



# Effects of Lifestyle Modification and Anti-diabetic Medicine on Prediabetes Progress: A Systematic Review and Meta-Analysis

Zhi Sheng<sup>1</sup>, Jia-Yu Cao<sup>1</sup>, Ying-Chang Pang<sup>1</sup>, Hang-Cheng Xu<sup>1</sup>, Jing-Wen Chen<sup>1</sup>, Jun-Hua Yuan<sup>2</sup>, Rui Wang<sup>2</sup>, Cai-Shun Zhang<sup>2</sup>, Liu-Xin Wang<sup>2</sup> and Jing Dong<sup>2,3\*</sup>

<sup>1</sup> Clinical Medicine Department, Medical College, Qingdao University, Shandong, China, <sup>2</sup> Special Medicine Department, Medical College, Qingdao University, Shandong, China, <sup>3</sup> Physiology Department, Medical College, Qingdao University, Shandong, China

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> \*Correspondence: Jing Dong dongjing6@hotmail.com

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Sheng Z, Cao J-Y, Pang Y-C, Xu H-C, Chen J-W, Yuan J-H, Wang R, Zhang C-S, Wang L-X and Dong J (2019) Effects of Lifestyle Modification and Anti-diabetic Medicine on Prediabetes Progress: A Systematic Review and Meta-Analysis. Front. Endocrinol. 10:455. doi: 10.3389/fendo.2019.00455 **Background:** Pre-diabetes is a risk factor for full-blown diabetes; it presents opportunities to prevent the actual diseases. It is therefore essential to identify effective preventive strategies, and to clarify the direction of future research.

**Methods:** PubMed, Embase and Cochrane Central Register of Controlled Trials were searched using key terms (**Supplementary Table 1**). We applied network meta-analysis to multiple comparisons among various diabetic preventive strategies, including lifestyle and pharmacological interventions; traditional meta-analysis for the synthesis of basal metabolic changes after interventions; and trial sequential analysis for determinations as to whether analysis conclusions meet expectations.

**Results:** We included 32 randomized controlled trials comprising 43,669 patients and 14 interventions in the meta-analysis. Both lifestyle modifications and anti-diabetic medications improved physical conditions, including weight loss, blood glucose, and blood pressure. Network meta-analysis suggested that the progression of diabetes could be delayed to varying degrees by lifestyle and pharmacological interventions, except for angiotensin-converting enzyme inhibitors, statins, sulfonylureas and vitamin D. The risk ratios (RR) [95% credible interval (Crl)] compared with control were: GLP-1RAs 0.28 (0.15, 0.50), Orlistat 0.33 (0.18, 0.55), TZM 0.33 (0.16, 0.63), TZD 0.39 (0.27, 0.53), LST 0.54 (0.32, 0.88), lifestyle 0.58 (0.49, 0.67), LSM 0.62 (0.45, 0.80), GI 0.66 (0.46, 0.88), SU 0.67 (0.40, 1.00), Vitamin D 0.91 (0.59, 1.40), ACEI 0.93 (0.62, 1.40), statins 1.20 (0.84, 1.60).

**Conclusions:** In adults with pre-diabetes, firm evidence supports the notion that lifestyle modifications and metformin reduces the incidence of diabetes with an average of 20% relative risk reduction, while statins increase the relative risk 20%. We found that lifestyle modifications, promising long-term strategies involving three factors (nutrition,

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exercise, and weight loss) contribute to health by reducing BMI, body weight, waist and hip circumference, systolic and diastolic pressure, fasting, and 2-h postprandial blood glucose, total cholesterol and by increasing HDL. We made this determination using TSA, avoiding further waste of experimental resources.

Keywords: prediabetic state, drug therapy, healthy lifestyle, diabetes mellitus, type 2, randomized controlled trial, network meta-analysis, trial sequential analysis

## INTRODUCTION

Type 2 diabetes mellitus (hereafter referred to as diabetes) is a major health problem associated with excessive morbidity and mortality, affecting approximately 5% of adults worldwide with rapidly rising prevalence (1, 2). Pre-diabetes, the precursor stage of diabetes, includes impaired fasting glucose (IFG), and impaired glucose tolerance (IGT), characterized by fasting plasma glucose (PFG)  $\geq$  6.1 and <7.0 or 2-h plasma glucose (2hPG)  $\geq$ 7.8 and <11.1 (3). There were recently introduced as risk factors for both diabetes and cardiovascular disease by the American Diabetes Association (4). As many as 5–10% of individuals with pre-diabetes develop diabetes each year (5), and approximately 70% of these will progress to diabetes during their lifetime (6). Fortunately, prevention of diabetes in the prediabetes stage can restore normal blood glucose levels (FPG <6.1, 2hPG <7.8), making early intervention crucial (7).

Guidelines from the American Diabetes Association suggest that individuals with pre-diabetes should undertake lifestyle modification to prevent the onset of diabetes, with healthy meals, increased physical exercise and weight reduction (8). Prescription medication has also been considered for the prediabetic population. Evidence supports that not only classic anti-diabetes drugs such as metformin and acarbose, but also newer agents such as GLP-1 receptor agonists help prevent the development of diabetes. Several randomized controlled trials (RCTs) diabetes-prevention strategies (lifestyle and/or pharmacological interventions) have been conducted (9, 10) and the literature has reviewed current achievements (11). Nevertheless, modern clinical therapies demand complex analyses for decision-making processes (12), in spite of traditional meta-analyses. Therefore, to assess physical outcomes of pre-diabetes interventions and to interpret the contemporary state of pre-diabetes research, we performed a Bayesian network meta-analysis and trial sequential analysis.

### **METHODS**

#### **Search Strategies**

The protocol of this review was registered in PROSPERO (ID: CRD 42018095121). Two review authors individually searched

PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) with database-appropriate terms and the text words (**Supplementary Table 1**). The reference lists of potentially relevant reviews were also screened. All references were eligible for inclusion regardless of language, published year and status.

#### **Inclusion Criteria**

- (i) RCTs published in peer-reviewed journals between 1/1/1965 and 1/5/2018;
- (ii) Patients were adults with pre-diabetes;
- (iii) Group allocation was based on lifestyle or medication interventions;
- (iv) Participants were randomly assigned;
- (v) Cumulative duration of interventions and follow-ups had a minimum with 1 year;
- (vi) Objective results were available, including the incidence of diabetes, regression of pre-diabetes, and physical condition changes.

#### **Exclusion Criteria**

- (i) Medications that were forbidden in routine clinical practice, e.g., troglitazone (13) and phenformin (14) (Supplementary Table 3);
- (ii) With the compliance of American Diabetes Association guidelines, lifestyle modification standardized to include both adjusted healthy meals and increased physical exercise (Supplementary Table 2) to ensure homogeneity, e.g., a study that only included health education (15);
- (iii) Patients with a history of cardiovascular events and other diseases.

#### **Data Extraction and Quality Assessment**

We extracted the incidence of diabetes, remission rate of pre-diabetes, and physical consequences with the principle of intention to treat analysis. Study quality was assessed using the Cochrane Collaboration's tool for risk bias (16).

#### **Statistical Analysis**

Analyses were performed using Mantel-Haenszel and Bayesian random effects models using RevMan (version 3.4.3) and R software (version 3.4.4, www.r-project.org), respectively. The Cochran-Mantel-Haenszel test (CMH) was used in the analysis of stratified or matched categorical data, allowing an investigator to test the association between a binary predictor or treatment and a binary outcome. The Bayesian random effects model, a classical statistical methods of network meta-analysis, uses posterior probability to rank all the interventions involved in the

Abbreviations: ACEI, Angiotensin converting enzyme inhibitors; BMI, Body mass index; CENTRAL, Cochrane Central Register of Controlled Trials; CrI, Credible interval; GI,  $\alpha$ -glycosidase inhibitors; GLP-1RAs, Glucagon-like peptide 1 receptor agonists; LSM, Lifestyle modification plus metformin; LST, Lifestyle modification plus thiazolidinedione; RCT, Randomized controlled trials; SUCRA, Surface under the cumulative ranking probabilities; TZD, Thiazolidinedione; TZM, Thiazolidinedione plus metformin.



comparisons and avoids the bias caused by repeated iteration in the estimation of parameters by frequency theory.

Consistent and simultaneous estimates of all interventions were obtained using Markov Chain Monte Carlo simulations using WinBugs software (version 1.4.3, http://www.mrc-bsu. cam.ac.uk/software/bugs/the-bugs-project-winbugs/). The results were recorded with RR and 95% credible interval (CrI). Trial sequential analysis (TSA, version 0.9.5.10 Beta, http:// www.ctu.dk/tsa/downloads.aspx) was managed to evaluate the cumulative evidence according to the information size achieved to date. When the same studies were repeatedly observed, the probability of a Type 1 error increased. Therefore, trial sequential analysis was intended to evaluate the overall Type 1 error rate assured at the desired level. Furthermore, with the trial sequential analysis, a conclusion may sometimes be reached at a much earlier stage once significant results are observed, at consequently lower financial and/or human cost. The cumulative ranking plot and the surface under the cumulative ranking (SUCRA) helps the researcher make decisions. The values of SUCRA are between 0 and 1 ( $0 \le$  SUCRA  $\le 1$ ). When SUCRA is 1, the intervention is absolutely valid, and when it is 0, the intervention is absolutely invalid.

# RESULTS

### PRISMA Flow Diagram and Baseline PRISMA Flow Diagram

Results relating to identification and selection of eligible 32 RCTs with outcome data for the incidence of diabetes are summarized in **Figure 1**. These studies included 43,669 participants with a mean follow-up of 3.3 years ranging from 1 to 6 years.

#### **Baseline Characteristics of Included Trials**

The 32 RCTs included in the network meta-analysis are summarized in **Table 1**. In the network of available intervention comparisons, twelve trials focused solely on the effectiveness of

 TABLE 1 | Baseline characteristics of included trials.

