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# OUTCOMES OF DIETARY INTERVENTIONS IN HFPEF

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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 insuffienc\*)) 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 kalori\* 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"

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**Embase** 1974 to 2019 August 02

- 1 (chf or hfpef or "preserved ejection fraction" or ((cardia\* or myocardial or heart) adj (failure or insuffienc\*)) 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 kalori\* 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"

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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
S8	(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 "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 kalori\* or high-calori\* or low-calori\*)

S6 S4 OR S5 Search modes - Boolean/Phrase

(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")

S5 Search modes - Boolean/Phrase

(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\*)

S4 Search modes - Boolean/Phrase

S3 S1 OR S2 Search modes - Boolean/Phrase

S2 (MH "Heart Failure+") Search modes - Boolean/Phrase

(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\*)))

S1 Search modes - Boolean/Phrase

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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/

1. (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 kalori\* 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, Design	Population		Intervention & Control	Outcomes (change between baseline and follow-up unless otherwise stated)				
					Haemodynamic	Function	Anthropometric	HF Status	Quality of Life
DASH	Hummel <i>et al.</i> 2018 (33)  GOURMET HFpEF  Randomised controlled, parallel group trial	<i>n</i>	66	<b>Intervention:</b> 28 days of prepared food matching the DASH eating pattern nutritional content (carbohydrate: 55%, protein: 20%, fat: 30%) with daily sodium intake of 50 mmol (1150 mg)/2100 kcal  <b>Control:</b> usual care	Systolic BP (mmHg) Intervention: -5; Control: 0; p=0.46	-	-	BNP (log transformed) Intervention: +56; Control: +82; p=0.59	KCCQ Summary Score (points) Intervention: +13; Control: +10; p=0.46
		HFpEF (%)	24						
		Other key inclusion criteria	Hypertension						
		Age years (mean SD)	71±8						
		Female (%)	30						
		NYHA II (%)	NR						
	NYHA III (%)	NR							
	Rifai <i>et al.</i> 2015 (34)  NA  Randomised controlled, parallel group trial	<i>n</i>	48	<b>Intervention:</b> 91 days of personalised DASH eating plan and shopping list augmented by in-person and/or bi-weekly phone counselling from dietitian  <b>Control:</b> usual care	-	6MWD (meters) Intervention: +38; Control: -5; p=0.018	-	BNP (pg/ml) Intervention: -8; Control: +61; p=0.081	MLWHFQ (points) Intervention: -8; Control: +1; p=0.006
		HFpEF (%)	44						
		Other key inclusion criteria	None						
		Age years (mean SD)	62±11*						
		Female (%)	39						
NYHA II (%)		23							
NYHA III (%)	52								
SALT REDUCTION	Colin-Ramirez <i>et al.</i> 2004 (35)  NA	<i>n</i>	65	<b>Dose:</b> 182 days of individualised diets (carbohydrate: 50-55%, protein: 15-20%, fat: 25-35%) with salt restricted to 2.0-2.4 grams/day and fluid restricted to 1.5L/day  <b>Control:</b> usual care	-	BMI (kg/m <sup>2</sup> ) Intervention: -0.4; Control: -0.1; p=not significant	Weight (kg) Intervention: -0.5; Control: -0.1, p=not significant.	NYHA I/ II/III (n) Intervention: +15/-4/-15.1; Control: -7.8/-10.6/+2.8	Bespoke HF questionnaire Intervention: +19.3%, Control: +3.2%; p=0.02
		HFpEF (%)	37						
		Other key inclusion criteria	None						
		Age years (mean SD)	62±16*						
	Female (%)	64							

