda-Juarez <i>et al.</i> 2015 (40)	HFpEF (%)	6	Intervention: 84 days of individualised diets (50% carbohydrates, 20% protein [protein partly replaced by branched	Systolic BP (mmHg)	VO2 Peak (ml/kg/min)	-	BMI (kg/m²) Intervention: - .38%; Control: - .67%; p=not significant	
PROTEIN MANIPULATION		Other key inclusion criteria	None	chain amino acids] and 30% fat) + plus resistance exercise					
MANIF		Age years (mean SD)	73±14*		Intervention -1.6%; control +5.2%;	Intervention +16.6%; Control:			-
ROTEIN		Female (%)	40.9		p=not significant	+50.1%; p=not significant			
Id	Randomised controlled, parallel	NYHA II (%)	20	<b>Control:</b> 84 days of resistance exercise only					
	group trial	NYHA III (%)	4						
		n	23						
	Azhar <i>et al.</i> 2020 (41)	HFpEF (%)	100	Intervention: 84 days of whey protein to supplement usual intake to reach an					
		Other key inclusion criteria	High BMI	equivalent of 1.2g protein/kg bodyweight per day plus exercise	Systolic BP (mmHg)	6MWD (meters)			
	NA	Age years (mean SD)	70±2		Intervention: - 11.9; Control: -2.8;	Intervention: +36.63; Control: -	-	-	-
		Female (%)	35	Controls: 1) whey protein to	p=<0.05	9.55; p=<0.05			
	Randomised controlled, parallel	NYHA II (%)	NR	supplement usual intake to reach an equivalent of 1.2g protein/kg					
	group trial	NYHA III (%)	NR	bodyweight (NO EXERCISE) 2) usual care					

	Cocco & Chu 2007 (42) NA	n HFpEF (%) Other key inclusion criteria Age years (mean SD)	70 100 Hypertension, High BMI NR	Intervention: 182 days of prescribed calorie restricted weekly diets designed to achieve a weight loss of >5 kg within 6 months.	Systolic BP (mmHg) Intervention: -3; Control: +2, p=not	6MWD (meters) Intervention: +26; Control: 0;	BMI (kg/m²) Intervention: -2; Control: 0; p=<0.0001	NTproBNP (pg/ml) Intervention: -368; Control: 0;	-
z		Female (%) NYHA II (%)	NR	Control: usual care	significant	p=<0.000002	Weight (kg) Intervention: -7; Control: 0; p=<0.0000	p=0.00005	
CALORIC RESTRICTION	Non-randomised, controlled study	Non-randomised,							
DRIC RE		n	100	Intervention: 140 days of meal					
CALC	Kitzman <i>et al.</i> 2016 (29)	HFpEF (%)	100	provision approach aiming for a calorie deficit of 350-400 kcal/day.					
	Other key inclusi criteria		High BMI	Macronutrients: 1.2 g of protein/kg ideal body weight, 25% to 30% fat calories, remainder as carbohydrate +				/ / N	
	SECRET	Age years (mean SD)	66±5*	exercise	-	6MWT (feet) Intervention: +281; Control: +27	Weight (kg) Intervention: -16; Control: 0	BNP (pg/ml) Intervention: +4; Control: +5.	-
	SECKET	Female (%)	81						
	Randomised controlled, parallel	NYHA II (%)	60	<b>Control intervention:</b> 140 days of either diet alone, exercise alone, attention control					
	group trial	NYHA III (%)	40						
		п	20						
	Eggebeen <i>et al.</i> 2016 (46)	HFpEF (%)	100	Intervention: 7 day consumption of					
ATE		Other key inclusion criteria	Exercise Intolerance	70ml bottle of beetroot juice (6.1 mmol nitrate).		VO <sub>2</sub> Peak			
INORGANIC NITRATE	NA	Age years (mean SD)	69±7		-	(ml/kg/min) Intervention: 0;	-	-	-
RGANI	NA	Female (%)	85			Control: 0, p=0.79			
NI	Randomized	NYHA II (%)	70	Control: Identical nitrate-depleted placebo					
	controlled, crossover trial	NYHA III (%)	30						
	Shaltout <i>et al.</i> 2017 (47)	n	20	Intervention: 28 days of 70ml bottle of beetroot juice (6.1 mmol nitrate)	-	Vo₂ Peak (ml/kg/min)	-	-	-