Study	Year	Center (N)	Duration (y)	Inclusion criteria	Diagnosis <sup>a</sup>	Population <sup>b</sup>	Treatment	Diabetic incidence, n/N (%
ACT NOW (10)	2011	8	2.4	IGT	ADA 2008	Age: 52, 53	Placebo vs. pioglitazone	50/299 (17)
						Male (%): 42, 42	(30–45 mg daily)	15/303 (5)
						BMI: 35, 33		
						Weight: NR		
CANOE (17)	2010	9	3.9*	IGT	WHO 1999	Age: 55, 50	Placebo vs. Rosiglitazone (2 mg)	41/104 (39)
						Male (%): 32, 35	plus Metformin (500 mg) twice	14/103 (14)
						BMI: 32, 31	daily	
						Weight: 86, 90		
Da Qing (18)	1997	33	6	IGT	WHO-	Age: 47, 44	Control vs. Lifestyle modification	90/133 (68)
						Male (%): 55, 56		58/126 (46)
						BMI: 26, 26		
						Weight: NR		
DPP (19)	2002	27	2.8	IFG/IGT	ADA 1997	Age: 50, 51, 51	Placebo vs. Metformin (850 mg	313/1082 (29)
						Male (%): 31, 34, 32	twice daily) vs. Lifestyle	233/1073 (22)
						BMI: 34, 34 34	modification	155/1079 (14)
						Weight:94, 94, 94		
DPS (9)	2001	5	3.2	IGT	WHO 1985	Age: 55, 55	Control vs. Lifestyle modification	59/257 (23)
						Male (%): 32, 34		27/265 (10)
						BMI: 31, 31		
						Weight: NR		
DREAM (20)	2006	191	3*	IGT, IFG	ADA 2003	Age: 55, 55	Placebo vs. Ramipril (5-15 mg	489/2646 (18)
						Male (%): 40, 41	daily)	449/2623 (17)
						BMI: 31, 31		
						Weight: 85, 85		
DREAM (21)	2006	191	3*	IGT, IFG	ADA 2003	Age: 55, 55	Placebo vs. Rosiglitazone (8 mg	658/2634 (25)
. ,						Male (%): 40, 42	daily)	280/2635 (11)
						BMI: 31, 31		
						Weight: 85, 85		
EDIPS (22)	2009	6	3.1	IGT	WHO 1999	Age: 57, 57	Control vs. Lifestyle modification	11/51 (22)
. /						Male (%): 39, 41		5/ 51 (10)
						BMI: 34, 34		
						Weight: 91, 93		
Eriksson et al. (23)	2006	4	1.5	IGT	WHO 1999	Age: 53, 58	Placebo vs. Glipizide (2.5 mg daily)	5/17 (29)

(Continued)

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Study	Year	Center (N)	Duration (y)	Inclusion criteria	Diagnosis <sup>a</sup>	Population <sup>b</sup>	Treatment	Diabetic incidence, n/N (%
						Male (%): 41, 12		1/17 (6)
						BMI: 29, 28		
						Weight: NR		
FDP (24)	2006	5	4*	IGT	WHO 1985	Age: NR	Control vs. Lifestyle modification	110/257 (43)
						Male (%): NR		75/265 (28)
						BMI: NR		
						Weight: 86, 87		
Heymsfield et al.	2000	39	1.6	IGT	WHO 1980	Age: 44, 44	Placebo vs. Orlistat (120 mg 3	4/53 (8)
(25)						Male (%):16, 17	times daily)	2/67 (3)
						BMI: 36, 36		
						Weight: 100, 99		
IDPP-1 (26)	2006	NR	3	IGT	WHO 1999	Age: 45, 46, 46, 46	Control vs. Lifestyle modification	75/136 (55)
						Male (%): 79, 76, 80, 81	vs. Metformin (500 mg daily) vs.	52/133 (39)
						BMI: 26, 26, 26, 26	Lifestyle modification plus Metformin	54/133 (41)
						Weight: NR	Metornin	51/129 (40)
IDPP-2 (27)	2010	NR	3	IGT	WHO 1999	Age: 46, 46	Lifestyle modification vs. Lifestyle	64/203 (32)
						Male (%): 84, 79	modification plus Pioglitazone	61/204 (30)
						BMI: 26, 26	(30 mg daily)	
						Weight: NR		
Jorde et al. (28)	2016	1	5	IFG, IGT, IFG/IGT	WHO 1999	Age: 62, 62	Placebo vs. Vitamin D (20,000 IU	112/255 (44)
						Male (%): 60, 63	per week)	103/256 (40)
						BMI: 30, 30		
						Weight: NR		
JUPITER (29)	2012	4	5	MS or IFG or BMI≥30	NR	Age: 66	Placebo vs. Rosuvastatin (20 mg	204/5765 (4)
				or HbA1c>6%		Male (%): 59	daily)	258/5743 (4)
						BMI: 31		
						Weight: NR		
Kawamori et al.	2009	103	3	IGT	WHO 1999	Age: 56, 56	Placebo vs. Voglibose (0.2 mg 3	84/883 (10)
(30)						Male (%): 60, 60	times daily)	40/897 (4)
						BMI: 26, 26		
						Weight: NR		

(Continued)

TABLE 1	Continued
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Study	Year	Center (N)	Duration (y)	Inclusion criteria	Diagnosis <sup>a</sup>	Population <sup>b</sup>	Treatment	Diabetic incidence, n/N (%
Kosaka et al. (31)	2005	NR	4	IGT	WHO 1980	Age: 51.5	Control vs. Lifestyle modification	32/356 (9)
						Male (%): NR		3/102 (3)
						BMI: 24, 24		
						Weight: NR		
Le Roux et al. (32)	2017	191	3	Prediabetes	ADA 2010	Age: 47, 48	Placebo vs. Liraglutide (3.0 mg	46/749 (6)
						Male (%): 24, 24	daily)	26/1505 (2)
						BMI: 39, 39		
						Weight: 108, 108		
Li et al. (33)	1999	NR	1	IGT	WHO 1985	Age: 50, 49	Placebo vs. Metformin (250 mg 3	6/43 (14)
						Male (%): 73, 70	times daily)	3/42 (7)
						BMI: 26, 26		
						Weight: NR		
Liao et al. (34)	2002	NR	1.5	IGT	WHO 1999	Age: 52, 56	Control vs. Lifestyle modification	2/38 (5)
						Male (%): 53, 37		1/36 (3)
						BMI: 27, 26		
						Weight: 70, 66		
Lindahl et al. (35)	2009	4	5	IGT	WHO 1985	Age: 54, 52	Control vs. Lifestyle modification	63/150 (42)
( )						Male (%): 39, 30	,	34/151 (23)
						BMI: 30, 31		
						Weight: 84, 86		
Lindblad et al. (36)	2010	23	5	IFG	NR	Age: 60, 60	Placebo vs. glimepiride (1 mg	55/138 (40)
			-			Male (%): 75, 88	once daily)	41/136 (30)
						BMI: 30, 30		
						Weight: NR		
LIPID (37)	2003	5	5	IFG	WHO 1999	Age: 63	Placebo vs. Pravastatin (40 mg	43/466 (9)
(0.)						Male (%): 85	daily)	46/474(10)
						BMI: NR		
						Weight: NR		
Polanco et al. (38)	2015	NR	6	prediabetes	NR	Age: NR	Lifestyle modification vs. Lifestyle	19/50 (38)
	2010		0	produced		Male (%): NR	modification plus Metformin (850	10/52 (19)
						BMI: NR	mg twice daily)	
						Weight: NR		
Saito et al. (39)	2011	38	3	IFG	ADA 2003	Age: 48, 50	Control vs. Lifestyle modification	51/330 (15)
x/						Male (%): 71, 72		35/ 11 (11)

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(Continued)

Study	Year	Center (N)	Duration (y)	Inclusion criteria	Diagnosis <sup>a</sup>	Population <sup>b</sup>	Treatment	Diabetic incidence, n/N (
						BMI: 27,27		
						Weight: 75, 74		
Sakane et al. (40)	2011	32	3	IFG, IGT	WHO 1985	Age: 30-60	Control vs. Lifestyle modification	18/152 (12)
						Male (%): NR		9/152 (6)
						BMI: 25, 25		
						Weight: 64, 65		
SLIM (41)	2008	1	3	IGT	WHO 1999	Age: 51, 51	Control vs. Lifestyle modification	18/73 (25)
						Male (%): 56, 54		8/74 (11)
						BMI: 29, 30		
						Weight: 83, 88		
STOP-NIDDM (42)	2002	23	3.3	IGT	WHO 1985	Age: 55, 54	Placebo vs. Acarbose (100 mg 3	285/686 (42)
						Male (%): 50, 48	times daily)	221/682 (32)
						BMI: 31, 31		
						Weight: 87, 88		
Weber et al. (43)	2016	1	3	IFG, IGT, IFG/IGT	ADA 1997	Age: 44,45	Placebo vs. Metformin (500 mg	98/295 (33)
						Male (%): 63, 64	daily)	69/283 (24)
						BMI: 28, 28		
						Weight: 75, 75		
XENDOS (44)	2004	22	4	IGT	WHO 1994	Age: 44, 43	Lifestyle modification plus	99/344 (29)
						Male (%): 45, 45	placebo vs. Lifestyle modification	66/350 (19)
						BMI: 37, 37	plus orlistat (120 mg daily)	
						Weight: 110, 110		
Xu et al. (45)	2012	1	1	IGR	ADA 2003	Age: 54, 41	Control vs. Lifestyle modification	7/42 (17)
						Male (%): 45,45		6/46 (13)
						BMI: 27, 26		
						Weight: 70, 68		
Zong et al. (46)	2015	6	2	Prediabetes	NR	Age: NR	Control vs. Lifestyle modification	11/107 (10)
						Male (%): NR		3/107 (3)
						BMI: NR		
						Weight: NR		

Date are mean (SD or range). \*Median (range).

2hPG, 2-h plasma glucose; ADA, American Diabetes Association; BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NR, not reported; OGTT, oral glucose tolerance test; WHO, World Health Organization.

<sup>a</sup>WHO Criteria 1980: IGT: FBG <140 mg/dl and OGTT 140–199 mg/dl. WHO Criteria 1985: normal: not defined; IGT: FBG <140 mg/dL and OGTT 140-200 mg/dL; IFG: not defined. WHO Criteria 1994: Not Found. WHO Criteria 1999: normal: FBG < 110 mg/dL; IGT: FBG <126 mg/dL and OGTT 140-200 mg/dL; IFG: FBG 110–126 mg/dL and OGTT <140 mg/dL. ADA Criteria 1997: normal: FBG <110 mg/dL and OGTT <140 mg/dL; IGT: OGTT 140 ng/dL. IGT: OGTT 140 ng/dL, IFG: FBG 110–126 mg/dL and OGTT <140 mg/dL; IGT: OGTT 140 mg/dL; IGT: OGTT 140 mg/dL, IFG: FBG 110–126 mg/dL. ADA Criteria 2003: normal: FBG < 110 mg/dL and OGTT <140 mg/dL; IGT: OGTT 140 mg/dL; IGT: OGTT 140 mg/dL, IFG: FBG 110–126 mg/dL, IFG: FBG 110–126 mg/dL, IFG: FBG 110–126 mg/dL, IFG: FBG 100-124 mg/dL, IFG: FBG 100-124 mg/dL, IFG < 100 mg/dL and OGTT <140 mg/dL; IGT: OGTT 140 mg/dL; IGT: OGTT 140 mg/dL, IFG < 100 mg/dL, IFG <100 mg

<sup>b</sup>Age is reported in years and weight is reported in kilograms.