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

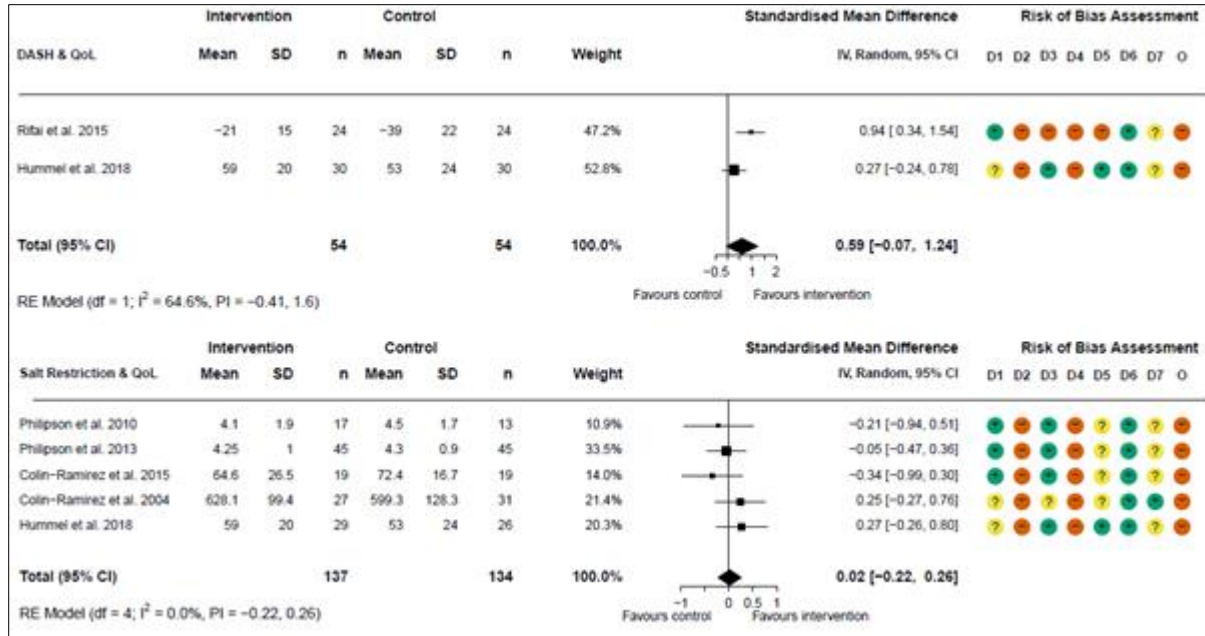
	Randomised controlled, parallel group trial	NYHA III (%)	73								
PROTEIN MANIPULATION	Evangelista <i>et al.</i> 2021 (39)	<i>n</i>	76	Intervention: 91 days of a high protein, hypocaloric diet (30% protein, 40% carbohydrates, 30% fat)	Systolic BP (mmHg) Intervention: -10.8; Control: +0.7; p=0.001	-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

CALORIC RESTRICTION	Cocco & Chu 2007 (42)	<i>n</i>	70	<b>Intervention:</b> 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 significant	6MWD (meters) Intervention: +26; Control: 0; p<<0.000002	BMI (kg/m <sup>2</sup> ) Intervention: -2; Control: 0; p<<0.0001	NTproBNP (pg/ml) Intervention: -368; Control: 0; p=0.00005	-
		HFpEF (%)	100						
		Other key inclusion criteria	Hypertension, High BMI						
		Age years (mean SD)	NR						
		Female (%)	NR						
		NYHA II (%)	NR						
	Non-randomised, controlled study	NYHA III (%)	NR	<b>Control:</b> usual care					
	Kitzman <i>et al.</i> 2016 (29)	<i>n</i>	100	<b>Intervention:</b> 140 days of meal provision approach aiming for a calorie deficit of 350-400 kcal/day. Macronutrients: 1.2 g of protein/kg ideal body weight, 25% to 30% fat calories, remainder as carbohydrate + exercise	-	6MWT (feet) Intervention: +281; Control: +27	Weight (kg) Intervention: -16; Control: 0	BNP (pg/ml) Intervention: +4; Control: +5.	-
		HFpEF (%)	100						
		Other key inclusion criteria	High BMI						
		Age years (mean SD)	66±5*						
Female (%)		81							
NYHA II (%)		60							
NYHA III (%)		40							
SECRET			<b>Control intervention:</b> 140 days of either diet alone, exercise alone, attention control						
Randomised controlled, parallel group trial									
INORGANIC NITRATE	Eggebeen <i>et al.</i> 2016 (46)	<i>n</i>	20	<b>Intervention:</b> 7 day consumption of 70ml bottle of beetroot juice (6.1 mmol nitrate).	-	VO <sub>2</sub> Peak (ml/kg/min) Intervention: 0; Control: 0, p=0.79	-	-	-
		HFpEF (%)	100						
		Other key inclusion criteria	Exercise Intolerance						
		Age years (mean SD)	69±7						
	NA	Female (%)	85	<b>Control:</b> Identical nitrate-depleted placebo					
		NYHA II (%)	70						
		NYHA III (%)	30						
	Randomized controlled, crossover trial								
Shaltout <i>et al.</i> 2017 (47)	<i>n</i>	20	<b>Intervention:</b> 28 days of 70ml bottle of beetroot juice (6.1 mmol nitrate)	-	Vo <sub>2</sub> Peak (ml/kg/min)	-	-	-	