	NA Randomised controlled, parallel group trial	HFpEF (%) Other key inclusion criteria Age years (mean SD) Female (%) NYHA II (%)	100 Exercise Intolerance 69±7* 84 68 31	consumed 3 x week plus exercise 3 x per week. Control: 28 days of matched placebo plus exercise 3 x week	-	Intervention: 0; Control: -0.1; p=0.89			
		n	20						
	Zamani <i>et al.</i> 2015 (48)	HFpEF (%)	100	Intervention: One dose of beetroot					
		Other key inclusion criteria	None	juice containing 12.9 mmols nitrate consumed before exercise testing		Vo₂ Peak (ml/kg/min)			
	NA	Age years (mean SD)	66±9		-	Difference between groups	-	-	-
	NA	Female (%)	12			0.1; p=0.005			
	Randomized controlled,	NYHA II (%)	71	Control: Identical nitrate-depleted placebo					
	crossover trial	NYHA III (%)	24						
		n	420	_					
	Mortensen <i>et al.</i> 2014 (49)	HFpEF (%)	7	Intervention: 730 days of CoQ10 100					
5		Other key inclusion criteria	none	mg 3 times daily.	Ejection Fraction				
ıentati	Q-SYMBIO	Age years (mean SD)	62±11*		(%) Intervention: +4;	-	-	-	-
uppler		Female (%)	27		Control: 2				
CoQ10 Supplementation	Randomised controlled, parallel	NYHA II (%)	3	Control: Matched placebo					
0	group trial	NYHA III (%)	87						
	Sobirin <i>et al.</i> 2019	п	30	Intervention: 30 days of CoQ10 100 mg	Ejection Fraction (%)	-	-	-	
	(50)	HFpEF (%)	100	three times a day.	Intervention: +1; Control: -1; p=0.73				

		Other key inclusion criteria	None						
		Age years (mean SD)	62±8						
	NA	Female (%)	50						
	Randomised	NYHA II (%)	NR	Control: usual care					
	controlled, parallel group trial	NYHA III (%)	NR						
		п	88						
5	Gonzales Islas <i>et al.</i> 2017 (53)	HFpEF (%)	18	Intervention: individualised normocaloric diet with low % of energy	Systolic BP (mmHg)	Weight (kg)			
Carbohydrate Restriction		Other key inclusion criteria	none	from carbohydrate (40% carbohydrates, 20% protein, 40% fat)					
drate Re	NA	Age years (mean SD)	69±12		Intervention: -4.9; Control: -1;	Intervention: -6.3; Control: +2.6;	-	-	-
Irbohyd	NA	Female (%)	60	Control: individualised normocaloric	p=0.385.	p=0.145			
ů	Randomised controlled, parallel	NYHA II (%)	22	diet with normal % of energy from carbohydrate (carbohydrate 50%, 20%					
	group trial	NYHA III (%)	8	protein, 30% fat)					
Abbrevia	tions	(KCCQ); Millimoles (mr	nol), Minnesota Liv	<ul> <li>All), Dietary Approaches to Stop Hypertensio ing with Heart Failure Questionnaire (MLWH ), Six minute walk test distance (6MWD)</li> </ul>			· · /·		
Symbols				d by group only, these were combined using e median was treated as the mean and stan	•		• •	commended by Cochra	ne, Chapter 6 (28).

# **1.3** Forest plots showing the effects of dietary interventions on QoL outcomes in HFpEF:

	Interve	Intion		Con	trol			Standard	ised Mean Difference		R	sk	of B	las	Ass	<b>e</b> 55	mer
DASH & GoL	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% Ci	D1	D2	03	D4	D		D7	0
Rifai et al. 2015	-21	15	24	-39	22	24	47.2%		0.94 [0.34, 1.54]		•			•		1	
Hummel et al. 2018	59	20	30	53	24	30	52.8%	-	0.27 [-0.24, 0.78]	2	•	•	•	•	•	2	•
Total (95% CI)			54			54	100.0%	-05 1 2	0.59 [-0.07, 1.24]								
RE Model (df = 1; 1 <sup>2</sup> = 64	.6%, P1 = -	0.41, 1.6	5)				Favou	and the second second	ntervention								
	Interve	Intion		Con	trol			Standard	ised Mean Difference		R	isk)	of B	lias	Ast	ess	me
Salt Restriction & QoL	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1	D2	D3	D4	D	5 De	07	0
Sal Restriction & Goc	mean	30											-	-	_	_	
	4.1	1.9	17	4.5	1.7	13	10.9%		-0.21 [-0.94, 0.51]					2		1 2	
Philpson et al. 2010	0050000 2000	1000		4.5 4.3	1.7	13 45	10.9% 33.5%	-	-0.21 [-0.94, 0.51] -0.05 [-0.47, 0.36]				:	2		2	e
Philipson et al. 2010 Philipson et al. 2013	4.1	1.9	17	1000	- 30	- 100	22.53										
Philipson et al. 2010 Philipson et al. 2013 Colin-Raminez et al. 2015	4.1 4.25	1.9 1	17 45	43	0.9	45	33.5%	-	-0.05 [-0.47, 0.36]							2 2 2	
Philpson et al. 2010 Philpson et al. 2013 Coln-Ramirez et al. 2015 Coln-Ramirez et al. 2004	4.1 4.25 64.6	1.9 1 26.5	17 45 19	43 72.4	0.9 16.7	45 19	33.5% 14.0%	+	-0.05 [-0.47, 0.36] -0.34 [-0.99, 0.30]	0 0 2 2						3	
Philipson et al. 2010 Philipson et al. 2013 Colin-Ramirez et al. 2015 Colin-Ramirez et al. 2014 Hummel et al. 2018 Total (95% CI)	4.1 4.25 64.6 628.1	1.9 1 26.5 99.4	17 45 19 27	4.3 72.4 599.3	0.9 16.7 128.3	45 19 31	33.5% 14.0% 21.4%		-0.05 [-0.47, 0.36] -0.34 [-0.99, 0.30] 0.25 [-0.27, 0.76]	0 0 2 7						3 3 3 3 3	