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lifestyle modification (all of these combined diet and exercise and health education was excluded), fourteen studies compared the effectiveness of only pharmacological interventions (nine





anti-diabetic, two lipid lowering, one anti-obesity, one antihypertensive and one steroid), five studies combined lifestyle and pharmacological intervention groups and one combined the effect of the two medicines. No studies examined the effectiveness of surgical interventions.

Inclusion criteria of the valid 32 RCTs includes IGT, IFG and IGR. The diagnosis consists of World Health Organization (1980, 1985, 1994 and 1999); American Diabetes Association (1997, 2003, 2008, 2010). Population characteristics, including age, gender, BMI, weight and other data are displayed in **Table 1**.

#### **Network Meta-Analysis**

As opposed to those of previous studies, in our review, diabetic prevention strategies were divided into 14 groups comprising the considerable baseline of all included studies: Control (standard care or placebo), GI ( $\alpha$ -glucosidase inhibitor), GLP-1RAs (glucagon-like peptide 1 receptor agonists), Lifestyle (lifestyle modification), LSM (lifestyle modification plus metformin), LST (lifestyle modification plus thiazolidinedione), Metformin (metformin), Orlistat (orlistat), Statins (statins), SU (sulfonylureas), TZD (thiazolidinedione), TZM (thiazolidinedione plus metformin) Vitamin D (vitamin D) and ACEI (angiotensin converting enzyme inhibitors).

Network meta-analysis uses indirect comparison technology to comprehensively evaluate and rank all interventions in a body of evidence. The network of all direct and indirect comparisons of all commonly using anti-pre-diabetes strategies can be seen in **Figure 2B**.

Compared with the control group, current evidence suggests that nine strategies credibly reduced incidence of diabetes with RR ranging from 0.28 (0.15, 0.50) to 0.73 (0.54, 0.92), including GLP-1RAs, Orlistat, TZM, TZD, LST, Lifestyle, LSM, SU and Metformin. Nevertheless, SU, ACEI, statins and Vitamin D all intersect the ineffective line (**Figure 2A**).

After comparing several interventions, the investigator is informed of the optimal intervention. However, if optimal intervention is not available, or is difficult to implement or