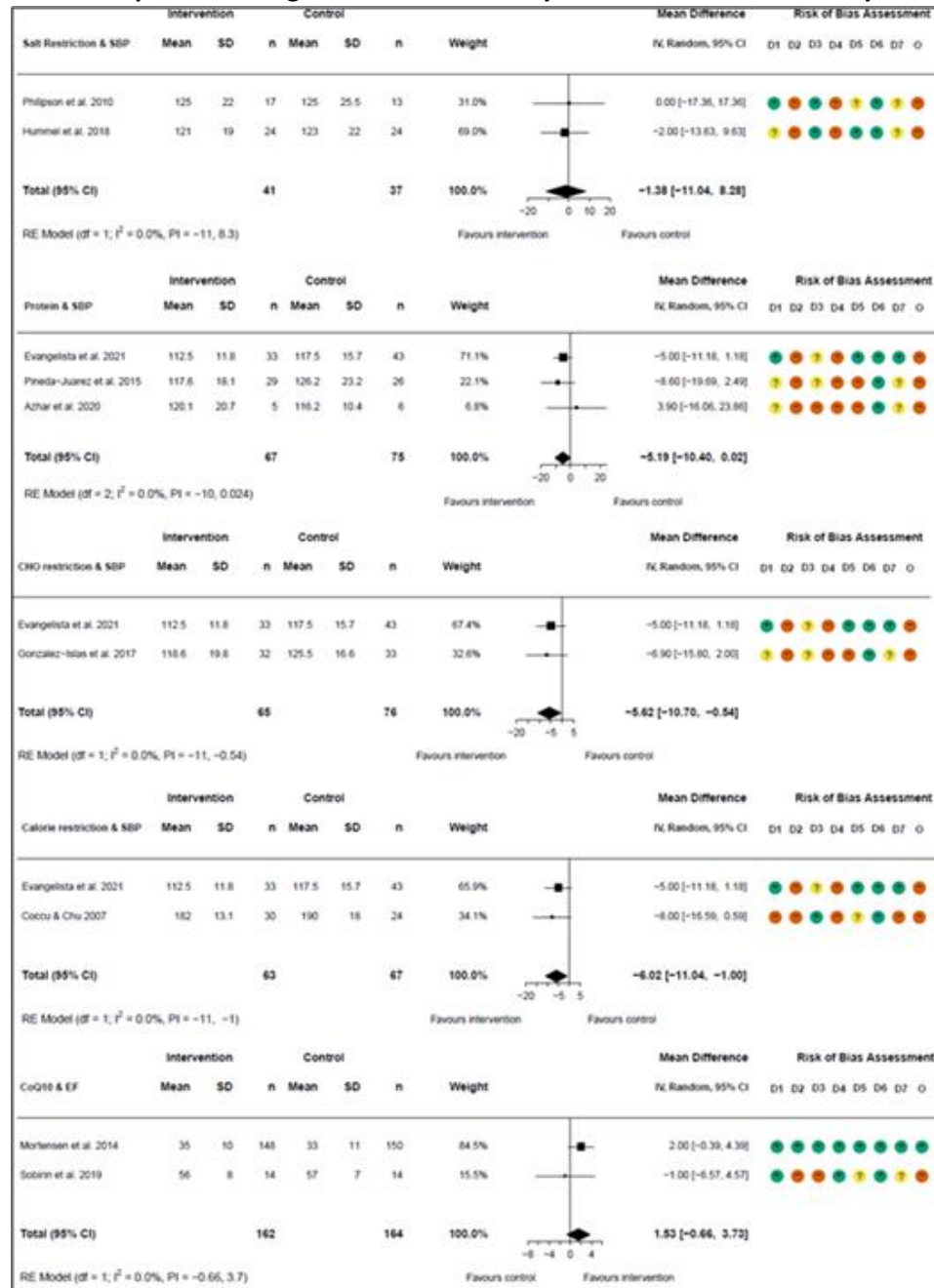
	NA  Randomised controlled, parallel group trial	HFpEF (%)	100	consumed 3 x week plus exercise 3 x per week.		Intervention: 0; Control: -0.1; p=0.89			
		Other key inclusion criteria	Exercise Intolerance						
		Age years (mean SD)	69±7*						
		Female (%)	84	Control: 28 days of matched placebo plus exercise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