# 1.4 Forest plots showing the effects of dietary interventions on haemodynamic outcomes in HFpEF

		ention .		Con	201				Mean Difference	Risk of Bias Assessment
Salt Restriction & SEP	Mean	so	n	Mean	SD	n	Weight		N, Random, 95% Cl	D1 02 03 D4 D5 D6 D7 O
Philipson et al. 2010	125	22	17	125	25.5	13	31.0%		0.00 [-17.36, 17.36]	
Hummel et al. 2018	121	19	24	123	22	24	69.0%		-2.00(-13.63, 9.63)	
Total (95% CI)			41			37	100.0%	-20 0 10 20	-1.38 [-11.04, 8.28]	
RE Model (df = 1; t <sup>2</sup> = 0)	0%, P1 = -	11, 8.3)					Favours inte		Favours control	
	Interv	ention		Con	trol				Mean Difference	Risk of Bias Assessment
Protein & SBP	Mean	50	•	Mean	SD	•	Weight		N, Random, 95% Cl	D1 D2 D3 D4 D5 D6 D7 O
Evangelista et al. 2021	112.5	10	33	117.5	15.7	0	71.1%		-5.00 [-11.18, 1.18]	
Pineda-Juarez et al. 2015	117.6	18.1	29	126.2	23.2	26	22.1%	+	-8.60 (-19.69, 2.49)	
Azhar et al. 2020	120.1	20.7	5	116.2	10.4	6	6.8%		3.90 [-16.06, 23.86]	*******
Total (95% CI)			67			75	100.0%	-20 0 20	-5.19 [-10.40, 0.02]	
RE Model (df = 2, t <sup>2</sup> = 0.	0%, PI = -	10, 0.024	9				Favours interve		avours control	
	Interve	ntion		Cont	lion				Mean Difference	Risk of Bias Assessment
CNO restriction & SBP	Mean	SD	n	Mean	SD	n	Weight		N. Random, 95% CI	D1 02 03 D4 05 D6 07 0
Evangelista et al. 2021	112.5	11.0	33	117.5	15.7	40	67.4%		-5.00[-11.18, 1.18]	
Concalec-Islas et al. 2017	118.6	19.8	32	125.5	16.6	33	32.6%		-6.90 [-15.80, 2.00]	
Total (95% CI)			65			76	100.0%	20 -5 5	-5.62 [-10.70, -0.54]	
Total (95% CI) RE Model (3t = 1; 1 <sup>2</sup> = 0.0	nk, Pi = −1	1, -0.54)						20 -5 5 Favours	control	
	fis, Pi = -1 Interve			Con	troi		11			Risk of Bias Assessment
RE Model (st = 1; t <sup>2</sup> = 0.0				Con Mean	trol SD		11		control	Risk of Bias Assessment D1 D2 D3 D4 D5 D6 D7 O
	Interve	ention					Favours intervention		control Mean Difference	
RE Model (df = 1; P <sup>2</sup> = 0.0 Calorie restriction & \$80P Evangelista et al. 2021	Interve Mean	sD	n	Mean	SD	n	- Favours intervention Weight	Favours	eorod Mean Difference N; Random, 95% Cl	
RE Model (df = 1; i <sup>2</sup> = 0.0 Calorie restriction & SBP	Interve Mean	sD	n 33	Mean	5D	n 43	Favours intervention Weight 65.9%	Favours	Nean Difference NC Random, 95% Cl -5.00 [-11.18, 1.18]	
RE Model (df = 1; F <sup>2</sup> = 0.0 Catorie restriction & \$BP Exangeinta et al. 2021 Coccu & Chu 2007	Interve Mean 112.5 182	tt.8	n 33 30	Mean	5D	n 43 24	Favours intervention Weight 05.9% 34.1%	Failura 	corool Mean Difference Ri, Raedon, 95% Cl -5.00 [-11.18, 1.18] -8.00 [-15.58, 0.50] -6.02 [-11.04, -1.00]	