Study or Subgroup Liao 2002 Lindahl 2009	Mean	modificat SD	Total		SD SD	Total	S Weight	td. Mean Difference IV. Random, 95% CI	Std. Mean Di IV, Random		
indahl 2009	-0.7	0.2	36	0.2	0.2	38	12.5%	-4.45 [-5.32, -3.59]			
Saito 2011	-1.8	1.6 1.2	151 311	-0.3 -0.4	1.53	150 330	17.8% 18.2%	-0.96 [-1.19, -0.72] -0.42 [-0.57, -0.26]			
Sakane 2011	-0.5	3.65	152	-0.1	3.25	152	17.9%	-0.12 [-0.34, 0.11]	+		
SLIM 2008	-0.36 -0.66	1.47 0.88	61 46	0.08	1.8	60	17.1%	-0.27 [-0.62, 0.09]	-		
Ku 2012	-0.00	0.08		-0.22	0.8/	42	16.6%	-0.47 [-0.90, -0.05]			
Fotal (95% CI) Heterogeneity: Tau <sup>2</sup> = 1	0.40.052-	107.00 4	757	~ 0.000	041.12	772	100.0%	-0.94 [-1.48, -0.41]	•		
Test for overall effect: 2			r=5 (P	< 0.000	01); 1* =	= 95%			-4 -2 0 Llifestyle modification C	2 ontrol	4
b	Lifestyle		tion		ontrol			Mean Difference	Mean Diffe		
Study or Subgroup	Mean	SD	Total		SD	Total	Weight	IV. Random, 95% C	IV. Random		
DPS 2001	-4.2	5.1	265	-0.8	3.7	257	16.5%	-3.40 [-4.16, -2.64]	-		
.iao 2002 .indahl 2009	-1.8 -5	0.5 4.12	36 151	0.7	0.6 4.17	38 150	19.1% 15.3%	-2.50 [-2.75, -2.25] -4.30 [-5.24, -3.36]			
Saito 2011	-2.5	3.2	311	-1.1	3.2	330	18.1%	-1.40 [-1.90, -0.90]			
Sakane 2011	-1.8	12.9	152	-1.4	11.46	152	5.8%	-0.40 [-3.14, 2.34]		_	
SLIM 2008 Ku 2012	-1.08 -1.75	4.3 2.37	61 46	0.16	4.91 2.59	60 42	10.6% 14.6%	-1.24 [-2.89, 0.41] -1.20 [-2.24, -0.16]	-		
	-1.75	2.07		-0.00	2.00						
Fotal (95% CI) Heterogeneity: Tau <sup>2</sup> =	0.84· Chi2 =	47.60 df	1022	0.0000	1)  2 =	1029	100.0%	-2.28 [-3.07, -1.49]			
Test for overall effect: 2	Z = 5.64 (P +	< 0.00001	- 0 (F < )	0.0000	n), r =	07 76			-10 -5 0 Lifestyle modification	5 Control	10
0	Lifestyle	modifica	tion	с	ontrol			Mean Difference	Mean Diffe		
Study or Subgroup	Mean	SD		Mean		Total	Weight	IV. Random, 95% CI	IV. Random		
DPS 2001	-4.4	5.2	46	-1.77	3.63	42	13.5%	-2.63 [-4.49, -0.77]			
Liao 2002 Lindahl 2009	-1.2	0.9	61 151	1.3	7.38	60 150	13.4% 14.9%	-2.50 [-4.38, -0.62] -5.90 [-7.33, -4.47]	-		
Saito 2011	-3.1	4.3	152		9.45	152	14.2%	-2.90 [-4.55, -1.25]	-		
Sakane 2011	-1.2	11.43	311	-1.3	4.7	330	15.1%	0.10 [-1.27, 1.47]			
SLIM 2008	-0.33	6.77	36	0.9	0.9	38	12.2%	-1.23 [-3.46, 1.00]	-		
Xu 2012	-4.02	5.09	265	-1.3	4.8	257	16.6%	-2.72 [-3.57, -1.87]			
Total (95% CI)	0.00.01.0	20.05	1022				100.0%	-2.57 [-3.98, -1.16]	•	_	
Heterogeneity: Tau <sup>2</sup> = Test for overall effect:			= 6 (P <	< 0.000	J1);  ² =	84%			-10 -5 0		10
									Concentrative Concentration (Co	Control	
d Study or Subgroup	Lifestyle				ontrol	Tet-!	Weight	Mean Difference	Mean Diffe		
Study or Subgroup Liao 2002	Mean -5	<u>SD</u> 6.18	Total 36	Mean -0.6	6.03	Total 38	Weight 35.3%	IV. Random, 95% CI -4.40 [-7.18, -1.62]	IV. Random	. 95% CI	
Ku 2012	-1.59	2.65	46		3.18	42	64.7%	-2.05 [-3.28, -0.82]			
Total (95% CI)			82			0.0	100 09/	2 88 1.5 09 0.001			
Total (95% CI) Heterogeneity: Tau <sup>2</sup> =	1.56; Chi <sup>2</sup> =	2.29. df =		0.13): F	2 = 56%		100.0%	-2.88 [-5.08, -0.68]		-	
Test for overall effect:						~			-20 -10 0 Lifestyle modification C	10 Control	20
9	Lifestyle	modifica	tion	0	ontrol			Mean Difference	Mean Diffe		
Study or Subgroup	Mean	SD	Total	Mean	SD		Weight	IV. Random, 95% C			
DPS 2001 Lindahl 2009	-5 -5.9	14 13.51	265 151	-1 1.9	15 13.44	257 150	24.5%	-4.00 [-6.49, -1.51] -7.80 [-10.84, -4.76]	-		
Saito 2011	-5.9	13.51	311	-3	13.44	330	25.9%	-1.00 [-3.09, 1.09]			
SLIM 2008	-3.6	15.8	61	-3.5	15.6	60	13.9%	-0.10 [-5.69, 5.49]		-	
Ku 2012	-2.59	16.21	46	1.24	11.67	42	13.2%	-3.83 [-9.70, 2.04]			
Total (95% CI)			834				100.0%	-3.51 [-6.36, -0.66]	•		
Heterogeneity: Tau <sup>2</sup> = Test for overall effect: 2			= 4 (P =	0.006)	; l <sup>2</sup> = 73	3%			-20 -10 0	10 20	(
¢			tion					Moon Differen	Lifestyle modification C		
f	Lifestyle Mean	modifica		C Mean	ontrol SD	Total	Weight	Mean Difference IV. Random, 95% CI	Lifestyle modification C Mean Diffe	erence	
f <u>Study or Subgroup</u> DPS 2001	Lifestyle <u>Mean</u> -5	modifica SD 9	Total 265	Mean -3	<b>SD</b> 9	Total 257	30.1%	IV. Random, 95% CI -2.00 [-3.54, -0.46]	Lifestyle modification C	erence	
f <u>Study or Subgroup</u> DPS 2001 Lindahl 2009	Lifestyle Mean -5 -3.7	modifica SD 9 7.56	Total 265 151	Mean -3 -0.4	SD 9 7.42	257 150	30.1% 25.6%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61]	Lifestyle modification C Mean Diffe	erence	
f <u>Study or Subgroup</u> DPS 2001	Lifestyle Mean -5 -3.7 -2	modifica SD 9	Total 265 151 311	Mean -3	9 7.42 10	257	30.1%	IV. Random, 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55]	Lifestyle modification C Mean Diffe	erence	
f <u>Study or Subgroup</u> DPS 2001 Lindahl 2009 Saito 2011	Lifestyle Mean -5 -3.7	modifica SD 9 7.56 10	Total 265 151	Mean -3 -0.4 -1	SD 9 7.42	257 150 330	30.1% 25.6% 29.9%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61]	Lifestyle modification C Mean Diffe	erence	
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SLIM 2008 Ku 2012	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2	modifica SD 9 7.56 10 7.4	Total 265 151 311 61 46	Mean -3 -0.4 -1 -3.1	9 7.42 10 8.2	257 150 330 60 42	30.1% 25.6% 29.9% 10.2% 4.1%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28]	Lifestyle modification C Mean Diffe	erence	
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SLIM 2008 Xu 2012 Total (95% CI) Heterogeneity: Tau <sup>2</sup> =	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> =	modifica SD 9 7.56 10 7.4 11.33 4.37, df =	Total 265 151 311 61 46 834 * 4 (P =	Mean -3 -0.4 -1 -3.1 -2	SD 9 7.42 10 8.2 9.98	257 150 330 60 42	30.1% 25.6% 29.9% 10.2%	IV, Random, 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32]	Lifestyle modification C Mean Diffe IV. Random	erence 95% CI	
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SLIM 2008 Xu 2012 Total (95% CI) Heterogeneity: Tau <sup>2</sup> =	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> =	modifica SD 9 7.56 10 7.4 11.33 4.37, df =	Total 265 151 311 61 46 834 * 4 (P =	Mean -3 -0.4 -1 -3.1 -2	SD 9 7.42 10 8.2 9.98	257 150 330 60 42	30.1% 25.6% 29.9% 10.2% 4.1%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28]	Lifestyle modification C Mean Diffe IV. Random	erence	20
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SLIM 2008 Ku 2012 Total (95% CI)	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P	modifica SD 9 7.56 10 7.4 11.33 4.37, df = < 0.00001	Total 265 151 311 61 46 834 : 4 (P = )	<u>Mean</u> -3 -0.4 -1 -3.1 -2 0.36); F	SD 9 7.42 10 8.2 9.98 ₹ = 9%	257 150 330 60 42	30.1% 25.6% 29.9% 10.2% 4.1%	IV. Random. 95% Cl -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28] -2.15 [-3.06, -1.24]	Lifestyle modification 0 Mean Diffe IV. Random	introl	20
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SulM 2008 Ku 2012 Total (95% CI) Heterogeneity: Tau <sup>2</sup> = Test for overall effect: . g Study or Subgroup	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle <u>Mean</u>	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = <0.00001 modifica <u>SD</u>	Total 265 151 311 61 46 834 4 (P = ) tion Total	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean	SD 9 7.42 10 8.2 9.98 * = 9% ontrol SD	257 150 330 60 42 839 Total	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28] -2.15 [-3.06, -1.24] Mean Difference IV. Random. 95% CI	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f Study or Subgroup DPS 2001 Lindahl 2009 Saito 2011 SLIM 2008 Ku 2012 Total (95% CI) Heterogeneity: Tau <sup>2</sup> = Test for overall effect: : g Study or Subgroup DPS 2001	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle <u>Mean</u> -0.22	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67	Total 265 151 311 61 46 834 4 (P = ) tion Total 265	<u>Mean</u> -3 -0.4 -1 -3.1 -2 0.36); F C <u>Mean</u> 0.06	SD 9 7.42 10 8.2 9.98 <sup>2</sup> = 9% ontrol SD 0.67	257 150 330 60 42 839 Total 257	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28] -2.15 [-3.06, -1.24] Mean Difference IV. Random. 95% CI -0.28 [-0.39, -0.17]	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f Study or Subgroup DPS 2001 Lindahl 2009 Salto 2011 Sult 2008 Ku 2012 Total (95% CI) Total (95% CI) Total (95% CI) Total (95% CI) Total (95% CI) Study or Subgroup DPS 2001 Lindahl 2009	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P <u>Lifestyle</u> <u>Mean</u> -0.22 -0.22	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.85	Total 265 151 311 61 46 834 4 (P = ) tion Total 265 151	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08	SD 9 7.42 10 8.2 9.98 ≥ = 9% ontrol SD 0.67 0.86	257 150 330 60 42 839 Total 257 150	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6%	IV. Random. 95% CI -2.00 [-3.54, -0.46] -3.30 [-4.99, -1.61] -1.00 [-2.55, 0.55] -3.10 [-5.88, -0.32] -2.17 [-6.62, 2.28] -2.15 [-3.06, -1.24] Mean Difference IV. Random. 95% CI -0.28 [-0.39, -0.17] -0.30 [-0.49, -0.11]	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f           Budy or Subgroup           DPS 2001           indahl 2009           Salto 2011           SLIM 2008           Ku 2012           Total (95% C1)           Heterogeneity: Tau't =           Test for overall effect:           g           Study or Subgroup           DPS 2001           Indahl 2009           Sakane 2011           Suldw 2011           Suldw 2011	Lifestyle Mean -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle Mean -0.22 -0.22 -0.22 0.1 0.32	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = <0.00001 modifica <u>SD</u> 0.67 0.85 0.7 0.83	Total 265 151 311 61 46 834 4 (P = ) tion Total 265	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08 -0.1 0.55	SD 9 7.42 10 8.2 9.98 * = 9% ontrol SD 0.67 0.86 0.78 0.82	257 150 330 60 42 839 Total 257 150 152 60	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% <u>Weight</u> 23.1% 20.6% 21.5% 16.8%	IV. Random, 95% Cl           -2.00 [53,4,0.46]           -3.00 [4,28,0.161]           -1.00 [2,25,0.55]           -3.10 [5,88,0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random, 95% Cl           -0.28 [0.39, -0.17]           -0.28 [0.39, -0.17]           -0.28 [0.49, -0.11]           -0.20 [0.24, -0.11]           -0.23 [0.25, 0.06]	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f Study or Subgroup PS 2001 indenh 2009 Salto 2011 SLIM 2008 Ku 2012 Total (95% Ct) Heterogeneity: Tau <sup>9</sup> = Test for overall effect: . g Study or Subgroup PD 2001 indenh 2009 Sakane 2011	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P <u>Lifestyle</u> <u>Mean</u> -0.22 -0.22 0.1	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           < 0.00001	Total 265 151 311 61 46 834 4 (P = ) ttion Total 265 151 152	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08 -0.1 0.55	SD 9 7.42 10 8.2 9.98 * = 9% ontrol SD 0.67 0.86 0.78	257 150 330 60 42 839 Total 257 150 152	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5%	IV. Random. 95% CI -2.00 (-3.54, -0.46) -3.30 (-4.99, -1.61) -1.00 (-2.55, 0.55) -3.10 (-5.88, -0.32) -2.17 (-6.62, 2.28) -2.15 (-3.06, -1.24) Mean Difference IV. Random. 95% CI -0.28 (-0.39, -0.17) -0.30 (-0.49, -0.11) -0.20 (-0.30, 0.37)	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f           Budy or Subgroup           DPS 2001           indahl 2009           Salto 2011           SLIM 2008           Ku 2012           Total (95% C1)           Heterogeneity: Tau't =           Test for overall effect:           g           Study or Subgroup           DPS 2001           Indahl 2009           Sakane 2011           Suldw 2011           Suldw 2011	Lifestyle Mean -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle Mean -0.22 -0.22 -0.22 0.1 0.32	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = <0.00001 modifica <u>SD</u> 0.67 0.85 0.7 0.83	Total 265 151 311 61 46 834 4 (P = ) ttion Total 265 151 152 61	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08 -0.1 0.55	SD 9 7.42 10 8.2 9.98 * = 9% ontrol SD 0.67 0.86 0.78 0.82	257 150 330 60 42 839 Total 257 150 152 60	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% <u>Weight</u> 23.1% 20.6% 21.5% 16.8%	IV. Random, 95% Cl           -2.00 [53,4,0.46]           -3.00 [4,28,0.161]           -1.00 [2,25,0.55]           -3.10 [5,88,0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random, 95% Cl           -0.28 [0.39, -0.17]           -0.28 [0.39, -0.17]           -0.28 [0.49, -0.11]           -0.20 [0.24, -0.11]           -0.23 [0.25, 0.06]	Lifestyle modification C Mean Diffe IV. Random IV. Random Lifestyle modification C Lifestyle modification C	erence . 95% CI	20