	<b>NA</b>  <b>Randomised controlled, parallel group trial</b>	<i>Other key inclusion criteria</i>	<i>None</i>						
		<i>Age years (mean SD)</i>	<i>62±8</i>						
		<i>Female (%)</i>	<i>50</i>	<b>Control:</b> usual care					
		<i>NYHA II (%)</i>	<i>NR</i>						
		<i>NYHA III (%)</i>	<i>NR</i>						
Carbohydrate Restriction	<b>Gonzales Islas et al. 2017 (53)</b>	<i>n</i>	<i>88</i>	<b>Intervention:</b> individualised normocaloric diet with low % of energy from carbohydrate (40% carbohydrates, 20% protein, 40% fat)	Systolic BP (mmHg) Intervention: -4.9; Control: -1; p=0.385.	Weight (kg) Intervention: -6.3; Control: +2.6; p=0.145	-	-	-
		<i>HFpEF (%)</i>	<i>18</i>						
		<i>Other key inclusion criteria</i>	<i>none</i>						
	<b>NA</b>  <b>Randomised controlled, parallel group trial</b>	<i>Age years (mean SD)</i>	<i>69±12</i>	<b>Control:</b> individualised normocaloric diet with normal % of energy from carbohydrate (carbohydrate 50%, 20% protein, 30% fat)					
		<i>Female (%)</i>	<i>60</i>						
		<i>NYHA II (%)</i>	<i>22</i>						
		<i>NYHA III (%)</i>	<i>8</i>						
<b>Abbreviations</b>	Blood pressure (BP), Body Mass Index (BMI), Dietary Approaches to Stop Hypertension (DASH), Heart Failure with preserved Ejection Fraction (HFpEF), Kansas City Cardiomyopathy Questionnaire (KCCQ); Millimoles (mmol), Minnesota Living with Heart Failure Questionnaire (MLWHFQ), Not Reported (NR); N-terminal pro b-type natriuretic peptide (NTproBNP), New York Heart Association Classification (NYHA); Quality of Life (QoL), Six minute walk test distance (6MWD)								
<b>Symbols</b>	*When descriptive statistics were reported by group only, these were combined using the formulae for combining summary statistics across two group recommended by Cochrane, Chapter 6 (28). Where median and IQR were reported, the median was treated as the mean and standard deviations imputed based on the formula $Q3-Q1/1.35$ .								

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



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









## 1.7 GRADE assessment

Outcomes of dietary interventions in patients with HFpEF						
Population		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).				
Intervention		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.				
Comparator		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.				
Outcomes		Outcomes selection was based on multiplicity (evidence driven); however combined outcomes are of interest in HFpEF. Longest follow-up time points were used in analyses. Outcomes not reported due to lack of multiplicity are summarised in our scoping review.				
ANALYSIS GROUP	Outcome	Illustrative comparisons		# participants & studies	Quality of the evidence (GRADE)	Clarifications of Judgements
		Usual care	Intervention	# participants HFpEF	High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very Low ⊕○○○	
DASH	<p>QoL</p> <p>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.</p> <p>Measure: MLWHFQ Score: scored in a 6-point Likert Scale (0 to 5), higher scores indicate more impairment. Scores &lt;24 = good QoL; 24-45 = moderate QoL; &gt;45 = poor QoL.</p>	<p>Mean KCCQ was 53±24 (fair to good)</p> <p>Mean MLWHFQ was 39±22 (moderate)</p>	<p>Mean KCCQ was 59±20 (fair to good)</p> <p>Mean MLWHFQ was 21±15 (good)</p> <p>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 24.8).</p>	Participants: 108	Very Low ⊕○○○	Risk of Bias: both studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 2 (2, 3)		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.
				% HFpEF: 24% (2), 44% (3)		Indirectness: No indirectness. Not downgraded
						Imprecision: the CI includes both meaningful benefit and no meaningful effect. Downgraded 1 level.
SALT	<p>Systolic blood pressure (SBP)</p> <p>Measured in mmHg via validated methods.</p>	<p>Mean SBP was 125±25.5 and 123±24</p>	<p>Mean SBP was: 125±17 and 121±19.</p> <p>There was a -1.38 mmHg change in BP in favour of intervention. A change of ≥5mmHg is associated with significant risk reduction in CVD (4).</p>	Participants: 78	Very Low ⊕○○○	Risk of Bias: both studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 2 (2, 5)		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.
				% HFpEF: 24% (2), unclear (5)		Indirectness: No indirectness. Not downgraded
						Imprecision: the CI includes both meaningful 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 ⊕○○○	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.  Measure: modified KCCQ  Measure: bespoke (0-7 with 7 representing higher scores)	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) 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).	Participants: 271  Studies: 5  % HFpEF: unclear (5), 23% (7), 37% (8), unclear (9), 24% (2).		Very Low ⊕○○○
PROTEIN	BMI  Measured in kg/m2 using validated methods.	Mean BMI was: 36.3±5.3, 28.07±61.  Difference in categories across studies obese and overweight.	Mean BMI was: 34.7±6.9, 26.84±5.1.  Difference in categories across studies obese and overweight.  Change of -1.42 kg/m2 favouring intervention, 95% CI -3.48 to 0.63.	Participants: 131  Studies: 2  % HFpEF: 43% (10), 6% (11)	Very Low ⊕○○○	
	Systolic blood pressure.  Measured in mmHg via validated methods.	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 associated with significant risk reduction in CVD (4).	Participants: 142  Studies: 3  % HFpEF: 43% (10), 6% (11), 100% (12).		Very Low ⊕○○○