RE Model (df = 1; i <sup>2</sup> = 0.0 Calorie restriction & SBP Evangelista et al. 2021 Caccu & Chu 2007 Total (85% CI)	Interve Mean 112.5 182	111)	n 33 30	Mean	SD 15.7 18	n 43 24	Favours intervention Weight 65.9% 34.1% 100.0%	Fators	corool Mean Difference Ri, Raedon, 95% Cl -5.00 [-11.18, 1.18] -8.00 [-15.58, 0.50] -6.02 [-11.04, -1.00]	D1 D2 D3 D4 D5 D6 D7 O
RE Model (df = 1; t <sup>2</sup> = 0.0 Calorie restriction & SEP Evargetista et al. 2021 Coccu & Chu 2007 Total (85% Cl) RE Model (df = 1; t <sup>2</sup> = 0.1	Interve Mean 112.5 182 0%, P( = -	111)	n 33 30	Mean 117.5 190	SD 15.7 18	n 43 24	Favours intervention Weight 65.9% 34.1% 100.0%	Fators	control Mean Difference N, Raedon, 19% CI -5.00 [-11 18, 1 18] -6.00 [-55.56, 0.56] -6.02 [-11.04, -1.00] s control	D1 D2 D3 D4 D5 D6 D7 O
RE Model (df = 1; I <sup>2</sup> = 0.0 Calorie restriction & SBP Evangelista et al. 2021 Caccu & Chu 2007 Total (85% CI)	Interve Mean 112.5 182 0%, PI = -	tt.8 11.1 111)	n 33 30	Mean 117.5 190	5D 15.7 18 0701	n 43 24 67	Favours intervention Weight 65.9% 34.1% 100.0% Favours intervents	Fators	corrol Mean Difference N, Raedon, 95% Cl -5.00 (-11.18, 1.18) -8.00 (-16.56, 0.50) -6.02 (-11.04, -1.00) i. control Mean Difference	Risk of Bias Assessment
RE Model (df = 1; l <sup>2</sup> = 0.0 Calore restriction & SBP Evargelista et al. 2021 Coccu & Chu 2007 Total (85% CI) RE Model (df = 1; l <sup>2</sup> = 0.1 Cocte & EF	Interv Mean 112.5 182 0%, PI = - Interv Mean	tt.8 tt.8 tt.1 tt.1 tt.1 tt.1 tt.1 tt.1	n 33 30 63	Mean 117.5 110 Con Mean	5D 15.7 18 5D	n 43 24 67	Favours intervention Weight 65.5% 34.1% 100.0% Favours interventio Weight	Faxour	corrol Mean Difference R(, Raedon, 95% Cl -5.00 [-11.18, 1.18] -8.00 [-15.58, 0.50] -6.02 [-11.04, -1.00] i control Mean Difference R(, Raedon, 95% Cl	D1 D2 D3 D4 D5 D4 D7 O
RE Model (df = 1; l <sup>2</sup> = 0.0 Calore restriction & SBP Evargelista et al. 2021 Caccu & Chu 2007 Total (85% CI) RE Model (df = 1; l <sup>2</sup> = 0.1 Co210 & EF	Interv Mean 112.5 182 0%, PI = - Interv Mean 35	tt.8 tt.1 tt.1 tt.1 tt.1 tt.1 tt.1 tt.1	n 33 30 63 n	Mean 117.5 110 Con Mean 33	50 15.7 18 50 11	n 43 24 67 8	Favours intervention Weight 65.9% 34.1% 100.0% Favours interventi Weight 64.5%	Faxour	corrol Mean Difference R(, Raedon, 95% Cl -5.00 [-11.18, 1.18] -8.00 [-15.59, 0.50] -6.02 [-11.04, -1.00] is control Mean Difference R(, Raedon, 95% Cl 2.00 [-0.39, 4.38]	D1 D2 D3 D4 D5 D4 D7 O