f         Subgroup.           PPS 2001         PPS 2001           Lindahl 2009         Subio 2001           Subio 2001         Vul 2012           Total (95% Ct)         Helerogeneity: Tau <sup>2</sup> =           Study or Subgroup         PPS 2001           Indahl 2009         Sakane 2011           SulM 2009         Sakane 2011           SulM 2009         Total (95% Ct)           Helerogeneity: Tau <sup>2</sup> =         Total (95% Ct)	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle <u>Mean</u> -0.22 -0.22 0.1 0.32 0.12 0.12	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.85 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.67 0.85 0.7 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.7 0.85 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7	Total 265 151 311 46 834 4 (P = ) tion Total 265 151 352 61 46 675	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08 -0.1 0.55 0.38	SD 9 7.42 10 8.2 9.98 2 = 9% 0.67 0.86 0.78 0.82 0.58	257 150 330 60 42 839 <b>Total</b> 257 150 152 60 42 661	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9%	V. Random. 95% C           2.00 [534, -0.46]           -3.00 [44.991.61]           -1.00 [255, 0.55]           -3.10 [58, -0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           V. Random, 95% C           -0.38 [-0.39, -0.17]           -0.30 [-0.49, -0.11]           -0.30 [0.49, -0.11]           -0.20 [0.03, 0.37]           -0.20 [0.03, 0.37]           -0.25 [-0.52, 0.06]           -0.26 [-0.52, 0.00]	Lifestyle modification C Kan Diffe V. Random -20 -10 0 Lifestyle modification C Lifestyle modification C Mean Diffe	erence . 95% CI	+20
f         Study or Subgroup           pPS 2001        ndahl 2009          ndahl 2009         Salto 2011           Suld 2011         Suld 2012           Total (95% CI)         Test for overall effect:           g         Study or Subgroup           pS 2001        ndahl 2009           Study or Subgroup         ppS 2001          ndahl 2009         Sakane 2011           SLM 2008         Xu 2012           Total (95% CI)         Total (95% CI)	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Lifestyle <u>Mean</u> -0.22 -0.22 0.1 0.32 0.12 0.12	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.85 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.67 0.85 0.7 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.85 0.7 0.7 0.85 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7	Total 265 151 311 46 834 4 (P = ) tion Total 265 151 352 61 46 675	Mean -3 -0.4 -1 -3.1 -2 0.36); F C Mean 0.06 0.08 -0.1 0.55 0.38	SD 9 7.42 10 8.2 9.98 2 = 9% 0.67 0.86 0.78 0.82 0.58	257 150 330 60 42 839 <b>Total</b> 257 150 152 60 42 661	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9%	V. Random. 95% C           2.00 [534, -0.46]           -3.00 [44.991.61]           -1.00 [255, 0.55]           -3.10 [58, -0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           V. Random, 95% C           -0.38 [-0.39, -0.17]           -0.30 [-0.49, -0.11]           -0.30 [0.49, -0.11]           -0.20 [0.03, 0.37]           -0.20 [0.03, 0.37]           -0.25 [-0.52, 0.06]           -0.26 [-0.52, 0.00]	Lifestyle modification C Maan Diffe IV. Randem -20 -10 C Lifestyle modification C Kean Diffe Maan Diffe	erence . 95% CI	
f         Subgroup           DPS 2001         Indahl 2009           Indahl 2009         Salto 2011           Sub 2011         Sub 2011           Sub 2012         Total (95% CI)           Total (95% CI)         Test for overall effect:           g         Study or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         SLM 2008           Ku 2012         Total (95% CI)           Total (95% CI)         Test for overall effect:           Test for overall (95% CI)         Test for overall effect:	Lifestyle <u>Mean</u> -5 -3,7 -2 -6,2 -4,17 0.10; Chi <sup>2</sup> = Z = 4,63 (P -0,22 -0,22 0,11 0.32 0,12 0.05; Chi <sup>2</sup> = Z = 1,56 (P Lifestyle	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.83 0.68 24.80, df = 0.12) modifica	$\begin{array}{c} \hline { Total } \\ 265 \\ 151 \\ 311 \\ 61 \\ 46 \\ 834 \\ 46 \\ (P = ) \\ \end{array} \\ \begin{array}{c} \hline { Total } \\ 265 \\ 151 \\ 152 \\ 61 \\ 46 \\ 675 \\ $	Mean         -3         -3         -0.4         -4         -1         -2         -2         -2         0.36); P         C         C         C         C         C         C         C         Mean         0.06         0.08         -0.1         0.55         0.38         <0.000         C </td <td>SD         9           9         7.42           10         8.2           9.98        </td> <td>257 150 330 60 42 839 70tal 257 150 152 60 42 661 84%</td> <td>30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9%</td> <td>IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 9.1.61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.57]           -0.28 [0.39, 0.64]           -0.28 [0.49, 0.46]           -0.28 [0.40, 0.49, 0.41]           -0.26 [0.45, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]</td> <td>Lifestyle modification C V. Random </td> <td>spence    </td> <td></td>	SD         9           9         7.42           10         8.2           9.98	257 150 330 60 42 839 70tal 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 9.1.61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.57]           -0.28 [0.39, 0.64]           -0.28 [0.49, 0.46]           -0.28 [0.40, 0.49, 0.41]           -0.26 [0.45, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]	Lifestyle modification C V. Random 	spence	
f study or Subgroup. DPS 2001 neth 2009 neth 2009	Lifestyle <u>Maan</u> -5 -3,7 -2 -6,2 -4,17 0,10; Chi <sup>2</sup> = Z = 4,63 (P <u>Lifestyle</u> <u>Maan</u> -0,22 0,1 0,32 0,12 0,05; Chi <sup>2</sup> = Z = 1,56 (P <u>Lifestyle</u> <u>Maan</u>	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.83 0.68 24.80, df = 0.12) modifica <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u> <u>SD</u>	Total           265           151           311           61           46           834           4 (P =           )           ttion           Total           265           151           265           151           265           151           265           151           265           151           265           151           265           152           61           675           = 4 (P            61           675           = 4 (P            ttion           Total	Mean         -3         -3         -0.4         -3         -1         -2         -2         -2         0.36); P         P         C         C         C         C         Mean         0.06         0.08         -0.1         0.55         0.38         <0.000°         C<	SD         9           9         7.42           10         8.2           9.98         8.2           9.98         0.67           0.66         0.78           0.62         0.58           1);  2 = .         0.58           1);  2 = .         0.51	257 150 330 60 42 839 Total 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 4.1% 100.0% <b>Weight</b> 23.1% 20.6% 21.5% 16.8% 100.0% <b>Weight</b>	V. Random. 95% CI           2.00 [534, 0.46]           -3.01 [4.49]. 1.61]           1.00 [255, 0.55]           -3.01 [548, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.47]           -0.28 [0.30, 0.37]           -0.28 [0.49, 0.41]           -0.28 [0.49, 0.41]           -0.28 [0.49, 0.41]           -0.28 [0.52, 0.00]           -0.27 [-0.38, 0.04]           Mean Difference           IV. Random, 95% CI	Lifestyle modification C V. Random -20 -10 0 Lifestyle modification C Lifestyle modification C Lifestyle modification C	spence	
f         Suby or Subgroup           DPS 2001         Indahl 2009           indahl 2009         Salto 2011           Sub 2011         Suby or Subgroup           Total (95% CI)         Test for overall effect:           g         Study or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         Suby or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         Sulk 2012           Total (95% CI)         Test for overall effect:           rest for overall effect:         Test for overall effect:           h         Study or Subgroup           DPS 2001         Suby OPS 2001	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P- Lifestyle <u>Mean</u> 0.22 0.12 0	modifica <u>SD</u> 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica <u>SD</u> 0.67 0.85 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7	Total           265           151           311           61           46           834           47           100           100           100           100           110           111      <	Mean         -3         -3         -0.4         -1         -3.1         -2         -2         0.36); if         F         C         C         Mean         0.06         0.08         -0.08         0.055         0.38         <0.38         <0.000         C         C         Mean         -0.28          <0.000         C         C         Mean         -0.28          <0.000         C         C         Mean         -0.28          <0.028         <0.028         <0.028         <0.028         <0.028         <0.028         <0.028         <0.028         <0.028 <th< th="">         &lt;0.28         &lt;0.28</th<>	SD         9           9         7.42           10         8.2           9.98         8.2           9.98         0.67           0.67         0.86           0.78         0.82           0.58         1); I² = -           ontrol         SD           2.22         2.22	257 150 330 60 42 839 Total 257 150 152 60 42 661 84% Total 257	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 9.1.6]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.53]           -0.28 [0.39, 0.64]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.41 [0.438, 0.04]           Mean Difference           IV. Random. 95% CI           -0.55 [0.90, 0.20]	Lifestyle modification C V. Random 	spence	
f         Suby or Subgroup           DPS 2001         Indahl 2009           Jandahl 2009         Salto 2011           Suld 2011         Suby or Subgroup           Total (95% CI)         Test for overall effect:           g         Study or Subgroup           DPS 2001         Jana 2009           Sakane 2011         Suby or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         Suldy 2012           Total (95% CI)         Test for overall effect:           rest for overall effect:         N           Pols 2001         Suby 2009           Study or Subgroup         DPS 2001           Jackane 2011         Suby 2009           Jackane 2011         Subara 2011	Lifestyle <u>Mean</u> -5 -3.7 -2.2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P- Lifestyle <u>Mean</u> -0.22 0.12 0.32 0.12 0.12 0.12 Lifestyle <u>Mean</u> -0.83 -0.71 -0.83 -0.71 -0.83	modifica SD 9 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica SD 0.67 0.85 0.73 0.68 24.80, df e 0.12) modifica SD 0.63 0.63 0.68 24.80, df 2.480, df 2.219 1.89 2.31 2.29	Total           265           151           311           61           46           834           4 (P =           )           ttion           Total           265           151           265           151           265           151           265           151           265           151           265           151           265           152           61           675           = 4 (P            61           675           = 4 (P            ttion           Total	Mean         -3         -3         -0.4         -3         -1         -2         -2         -2         0.36); P         P         C         C         C         C         Mean         0.06         0.08         -0.1         0.55         0.38         <0.000°         C<	SD         9           9         7.42           10         8.2           9.98         8.2           9.98         0.67           0.67         0.86           0.78         0.82           0.58         1); I² = -           ontrol         SD           2.22         2.22	257 150 330 60 42 839 Total 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 24.7%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 0.16]           -1.00 [2.55, 0.55]           -3.10 [588, 0.32]           -2.17 [66.2, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.53]           -0.28 [0.39, 0.54]           -0.28 [0.49, 0.41]           0.20 [0.49, 0.41]           0.20 [0.49, 0.41]           0.21 [0.52, 0.06]           -0.28 [0.49, 0.43]           -0.28 [0.49, 0.44]           -0.28 [0.40, 0.49, 0.41]           0.20 [0.45, 0.06]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.40 [0.40, 0.40]           -0.55 [0.90, 0.20]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]	Lifestyle modification C V. Random 	spence	