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

			Change: 26 meters (CI: 14.66-to 37.346). A change of $\geq 30$ meters has been established as clinically meaningful (15)			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.
CARB.	Systolic blood pressure.  Measured in mmHg via validated methods.	Mean: 117.5 $\pm$ 15.7, 125.5 $\pm$ 16.6.	Mean 112.5 $\pm$ 11.8, 118.6 $\pm$ 19.8.  Change: -5.62 (CI: -10.70, -0.54). . A change of $\geq 5$ mmHg is associated with significant risk reduction in CVD (4)..	Participants: 141	Moderate $\oplus\oplus\oplus\bigcirc$	Risk of Bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 2		Inconsistency: $I^2$ 0%, $PI = -11, -0.54$ Direction of effect consistent. Not downgraded
	% HFpEF: 43% (10), 18% (16)	Indirectness: No indirectness. Not downgraded				
		Imprecision: the CI includes the potential for meaningful benefit, not downgraded.				
CARB.	Weight.  Measured in kg using validated methods.	Mean: 108.8 $\pm$ 18.2, 88.3 $\pm$ 28.9.  Difference of 18.5 kg between studies	Mean: 101.9 $\pm$ 21.7, 86.1 $\pm$ 27.  Difference of 15.8 kg between studies.  Change -4.08 (CI: -11.75, 3.59). 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: 5.275, 4.62 kg	Participants: 138	Very Low $\oplus\bigcirc\bigcirc\bigcirc$	Risk of Bias: two studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 2		Inconsistency: $I^2$ 0%, $PI = -12, 3.6$ demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level..
	% 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 validated methods.	Mean: 12 $\pm$ 2.2, 12.2 $\pm$ 1.9, 11.6 $\pm$ 3.1	Mean: 12 $\pm$ 2.6, 11.6 $\pm$ 3, 12.6 $\pm$ 3.7.  Change: 0.08 (CI: -1.01, 1.18). A change of 1.0 ml/kg/min is accepted as a clinically meaningful threshold .	Participants: 93	Very Low $\oplus\bigcirc\bigcirc\bigcirc$	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 3		Inconsistency: $I^2$ 0%, $PI = -1, 1.2$ demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level..
	% 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 methods.	Mean: 33 $\pm$ 11, 57 $\pm$ 7	Mean: 35 $\pm$ 10, 56 $\pm$ 8.  Change: 1.53 (CI: -0.66, 3.73).	Participants: 326	Very Low $\oplus\bigcirc\bigcirc\bigcirc$	Risk of Bias: three studies assessed to be at high risk of bias, level of evidence downgraded 1 level.
				Studies: 2		Inconsistency: $I^2$ 0%, $PI = -0.66, 3.7$ demonstrating significant uncertainty in the direction and size of the effect estimate. Downgraded 1 level..
	% 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