# 1.5 Forest plots showing effects of dietary interventions of anthropometric outcomes

	Interve	ention		Cont	rol				Mean Difference	Risk of Bias Assessment
Salt restriction & weight	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Philipson et al. 2010	84	18.5	17	83	16	13	14.2%		1.00 [-11.37, 13.37]	
Philipson et al. 2013	83	16	45	83	17	45	46.7%	_ <b>+</b> _	0.00 [ -6.82, 6.82]	
Colin-Ramirez et al. 2004	63.4	15.9	27	67.5	12.6	31	39.1%		-4.10 [-11.56, 3.36]	? • ? • ? • • •
Total (95% CI)			89			89	100.0%		-1.46 [-6.12, 3.20]	
RE Model (df = 2; l <sup>2</sup> = 0.0	)%, PI = -(	6.1, 3.2)					Favours inter-		15 avours control	
	Interve	ention		Cont	rol				Mean Difference	Risk of Bias Assessment
CHO restriction & weight	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Evangelista et al. 2021	101.9	21.7	33	106.8	18.2	43	69.7%		-4.90 [-14.09, 4.29]	
Gonzalez-Islas et al. 2017	86.1	27	29	88.3	28.9	33	30.3%		-2.20 [-16.12, 11.72]	••••••
Total (95% CI)			62			76	100.0%	-20 -5 5 19	-4.08 [-11.75, 3.59]	
RE Model (df = 1; I <sup>2</sup> = 0.0	%, PI = -1	12, 3.6)					Favours	intervention	Favours control	
	Interve	Intion		Cont	rol				Mean Difference	Risk of Bias Assessment
Calorie restriction & Weigh	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% Cl	D1 D2 D3 D4 D5 D6 D7 O
Evangelista et al. 2021	101.9	21.7	33	106.8	18.2	43	3.1%		-4.90 [-14.09, 4.29]	
Cocco & Chu 2007	101	5.5	30	108	4.5	24	36.9%	•	-7.00 [ -9.67, -4.33]	$\bullet \bullet \bullet \bullet \circ \bullet \bullet \bullet \bullet$
Kitzman et al. 2016	97	6.5	46	104	3.2	46	60.0%	•	-7.00 [ -9.09, -4.91]	•••••
Total (95% CI)			109			113	100.0%	-15 -5 5	-6.93 [-8.56, -5.31]	
RE Model (df = 2; l <sup>2</sup> = 0.0	%, P1 = -8	3.6, -5.3)					Favours interve		uns control	
	Interve	ention		Cont	rol				Mean Difference	Risk of Bias Assessment
Protein & BMI	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Evangelista et al. 2021	34.7	6.9	33	36.3	5.3	43	52.6%		-1.60 [-4.44, 1.24]	
Pineda-Juarez et al. 2016	26.84	5.1	29	28.07	6.1	26	47.4%		-1.23 [-4.22, 1.76]	
						69	100.0%		-1401-240 0 00	
Total (95% CI)			62			63	100.0%	-6 -2 2	-1.42 [-3.48, 0.63]	

# 1.6 Forest plots showing effects of effects of dietary interventions on physical function outcomes

	Interve	ention		Con	trol				Mean Difference	Risk of Bias Assessmen
Caloric Rest. & 6MWD	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Cocco & Chu 2007	251	22	30	225	23	24	87.7%	-	26.00 [13.89, 38.11]	
Kitzman et al. 2016	453	29	46	427	108	46	12.3%		26.00 [-6.32, 58.32]	•••••
Total (95% CI)			76			70	100.0%	-20 20 60	26.00 [14.66, 37.34]	
RE Model (df = 1; I <sup>2</sup> = 0.0	0%, PI = 1	5, 37)					Favo	urs control Favou	rs intervention	
	Interv	ention		Con	trol			Standard	ised Mean Difference	Risk of Bias Assessmen
Protein & function	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Pineda-Juarez et al. 2015	22.56	11.3	29	15.57	11.2	26	83.6%		0.61 [0.07, 1.15]	
Azhar et al. 2020	466.63	125.9	5	370.45	118.5	6	16.4%	+	0.72 [-0.50, 1.95]	•••••
Total (95% CI)			34			32	100.0%	-1 0 1 2	0.63 [0.13, 1.13]	
RE Model (df = 1; I <sup>2</sup> = 0.0	0%, PI = 0	.13, 1.1)					Favours		ours intervention	
	Interve	ention		Con	trol				Mean Difference	Risk of Bias Assessmen
IN & Peak Vo2	Mean	SD	n	Mean	SD	n	Weight		IV, Random, 95% CI	D1 D2 D3 D4 D5 D6 D7 O
Eggebeen et al. 2016	12	2.6	20	12	2.2	20	53.5%	+	0.00 [-1.49, 1.49]	
Shaltout et al. 2017	11.6	3	10	12.2	1.9	9	23.9%	_+_	-0.60 [-2.84, 1.64]	
Zamani et al. 2015	12.6	3.7	17	11.6	3.1	17	22.6%	+	1.00 [-1.29, 3.29]	2 8 8 8 2 8 2 6
Total (95% CI)			47			46	100.0%	-4 0 2	0.08 [-1.01, 1.18]	
RE Model (df = 2; l <sup>2</sup> = 0.0	0%, PI = -	1, 1.2)					Favours		nention	