f         f           DPS 2001         DPS 2001           DPS 2001         DPS 2001           Lindami 2009         Salici 2011           Salici 2011         Sulva 2012           Total (95% CI)         Heterogeneity: Tau* =           Test for overall effect:         3           Study or Subgroup         DPS 2001           DPS 2001         Salane 2011           Sulva 2012         Total (95% CI)           Heterogeneity: Tau* =         Test for overall effect:           NBudy or Subgroup         DPS 2001           Salane 2011         Sulva or Subgroup           DPS 2001         DPS 2001           Jondani 2009         Salane 2011           Sulva or Subgroup         DPS 2001           DPS 2001         DPS 2001           Jondani 2009         Salane 2011           Sulva or Subgroup         DS 2001           Salane 2011         Sulva 2011	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = 2 Z = 4.63 (P <u>Mean</u> -0.22 -0.22 -0.22 0.12 0.05; Chi <sup>2</sup> = 2 0.13 0.05; Chi <sup>2</sup> = 0.22 0.08 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08 0.07 0.08	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           <0.0001	Total           265           151           311           61           46           834           e4 (P = )           100           Total           265           151           52           61           675           64 (P            152           61           265           151           152           61           265           151           265           151           265           151           265           151           265           151           265           151           265           151           265           152           61	Mean         -3         -0.4         -1         -3.1         -2         0.36); if         C         C         C         C         C         0.4         -0.5         0.38         -0.1         0.55         0.38         -0.28         -0.28         -0.219         -0.28         -0.219         -0.53         0.89         -0.89 <td>SD         9           9         7.42         10           8.2         9.98         2         9.98           ontrol         5D         0.67         0.86           0.78         0.82         0.58         1); I² =         0.82           ontrol         5D         2.22         2.34         2.11         1.9</td> <td>257 150 330 60 42 839 7 0152 57 150 152 60 42 661 84% 7 050 152 60 42 661 84%</td> <td>30.1% 25.6% 29.9% 10.2% 4.1% 100.0% 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 21.7% 21.7%</td> <td>IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [44.99, -1.6]           -1.00 [2.55, 0.55]           -3.10 [6.58, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           0.28 [0.33, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.52, 0.00]           -0.21 [0.43, 0.01]           Wean Difference           IV. Random. 95% CI           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.54 [-1.64, 0.24]</td> <td>Lifestyle modification C V. Random </td> <td>spence    </td> <td></td>	SD         9           9         7.42         10           8.2         9.98         2         9.98           ontrol         5D         0.67         0.86           0.78         0.82         0.58         1); I² =         0.82           ontrol         5D         2.22         2.34         2.11         1.9	257 150 330 60 42 839 7 0152 57 150 152 60 42 661 84% 7 050 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 21.7% 21.7%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [44.99, -1.6]           -1.00 [2.55, 0.55]           -3.10 [6.58, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           0.28 [0.33, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.52, 0.00]           -0.21 [0.43, 0.01]           Wean Difference           IV. Random. 95% CI           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.54 [-1.64, 0.24]	Lifestyle modification C V. Random 	spence	
f         Suby or Subgroup           DPS 2001         Indahl 2009           Indahl 2009         Salto 2011           Sub 2011         Suby or Subgroup           Total (95% CI)         Test for overall effect:           g         Study or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         Suby or Subgroup           DPS 2001         Indahl 2009           Sakane 2011         Suby 2012           Total (95% CI)         Test for overall effect:           rest for overall effect:         N           Post 2001         Suby 2009           Study or Subgroup         DPS 2001           Jostane 2011         Subara 2020	Lifestyle <u>Mean</u> -5 -3.7 -2.2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P- Lifestyle <u>Mean</u> -0.22 0.12 0.32 0.12 0.12 0.12 Lifestyle <u>Mean</u> -0.83 -0.71 -0.83 -0.71 -0.83	modifica SD 9 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica SD 0.67 0.85 0.73 0.68 24.80, df e 0.12) modifica SD 0.63 0.63 0.68 24.80, df 2.480, df 2.219 1.89 2.31 2.29	Total           2655           1511           311           61           46           834           e4 (P = )           tion           Total           265           1511           152           61           46           675           61           46           675           61           46           675           152           46           675           61           46           675           51           152	Mean         -3         -0.4         -1         -3.1         -2         0.36); if         C         C         C         C         C         0.4         -0.5         0.38         -0.1         0.55         0.38         -0.28         -0.28         -0.219         -0.28         -0.219         -0.53         0.89         -0.89 <td>SD         9           9         7.42         10           8.2         9.98         9.98           ontrol         0.67         0.86           0.82         0.58         0.58           1);  ² = .         0.78         2.22           2.34         2.1         2.34</td> <td>257 150 330 60 42 839 7 0 152 60 42 661 84% 7 0 152 60 42 661 84%</td> <td>30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 24.7%</td> <td>IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 0.16]           -1.00 [2.55, 0.55]           -3.10 [588, 0.32]           -2.17 [66.2, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.53]           -0.28 [0.39, 0.54]           -0.28 [0.49, 0.41]           0.20 [0.49, 0.41]           0.20 [0.49, 0.41]           0.21 [0.52, 0.06]           -0.28 [0.49, 0.43]           -0.28 [0.49, 0.44]           -0.28 [0.40, 0.49, 0.41]           0.20 [0.45, 0.06]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.40 [0.40, 0.40]           -0.55 [0.90, 0.20]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]</td> <td>Lifestyle modification C V. Random </td> <td>spence    </td> <td></td>	SD         9           9         7.42         10           8.2         9.98         9.98           ontrol         0.67         0.86           0.82         0.58         0.58           1);  ² = .         0.78         2.22           2.34         2.1         2.34	257 150 330 60 42 839 7 0 152 60 42 661 84% 7 0 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 24.7%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [4.49, 0.16]           -1.00 [2.55, 0.55]           -3.10 [588, 0.32]           -2.17 [66.2, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.53]           -0.28 [0.39, 0.54]           -0.28 [0.49, 0.41]           0.20 [0.49, 0.41]           0.20 [0.49, 0.41]           0.21 [0.52, 0.06]           -0.28 [0.49, 0.43]           -0.28 [0.49, 0.44]           -0.28 [0.40, 0.49, 0.41]           0.20 [0.45, 0.06]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.28 [0.40, 0.40]           -0.40 [0.40, 0.40]           -0.55 [0.90, 0.20]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]           -0.55 [0.40, 0.40]	Lifestyle modification C V. Random 	spence	
f study or Subgroup DPS 2001 indain 2009 Salto 2011 SLIM 2009 Ku 2012 Total (95% CI) Total (95% CI) Total (95% CI) Total (95% CI) Study or Subgroup DPS 2001 Total (95% CI) Study 2012 Total (95% CI)	Lifestyle Mean -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Lifestyle Mean -0.22 0.12 0.5; Chi <sup>2</sup> = 2 = 1.56 (P Lifestyle Mean -0.83 -0.71 -0.83 -0.05 -1.24	modifica SD 9 7.56 10 7.4 11.33 4.37, df = < 0.00001 modifica SD 0.67 0.75 0.75 0.75 0.75 0.75 0.75 0.0001 modifica SD 0.68 24.80, df = 0.12) modifica SD 2.31 2.31 2.37	$\begin{array}{c} \hline { Total } \\ 265 \\ 151 \\ 311 \\ 61 \\ 46 \\ 834 \\ e4 \\ (P= \\ ) \end{array}$	Mean. -3 -0.4 -1 -3.1 -2 0.36); F C C Mean. 0.06 0.08 0.08 0.038 ( 0.09 0.05 0.38 € 0.0000 C C Mean. -0.28 € 0.0000 C C Mean. -0.28 0.36); C C Mean. -0.44 0.45 0.45 0.45 0.45 0.45 0.45 0.45	SD         9         9           7.42         10         8.2           9.98         9.98         9.98           a         9.98         0.67           0.66         0.78         0.62           0.58         0.58         0.58           1); I² =         2.22         2.34           2.1         1.9         5.57	257 150 330 60 42 839 Total 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% 23.1% 20.6% 21.5% 16.8% 17.9% 100.0% Weight 37.8% 21.7% 21.7% 21.7%	IV. Random. 95% CI           2.00 [534, 0.46]           -3.00 [44.99, -1.6]           -1.00 [2.55, 0.55]           -3.10 [6.58, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           0.28 [0.33, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.43, 0.17]           0.20 [0.52, 0.00]           -0.21 [0.43, 0.01]           Wean Difference           IV. Random. 95% CI           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.52 [-0.50, 0.01]           0.54 [-1.64, 0.24]	Lifestyle modification C V. Random 	spence	