# 1.7 GRADE assessment

Population Intervention Comparator Outcomes		Patients with study defined HFpEF or likely HFpEF based on inclusion criteria and characteristics reported in study demographics (e.g. studies with mixed HF populations). Dietary interventions (whole food and supplement based manipulation); analysed and presented in 12 sub-groups that were derived based on broad similarity of manipulation component/target. In the case of multiple comparator interventions; the intervention group was defined as the group with the greatest number of active components. Active concurrent control (e.g. different variation of intervention); no treatment concurrent controls; external concurrent control. When studies employed more than one type of control, comparisons were made between interventions and no treatment concurrent control.														
											1	analyses. Outcomes not report	ed due to lack of multiplicity are sum	marised in our scopin	Ĩ	
												Illustrativ	e comparisons	# participants &	Quality of the evidenc (GRADE)	e
										ANALYSIS GROUP	Outcome			studies	High $\oplus \oplus \oplus \oplus$ Moderate $\oplus \oplus \oplus \oplus$	Clarifications of Judgements
	Usual care	Intervention	# participants HFpEF	Low ⊕⊕OC Very Low ⊕OOC												
DASH	QoL Measure: KCCQ Score: 1-100, higher scores represent better QOL Scores 0-24 = very poor to poor health status; 25-49 = poor to fair; 50-74 = fair to good. Measure: MLWHFQ Score: scored in a 6-point Likert Scale (0 to 5), higher scores indicate more impairment. Scores <24 =	Mean KCCQ was 53±24 (fair to good) Mean MLWHFQ was 39±22 (moderate)	Mean KCCQ was 59±20 (fair to good) Mean MLWHFQ was 21±15 (good) There was a 0.59 change (CI:- 0.41, 1.58) in favour of intervention which represents a moderate effect by Cochrane's rule of thumb. Re-expressed as KCCQ this change represents an +11.8 point change (CI: 0.02 to	Participants: 108 Studies: 2 (2, 3) % HFpEF: 24% (2), 44% (3)	Very Low ⊕OOO	Risk of Bias: both studies assessed to be at high risk of bias, level of evidence downgraded 1 level.         Inconsistency: I <sup>2</sup> 64.6%, PI = -0.41 to 1.6 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level.         Indirectness: No indirectness. Not downgraded         Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.										
SALT	good QoL; 24-45 = moderate QoL; >45 = poor QoL. Systolic blood pressure (SBP) Measured in mmHg via	Mean SBP was 125±25.5 and 123±24	24.8). Mean SBP was: 125±17 and 121±19. There was a -1.38 mmHg change in BP in favour of intervention. A	Participants: 78 Studies: 2 (2, 5)	- Very Low ⊕000	Risk of Bias: both studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI = -0.11 to 8.3 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level. Indirectness: No indirectness. Not										
validated methods.		change of ≥5mmHg is associated with significant risk reduction in CVD (4).	% HFpEF: 24% (2), unclear (5)		Imprecision: the CI includes both meaningf benefit and no meaningful effect. Downgraded 1 level.											

	Weight Measured in kg using validated methods.	Mean weight was 83±16, 83±17, 67.5±12.6. Difference of 15.5kg between studies.	Mean weight was 84±18.5, 83±16, 63.4±15.9. Difference of 21 kg. There was a -1.46kg change in favour of intervention. Weight loss of 5-10% improves cardiovascular risk factors in those with established metabolic disease (6). 5% weight loss in the intervention group based on mean would be: 4.25, 4.25, 3.195 kg for studies in review.	Participants: 178 Studies: 3 % HFpEF: unclear (5), 23% (7), 37% (8)	Very Low ⊕OOO	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI = -6.1 to 3.2 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level Indirectness: No indirectness. Not downgraded. Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.
	QoL Measure: KCCQ Score: 1-100, higher scores represent better QOL Scores 0-24 = very poor to poor health status; 25-49 = poor to fair; 50-74 = fair to good.	Mean QoL score was: 4.1±1.7, 4.3±0.9, 16.7±19, 599.3±128.3, 53±24. KCCQ: 53±254 = fair to good; 72.4±16.7 = fair to good. No scales to judge other measures	Mean QoL score was: 4.1±1.9, 4.25±1, 64.6±26.5, 628.1±99.4, 59±20. KCCQ: 59±2.0=fair to good. 64.6 = fair to good. Change of 0.02 (CI: -0.22 to 0.26)	Participants: 271 Studies: 5	Very Low ⊕000	Risk of Bias: five studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI =0.22,0.26 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level Indirectness: No indirectness. Not
	Measure: modified KCCQ Measure: bespoke (0-7 with 7 representing higher scores)		which by Cochrane rule of thumb equals a small effect. Re- expressed as KCCQ this change represents a 0.4 point change (CI: -4.4 to 5.2).	% HFpEF: unclear (5), 23% (7), 37% (8), unclear (9), 24% (2).		downgraded Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.
	BMI Measured in kg/m2 using	Mean BMI was: 36.3±5.3, 28.07±61. Difference in categories	Mean BMI was: 34.7±6.9, 26.84±5.1. Difference in categories across studies obese and overweight.	Participants: 131 Studies: 2	Very Low ⊕000	Risk of Bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI =0.3.5, 0.63 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level
PROTEIN	validated methods.	across studies obese and overweight.	Change of -1.42 kg/m2 favouring intervention, 95% CI -3.48 to 0.63.	% HFpEF: 43% (10), 6% (11)	downgraded Imprecision: the CI includes both	Imprecision: the CI includes both meaningful benefit and no meaningful effect.
TROTEIN	Systolic blood pressure. Measured in mmHg via	Mean SBP was: 117.5±15.7, 126.2±23.2, 116.2±10.4,	Mean SBP was: 112.5±11.8, 117.6±18.1, 120.1±20.7, Change of -5.19mmHg (CI-10.4 to 0.02) .A change of ≥5mmHg is	Participants: 142 Studies: 3	Very Low ⊕000	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI =0.10, 0.02 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level.
	validated methods.		associated with significant risk reduction in CVD (4).	% HFpEF: 43% (10), 6% (11), 100% (12).		Indirectness: No indirectness. Not downgraded Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.

<b></b>			Mean Vo2 peak: 22.56±11.3			Risk of Bias: two studies assessed to be at
			Difference of 7ml/kg/litre	Participants: 66		high risk of bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
			between intervention and			Inconsistency: I <sup>2</sup> 0%, PI = 0.13 to 1.13
			control.	Studies: 2		demonstrating consistency in the direction
						and size of the effect estimate. Not
	Function		Mean 6MWTD: 466±125			downgraded.
		Mean VO2 peak: 15.57±11.2				Indirectness: No indirectness. Not
	Measures: VO2 peak	ml/kg/min.	Difference of 96 meters between intervention and control.			downgraded
	measured in ml/kg/min via	1117 Kg/ 1111.				Imprecision: the CI includes the potential for
	validated methods.				Moderate $\oplus \oplus \oplus \bigcirc$	meaningful benefit, not downgraded.
		Mean 6MWTD: 370±118	Change of 0.63 favouring			
	Measure: 6MWT distance	meters	intervention, 95% CI 0.13 to 1.13,			
	measured in meters via		which by Cochrane's rule of	% HFpEF: 6%		
	validated methods.		thumb equals a moderate effect.	(11), 100% (12).		
			Re-expressed as Vo2 peak this change represents an +7.12			
			ml/kg/min change (CI: 1.47 to			
			12.78). A change of 1 ml/kg/min			
			is accepted as a clinically			
			meaningful threshold .			
			Mean weight: 101.9±21.7,			Risk of Bias: three studies assessed to be at
		Mean weight: 106.8±18.2, 108±4.5, 105±4.84	101±5.5, 99±4.73			high risk of bias, level of evidence
				Participants: 222		downgraded 1 level.
	Weight. Measured in kg using validated methods.		Change of -6.93 favouring	Studies: 3		Inconsistency: I <sup>2</sup> 0%, PI =8.3, -4.6.
			intervention, 95% CI -8.56 to -	Studies: 5		Direction of effect consistent. Not
			5.31. Weight loss of 5-10%			downgraded.
			improves cardiovascular risk		Moderate $\oplus \oplus \oplus \bigcirc$	Indirectness: No indirectness. Not
			factors in those with established			downgraded
			metabolic disease (6). 5% weight	% HFpEF: 45%		Imprecision: the CI includes the potential for
			loss in the intervention group	(10), 100% (13),		meaningful benefit, not downgraded.
			based on mean would be: 5.275,	100% (14)		
			5.4, 5.25 kg for studies in the review.			
			Mean SPB: 112.5±11.8, 182±13.1.			Risk of Bias: two studies assessed to be at
				Participants: 130		high risk of bias, level of evidence
CALORIE		Mean SBP: 117.5±15.7, 190±18	Difference between studies in	Farticipants. 150		downgraded 1 level.
RESTR.	Systolic blood pressure.		degree of hypertension across	Studies: 2		Inconsistency: I <sup>2</sup> 0%, PI =11, -1. Direction
-			studies. Normotensive and			of effect consistent. Not downgraded.
		Difference between studies	severely hypertensive		Moderate $\oplus \oplus \oplus \bigcirc$	Indirectness: No indirectness. Not
	Measured in mmHg via	in degree of hypertension				downgraded
	validated methods.	across studies. Normotensive	Change: -6.02 mmHg favouring	% HFpEF: 45%		Imprecision: the CI includes the potential for
		and severely hypertensive	intervention (CI: -11.04 to -1.00).	(10), 100% (13).		meaningful benefit, not downgraded.
		and severely hypertensive	A change of ≥5mmHg is	(10), 100/0 (13).		
			associated with significant risk			
			reduction in CVD (4).			Dials of Diago have shading a second to be a
		Mean 6MWTD: 225±23,	Mean 6MWTD: 251±22, 453±29.	Dortioincate: 140		Risk of Bias: two studies assessed to be at high risk of bias, level of evidence
	6MWT distance.	418±64.9.	Differences between studies in	Participants: 146		downgraded 1 level.
		Differences between studies	degree of impairment based on	Studies: 2	Moderate $\oplus \oplus \oplus \bigcirc$	Inconsistency: I <sup>2</sup> 0%. Direction of effect
	Measured in meters via	in degree of impairment	6MWTD means (202 meters	Studies. Z		consistent.
	validated methods.	based on 6MWTD means	difference).	% HFpEF: 100%	1	Indirectness: No indirectness. Not
		(193.2 meters difference).		(13), 100% (14)		downgraded.
		(19972 meters unterence).		(13), 100/0 (14)		uowngruueu.