f	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Z = 4.63 (P 0.22 0.12 0.12 0.12 0.12 Lifestyle <u>Mean</u> -0.22 0.12 0.12 Lifestyle <u>Mean</u> -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.72 -0.75 -0	modifies           SD         9           7.56         7.4           11.33         4.37, df =           4.37, df =         0.00001           modifies         0.67           0.83         0.66           24.80, df =         0.12)           modifies         2.31           2.31         2.32           2.37         5.00, df =	$\begin{array}{c} \hline {\bf Total} \\ 265 \\ 151 \\ 311 \\ 46 \\ 834 \\ 46 \\ (P = ) \end{array}$	Mean. -3 -0.4 -1 -3.1 -2 0.36); F C C Mean. 0.06 0.08 0.08 0.038 ( 0.09 0.05 0.38 € 0.0000 C C Mean. -0.28 € 0.0000 C C Mean. -0.28 0.36); C C Mean. -0.44 -0.44 -0.45 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.45 -0.44 -0.44 -0.44 -0.44 -0.44 -0.45 -0.45 -0.48 -0.49 -0.45	SD         9         9           7.42         10         8.2           9.98         9.98         9.98           a         9.98         0.67           0.66         0.78         0.62           0.58         0.58         0.58           1); I² =         2.22         2.34           2.1         1.9         5.57	257 150 330 60 42 839 Total 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 100.0% Weight 37.8% 21.7% 100.0%	IV. Random. 95% CI           -2.00 (5 3 4, 0.46)           -3.00 (4 99, -1.61)           -1.00 (2 55, 0.55)           -3.10 (5 88, 0.32)           -2.17 (5 6.62, 2.28)           -2.17 (5 6.62, 2.28)           -2.15 (-3.06, -1.24)           Mean Difference           IV. Random. 95% CI           0.28 (0.38, 0.17)           0.20 (0.38, 0.17)           0.20 (0.38, 0.37)           0.21 (0.48, 0.11)           0.20 (0.38, 0.37)           0.21 (0.52, 0.00)           -0.17 (-0.38, 0.04)           Mean Difference           IV. Random. 95% CI           -0.55 (-10.50, 0.01)           -0.56 (-10.50, 0.01)           -0.56 (-10.50, 0.01)           -0.30 (-178, 0.58)           -0.34 (-1.44, -0.24)           -0.35 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)	Lifestyle modification C V. Random 	spence	
f study or Subgroup DPS 2001 indain 2009 Salto 2011 SLIM 2009 Ku 2012 Total (95% CI) Total (95% CI) Total (95% CI) Total (95% CI) Study or Subgroup DPS 2001 Total (95% CI) Study 2012 Total (95% CI)	Lifestyle <u>Mean</u> -5 -3.7 -2 -6.2 -4.17 0.10; Chi <sup>2</sup> = Z = 4.63 (P Z = 4.63 (P 0.22 0.12 0.12 0.12 0.12 Lifestyle <u>Mean</u> -0.22 0.12 0.12 Lifestyle <u>Mean</u> -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.83 -0.71 -0.72 -0.75 -0	modifies           SD         9           7.56         7.4           11.33         4.37, df =           4.37, df =         0.00001           modifies         0.67           0.83         0.66           24.80, df =         0.12)           modifies         2.31           2.31         2.32           2.37         5.00, df =	$\begin{array}{c} \hline {\bf Total} \\ 265 \\ 151 \\ 311 \\ 46 \\ 834 \\ 46 \\ (P = ) \end{array}$	Mean. -3 -0.4 -1 -3.1 -2 0.36); F C C Mean. 0.06 0.08 0.08 0.038 ( 0.09 0.05 0.38 € 0.0000 C C Mean. -0.28 € 0.0000 C C Mean. -0.28 0.36); C C Mean. -0.44 -0.44 -0.45 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.44 -0.45 -0.44 -0.44 -0.44 -0.44 -0.44 -0.45 -0.45 -0.48 -0.49 -0.45	SD         9         9           7.42         10         8.2           9.98         9.98         9.98           arrow ontrol         SD         0.67           0.66         0.78         0.62           0.58         0.58         1); I² = -           arrow ontrol         SD         2.22           2.34         2.1         1.9           5.57         5.57	257 150 330 60 42 839 Total 257 150 152 60 42 661 84%	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 100.0% Weight 37.8% 21.7% 100.0%	IV. Random. 95% CI           -2.00 (5 3 4, 0.46)           -3.00 (4 99, -1.61)           -1.00 (2 55, 0.55)           -3.10 (5 88, 0.32)           -2.17 (5 6.62, 2.28)           -2.17 (5 6.62, 2.28)           -2.15 (-3.06, -1.24)           Mean Difference           IV. Random. 95% CI           0.28 (0.38, 0.17)           0.20 (0.38, 0.17)           0.20 (0.38, 0.37)           0.21 (0.48, 0.11)           0.20 (0.38, 0.37)           0.21 (0.52, 0.00)           -0.17 (-0.38, 0.04)           Mean Difference           IV. Random. 95% CI           -0.55 (-10.50, 0.01)           -0.56 (-10.50, 0.01)           -0.56 (-10.50, 0.01)           -0.30 (-178, 0.58)           -0.34 (-1.44, -0.24)           -0.35 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)           -0.36 (-1.05, 0.01)	Lifestyle modification C -20 -10 0 Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C -2 -1 0 Lifestyle modification C -2 -1 0 -2	In the second se	
filludo or Subgroup.           DPS 2001           DPS 2001           Jandahi 2009           Salto 2011           Salto 2011           Salto 2012           Total (95% C1)           Heterogeneity: Tau* =           Test for overall effect:           Salto 2019           Salto 2019           Salto 2019           Jindahi 2009           Saltor 2011           SulM 2008           Ku 2012           Total (95% C1)           Heterogeneity: Tau* =           Statum 2011           SulM 2008           Sular 2021           Total (95% C1)           Heterogeneity: Tau* =           Statame 2011           Sultar 2021           Total (95% C1)           Heterogeneity: Tau* =           Test for overall effect:           j	Lifestyle Maan -5 -3,7 -2 -4,17 0,10; Ch <sup>2</sup> = 4,63 (P -0,22 -4,63 (P -0,22 -	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           < 0.00001	$\begin{array}{c} \hline {\bf Total} \\ 265 \\ 151 \\ 311 \\ 61 \\ 46 \\ 834 \\ 46 \\ (P = \\ ) \end{array}$	Mean -3 -3 -4 -4 -4 -1 -3 -3 -1 -2 0.36); F C Mean 0.06 0.08 -0.11 0.55 0.38 < 0.000 C Mean -0.4 -0.5 0.89 0.85; F C C C C C C C C C C C C C	SD         9         9         9         7.42         10         8.2         9.96         8         2         9.96         8         2         9.96         0.67         0.67         0.86         0.78         0.86         0.78         0.86         0.78         0.52         2.22         2.34         2.11         1.9         5.57         5.57         2 = 20%         2	257 150 330 60 42 839 701 52 60 42 661 84% 7050 152 60 42 661 52 60 42 661	30.1% 25.6% 4.1% 10.2% 4.1% 100.0% Weight 123.1% 16.8% 17.9% 100.0% 10.0% Weight 37.8% 2.15% 100.0% S	IV. Random. 95% CI           2.00 [534, -0.46]           -3.00 [4.49, -1.61]           -1.00 [-2.55, 0.55]           -3.10 [548, -0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [-0.39, -0.67]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.70]           -0.28 [-0.39, -0.70]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.48, -0.41]           -0.55 [-0.90, -0.20]           -0.55 [-0.48, -0.42]           -0.36 [-0.78, 0.18]           -0.47 [-0.48, -0.42]           -0.57 [-0.48, -0.42]           -0.57 [-0.48, -0.42]           -0.57 [-0.48, -0.42]           -0.57 [-0.48, -0.42]           -0.57 [-0.48, -0.42]	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f         f           DPS 2001         DPS 2001           DPS 2001         DPS 2001           Lindami 2009         Salito 2011           Salito 2011         Salito 2011           Value Value         Value           Total (9%) CI)         Heterogeneity: Tau* =           Saldwor Subgroup         DPS 2001           Jindahl 2001         Salate 2011           Salum 2008         Ku 2012           Total (9%) CI)         Heterogeneity: Tau* =           Test for overall effect:         h           Study or Subgroup         DPS 2001           Salatene 2011         Salatene 2011           Salatene 2011         Salatene 2011 <td><math display="block">\label{eq:linear} \begin{split} &amp; \text{Lifestyle} \\ &amp; \text{Mean} \\ &amp; -5 \\ &amp; -3, \\ &amp; -2 \\</math></td> <td><math display="block">\begin{array}{c} \mbox{modifies}\\ \mbox{sp}\\ \mbox{9}\\ \mbox{9}\\ \mbox{7.56}\\ \mbox{10}\\ \mbox{7.4}\\ \mbox{11.33}\\ \mbox{4.37}, \mbox{df} \mbox{df} \mbox{4.37}\\ \mbox{4.37}, \mbox{df} \mbox{df} \mbox{6}\\ \mbox{sp}\\ \mbox{0.68}\\ 0.</math></td> <td>Total           265           151           311           61           46           834           47           7000           1000           1000           1000           1100</td> <td>Mean.         -3.3         -0.4         -1.         -0.4         -1.         -2.         0.36); if         C         C         C         Mean.         0.06         0.08         -0.15         0.38         0.000         C         C         Mean.         -0.28         -0.19         0.38         0.000         0.28         0.38         0.029         0.85         0.89         0.85         0.29); if         C</td> <td>SD         SD           9         9         9           7.42         10         8.2           9.98         9.98         8           * = 9%         0.67         0.67           0.67         0.82         0.58           0.1;  * =         2.22         2.34           2.1         1.9         5.57           ≈ = 20%         SD         SD</td> <td>257 150 330 60 42 839 Total 257 150 152 661 257 150 152 60 42 661 5 5</td> <td>30.1% 25.6% 4.1% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 16.6% 17.9% 24.7% 24.7% 13.6% 24.7% 13.0% 24.7% 13.0% 23.3% 23.3% 23.5% 24.5% 25</td> <td>IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.16 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.48, 0.13]           -0.28 [0.48, 0.14]           -0.29 [0.52, 0.00]           -0.17 [-0.38, 0.04]           Mean Difference           IV. Random. 95% CI           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]     <td>Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Mean Diffe Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C</td><td>i 95% Cl </td><td></td></td>	$\label{eq:linear} \begin{split} & \text{Lifestyle} \\ & \text{Mean} \\ & -5 \\ & -3, \\ & -2 \\$	$\begin{array}{c} \mbox{modifies}\\ \mbox{sp}\\ \mbox{9}\\ \mbox{9}\\ \mbox{7.56}\\ \mbox{10}\\ \mbox{7.4}\\ \mbox{11.33}\\ \mbox{4.37}, \mbox{df} \mbox{df} \mbox{4.37}\\ \mbox{4.37}, \mbox{df} \mbox{df} \mbox{6}\\ \mbox{sp}\\ \mbox{0.68}\\ 0.$	Total           265           151           311           61           46           834           47           7000           1000           1000           1000           1100	Mean.         -3.3         -0.4         -1.         -0.4         -1.         -2.         0.36); if         C         C         C         Mean.         0.06         0.08         -0.15         0.38         0.000         C         C         Mean.         -0.28         -0.19         0.38         0.000         0.28         0.38         0.029         0.85         0.89         0.85         0.29); if         C	SD         SD           9         9         9           7.42         10         8.2           9.98         9.98         8           * = 9%         0.67         0.67           0.67         0.82         0.58           0.1;  * =         2.22         2.34           2.1         1.9         5.57           ≈ = 20%         SD         SD	257 150 330 60 42 839 Total 257 150 152 661 257 150 152 60 42 661 5 5	30.1% 25.6% 4.1% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 16.6% 17.9% 24.7% 24.7% 13.6% 24.7% 13.0% 24.7% 13.0% 23.3% 23.3% 23.5% 24.5% 25	IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.16 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.48, 0.13]           -0.28 [0.48, 0.14]           -0.29 [0.52, 0.00]           -0.17 [-0.38, 0.04]           Mean Difference           IV. Random. 95% CI           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01]           -0.52 [-0.50, 0.01] <td>Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Mean Diffe Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C</td> <td>i 95% Cl </td> <td></td>	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Mean Diffe Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C	i 95% Cl 	