	Systolic blood pressure. Measured in mmHg via	Mean: 117.5±15.7, 125.5±16.6.	Change: 26 meters (CI: 14.66-to 37.346). A change of ≥30 meters has been established as clinically meaningful (15) Mean 112.5±11.8, 118.6±19.8. Change: -5.62 (CI: -10.70, -0.54) A change of ≥5mmHg is	Participants: 141 Studies: 2	Moderate⊕⊕⊕O	Imprecision: the CI includes the potential for meaningful benefit, not downgraded.Imprecision: the CI includes both meaningful benefit and no meaningful effect.Downgraded 1 level.Risk of Bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level.Inconsistency: I² 0%, PI = -11, -0.54 Direction of effect consistent. Not downgradedIndirectness: No indirectness. Not
	validated methods.		associated with significant risk reduction in CVD (4)	% HFpEF: 43% (10), 18% (16)		downgraded Imprecision: the CI includes the potential for meaningful benefit, not downgraded.
CARB.	Weight.	Mean: 108.8±18.2, 88.3±28.9.	Mean: 101.9±21.7, 86.1±27. Difference of 15.8 kg between studies. Change-4.08 (CI: -11.75, 3.59). Weight loss of 5-10% improves	Participants: 138 Studies: 2	Very Low ⊕000	Risk of Bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI =12, 3.6 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level
	Measured in kg using validated methods.	Difference of 18.5 kg between studies	cardiovascular risk factors in those with established metabolic disease (6). 5% weight loss in the intervention group based on mean would be: 5.275, 4.62 kg	% HFpEF: 43% (10), 18% (16)		Indirectness: No indirectness. Not downgraded Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.
IN	Function Measures: VO2 peak measured in ml/kg/min via	Mean: 12±2.2, 12.2±1.9, 11.6±3.1	Mean: 12±2.6, 11.6±3, 12.6±3.7. Change: 0.08 (CI: -1.01, 1.18). A change of 1.0 ml/kg/min is	Participants: 93 Studies: 3	Very Low ⊕000	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI = -1, 1.2 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level
	validated methods.		accepted as a clinically meaningful threshold .	% HFpEF: 100% (17), 100% (18), (19)		Indirectness: No indirectness. Not downgraded Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.
COQ10	Ejection Fraction Measured in % via validated	Mean: 33±11, 57±7	Mean: 35±10, 56±8.	Participants: 326 Studies: 2	Very Low ⊕000	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level. Inconsistency: I <sup>2</sup> 0%, PI = -0.66, 3.7 demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level
	methods.		Change: 1.53 (CI: -0.66, 3.73).	% HFpEF: 7% (20), 100% (21)		Indirectness: No indirectness. Not downgraded Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.

# 1.8 Visual Summary

Q	$\mathbf{Y}$	$\bigcirc$		\$ 2 2 5	
Search: 5 databases 12875 records	Screening: 12723 excluded 134 Full text reviews	Inclusion: 31 reports of 25 studies	Extraction: PICO & 5 outcome domains	Meta-analysis: 17 studies	
Quality of Life	Heart Failure Status	Haemodynamic	Anthropometric	Physical Function	ĭ ≍=
CMI = ≥5 point increase in QoL score	CMI = ↓ NYHA Class, ↓NPs	CMI = ≥5mmHg decrease in systolic BP ↓NA+ ⊕OOO	CMI = weight loss≥ 5% of body weight/ decrease in BMI	CMI = ≥ 30 meters in 6MWD / ≥1 ml/kg/min VO <sub>2</sub> Peak	Results & GRADE
<b>↓NA⁺⊕OOO</b> No evidence of CMI	DASH No superiority in improving NPs	No evidence of CMI $\uparrow$ PRO $\oplus$ OOO	<b>↓NA⁺⊕OOO</b> No evidence of CMI	↓Kcal ⊕⊕⊕О	assessment
DASH ⊕OOO	↓NA+	Possibility for CMI	<b>↑</b> PRO ⊕000	No evidence of CMI	
Possibility for CMI	Superior at improving NPs (n=1); no superiority (n=2)	<b>↓Kcal ⊕⊕⊕</b> О Possibility for CMI <b>↓CHO ⊕⊕⊕</b> О	Possibility for CMI $\psi$ CHO $\oplus$ OOO No evidence of CMI	↑ PRO ⊕⊕⊕O Possibility for CMI ↑ IN ⊕OOO	
	Superior at improving NYHA class (n=2); no superiority (n=1)	Possibility for CMI	<b>↓Kcal ⊕⊕⊕О</b> Possibility for CMI	No evidence of CMI	

Blood pressure (BP); Clinically meaningful improvement (CMI); Natriuretic Peptides (NPs); six-minute walk test distance (6MWD). Evidence quality: High  $\oplus \oplus \oplus \oplus$ ; Moderate  $\oplus \oplus \oplus \odot$ ; Low  $\oplus \oplus \odot \odot$ ; very low  $\oplus \odot \odot \odot$