filludo or Subgroup.           DPS 2001           DPS 2001           Jandahi 2009           Salto 2011           Salto 2011           Salto 2012           Total (95% C1)           Heterogeneity: Tau* =           Test for overall effect:           Salto 2019           Salto 2019           Salto 2019           Jindahi 2009           Saltor 2011           SulM 2008           Ku 2012           Total (95% C1)           Heterogeneity: Tau* =           Statum 2011           SulM 2008           Sular 2021           Total (95% C1)           Heterogeneity: Tau* =           Statame 2011           Sultar 2021           Total (95% C1)           Heterogeneity: Tau* =           Test for overall effect:           j	Lifestyle Maan -5 -3,7 -2 -4,17 0,10; Ch <sup>2</sup> = 4,63 (P -0,22 -4,63 (P -0,22 -	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           < 0.00001	$\begin{array}{c} \hline {\bf Total} \\ 265 \\ 151 \\ 311 \\ 61 \\ 46 \\ 834 \\ 46 \\ (P = \\ ) \end{array}$	Mean. -3.3 -0.4 -1 -2 0.36); F C C Mean. 0.06 0.08 0.055 0.38 <0.0000 C C Mean. -0.2 8 0.385 0.89 0.85 0.89 0.85 0.29); F C C C C C C C C C C C C C C C C C C C	SD         9         9         9         9         9         7.42         10         8.2         9.98         9.98         9.98         9.98         0.67         0.07         0.67         0.82         2.02         2.04         10         11         17         2         2         2.34         2.11         1.9         5.57         2         2.0%         0.00000000000000000000000000000000000	257 150 330 60 42 839 701 52 60 42 661 84% 7050 152 60 42 661 52 60 42 661	30.1% 25.6% 4.1% 10.2% 4.1% 100.0% Weight 123.1% 16.8% 17.9% 100.0% 10.0% Weight 37.8% 2.15% 100.0% S	IV. Random. 95% CI           2.00 [534, -0.46]           -3.00 [4.49, -1.61]           -1.00 [-2.55, 0.55]           -3.10 [548, -0.32]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [-0.39, -0.67]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.64]           -0.28 [-0.39, -0.70]           -0.28 [-0.39, -0.70]           -0.28 [-0.39, -0.70]           -0.28 [-0.39, -0.70]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.28 [-0.49, -0.41]           -0.45 [-0.40, -0.42]           -0.45 [-0.40, -0.43]           -0.45 [-0.40, -0.43]	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f         Study or Subgroup           DPS 2001         DPS 2001           Undahl 2009         Salte 2011           Salte 2011         Salte 2011           Salte 2011         Salte 2011           Salte 2012         Total (95% CI)           relerogeneity: Tau* =         Test for overall effect:           Salte 2013         Salte 2011           Salte 2013         Salte 2011           Salte 2014         Salte 2011           Salte 2015         Salte 2011           Salte 2016         Salte 2011           Salte 2017         Salte 100           Salte 2018         Salte 2011           Salte 2019         Salte 2011	Lifestyle Maanle Maanle 1.000000000000000000000000000000000000	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           <0.0001	$\begin{array}{c} \hline { Total } \\ 265 \\ 151 \\ 311 \\ 46 \\ 834 \\ 4 \ (P = ) \\ ) \\ \hline \\ 152 \\ 151 \\ 161 \\ 46 \\ 675 \\ 151 \\ 152 \\ 61 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 151 \\ 151 \\ 152 \\ 151 \\ 1$	Mean. -3.3 -0.4 -0.4 -1 -2 -0.36); F C C Mean. 0.06 0.08 0.08 0.085 0.38 € 0.000 C C Mean. -0.28 0.85 0.89 0.85 0.80 0.85 0.85 0.85 0.85 0.85 0.85	SD         SD           9         9         9           7.42         10         8.2           9.98         8         9%           ontrol         8.2         9%           0.67         0.86         0.82           0.58         0.58         0.78           1); I² = .         .         .           2.22         2.34         2.1           2.9         5.57         2           2.34         2.9         .           9.557         2         2.0%           ontrol         SD         .           2.8         0.56         2.6	257 150 330 330 60 42 839 70 150 42 661 84% 70 50 42 661 84% 70 50 42 661 527 150 60 42 661 527 152 60 42 57 152 57 150 152 60 42 57 150 152 152 60 42 152 152 152 152 152 152 152 152 152 15	30.1% 25.6% 4.1% 4.1% 4.1% Weight 23.1% 20.6% 21.5% 20.6% 21.5% 100.0% Weight 100.0% Weight 13.6% 2.3% 31.1% 13.6% 31.1% 13.3%	IV. Random. 95% CI           2.00 [534, -0.46]           -3.00 [4.49, -1.61]           -1.00 [-2.55, 0.55]           -3.01 [54, -0.46]           -2.01 [53, 0.55]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.63]           -0.28 [0.39, 0.64]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.45 [0.40, 0.42]           -0.45 [0.41, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f         Subdrars Subgroup.           DPS 2001         DPS 2001           Jundami 2009         Salito 2011           Salito 2011         Subdrars 2009           Salito 2011         Subdrars 2009           Total (98% CI)         Heterogeneity. Tau' =           res for overall effect:         Subdrars 2011           Subdrars 2011         Subdrars 2011           Subdrars 2012         Total (98% CI)           releterogeneity. Tau' =         Test for overall effect:           h         Subdrars 2011           Subdrars 2011         Subdrars 2011           Subdrars 2013         Subdrars 2011           Subdrars 2013         Subdrars 2011           Subdrars 2011         Subdrars 2011           Subdrars 2013         Subdrars 2011           Subdrars 2013         Subdrars 2011           Subdrars 2014         Subdrars 2011           Subdrars 2013         Subdrars 2011           Subdrars 2011         Subdrars 2011	$eq:linear_line$	modifica SD 9 7.56 10 7.4 4.37, df = 4.37, df = 0.67 0.85 0.67 0.85 0.67 0.83 0.68 24.80, df = 0.12) modifica SD 2.02 2.37 5.00, df = SD 2.52 2.6 0.55 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.85 2.6 0.55 2.6 0.85 2.6 0.55 2.6 0.85 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 2.6 0.55 0 0 0 0 0 0 0 0 0 0 0 0 0	$\begin{array}{c} {\rm Total} \\ {\rm 265} \\ {\rm 151} \\ {\rm 311} \\ {\rm 161} \\ {\rm 46} \\ {\rm 834} \\ {\rm e4} \\ {\rm (P} = \\ {\rm 0} \\ {\rm 151} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 152} \\ {\rm 61} \\ {\rm 265} \\ {\rm 61} \\ {\rm 152} \\ {\rm 61} \\ {\rm 152} \\ {\rm 61} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 152} \\ {\rm 61} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 151} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 151} \\ {\rm 151} \\ {\rm 151} \\ {\rm 152} \\ {\rm 151} \\ {\rm 15$	Mean -0.4 -0.4 -0.4 -0.4 -0.4 -0.4 -0.2 -0.36); F C Mean -0.28 <0.000 C Mean -0.28 0.38 0.085 0.38 0.085 0.38 0.085 0.38 0.085 0.38 0.085 0.38 0.085 0.38 0.085 0.38 0.085 0.295; F C C C C C C C C C C C C C	SD         SD           9         9         9           0         8.2         9,98           0.10         8.2         9,98           0.11         8.2         9,98           0.011         0.82         0.58           0.78         0.78         0.78           0.78         0.78         0.78           0.78         0.78         5.57           22         2.24         2.11           1.9         5.57         28           0.56         26         0.52           0.56         26         0.94	257 150 330 60 42 839 Total 257 150 152 60 152 60 42 661 84% Total 257 150 152 661 84%	30.1% 22.5% 29.9% 10.2% 4.1% 100.0% Weight 37.8% 2.1.5% 100.0% Weight 37.8% 2.2.3% 13.6% 2.3% 3.1.% 3.1.% 3.1.% 3.1.% 3.1.% 5.5%	IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.38 [0.48, 0.42]           Mean Difference           -0.35 [-4.68, 0.24]           -0.35 [-4.68, 0.24]           -0.35 [-4.68, 0.24]           -0.36 [-4.64, 0.24]           -0.37 [-0.85, 0.29]           -0.37 [-0.85, 0.29]           -0.37 [-0.85, 0.29]           -0.46 [-4.02, 0.44, 0.01]           -0.46 [-4.02, 0.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01] <td>Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V. Random V.</td> <td>i 95% Cl </td> <td></td>	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f         Study or Subgroup           DPS 2001         DPS 2001           Undahl 2009         Salte 2011           Salte 2011         Salte 2011           Salte 2011         Salte 2011           Salte 2012         Total (95% CI)           relerogeneity: Tau* =         Test for overall effect:           Salte 2013         Salte 2011           Salte 2013         Salte 2011           Salte 2014         Salte 2011           Salte 2015         Salte 2011           Salte 2016         Salte 2011           Salte 2017         Salte 100           Salte 2018         Salte 2011           Salte 2019         Salte 2011	Lifestyle Maanle Maanle 1.000000000000000000000000000000000000	modifica           SD           9           7.56           10           7.4           11.33           4.37, df =           <0.0001	$\begin{array}{c} \hline { Total } \\ 265 \\ 151 \\ 311 \\ 46 \\ 834 \\ 4 \ (P = ) \\ ) \\ \hline \\ 152 \\ 151 \\ 161 \\ 46 \\ 675 \\ 151 \\ 152 \\ 61 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 61 \\ 151 \\ 152 \\ 151 \\ 151 \\ 152 \\ 151 \\ 1$	Mean. -3.3 -0.4 -0.4 -1 -2 -0.36); F C C Mean. 0.06 0.08 0.08 0.085 0.38 € 0.000 C C Mean. -0.28 0.85 0.89 0.85 0.80 0.85 0.85 0.85 0.85 0.85 0.85	SD         SD           9         9         9           0         8.2         9,98           0.10         8.2         9,98           0.11         8.2         9,98           0.011         0.82         0.58           0.78         0.78         0.78           0.78         0.78         0.78           0.78         0.78         5.57           22         2.24         2.11           1.9         5.57         28           0.56         26         0.52           0.56         26         0.94	257 150 330 330 60 42 839 70 150 42 661 84% 70 50 42 661 84% 70 50 42 661 527 150 60 42 661 527 152 60 42 57 152 57 150 152 60 42 57 150 152 152 60 42 152 152 152 152 152 152 152 152 152 15	30.1% 25.6% 4.1% 4.1% 4.1% Weight 23.1% 20.6% 21.5% 20.6% 21.5% 100.0% Weight 100.0% Weight 13.6% 2.3% 31.1% 13.6% 31.1% 13.3%	IV. Random. 95% CI           2.00 [534, -0.46]           -3.00 [4.49, -1.61]           -1.00 [-2.55, 0.55]           -3.01 [54, -0.46]           -2.01 [53, 0.55]           -2.17 [-6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.39, 0.63]           -0.28 [0.39, 0.64]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.49]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.28 [0.40, 0.41]           -0.45 [0.40, 0.42]           -0.45 [0.41, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]           -0.45 [0.21, 0.41]	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f         Study or Subgroup.           DPS 2001         DPS 2001           DPS 2001         State 2019           Satio 2019         State 2019           Satio 2012         Total (95% CI)           Telest (or overall effect:         State 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Jondahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           DPS 2001         Contact (95% CI)           Heterogeneity: Tau <sup>2</sup> =         Teat (1000           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakoto 2011           Study 2001         Study 2001           Indahl 2003         Sakoto 2011           Study 2001         Study 2001           Study 2001         Study 2001           Study 2002         Study 2001	Lifestyle $Maan e = 1$ ( $Maan e = 1$ ) ( $Maan = 1$	modifica SD 9 9 7.56 10 7.4 4.37, df = 11.33 4.37, df = 0.67 0.85 24.80, df 24.80, df = 0.67 0.85 24.80, df = 0.12) modifica SD 0.67 0.85 2.13 1.89 2.03 2.19 2.00 2.00 0.0001 3.20 2.10 3.20	Total           265           151           311           61           46           834           47           675           675           675           675           675           676           677           676           677           675           676           677           675           676           677           675           676           677           7041           152           61           675           676           677           675           676           677           676           677           7041           152           615           311           616           834	Maan -3 -0.4 -0.4 -1 -2 0.36); F C Mean 0.06 0.08 -0.19 -0.29; F C C Mean -0.29; F C C Mean -0.49 -0.55 0.38 -0.4 -0.4 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	$\frac{\text{SD}}{\text{P}} = 7.42$ 100 8.2 9.98 and and a set of the set of	257 150 330 60 42 839 701 50 152 60 42 661 84% 700 152 60 152 60 42 661 5 757 150 152 60 42 661 5 757 150 152 60 42 839	30.1% 22.5% 29.9% 10.2% 4.1% 100.0% Weight 37.8% 2.1.5% 100.0% Weight 37.8% 2.2.3% 13.6% 2.3% 3.1.% 3.1.% 3.1.% 3.1.% 3.1.% 5.5%	IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.38, 0.17]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.28 [0.48, 0.41]           -0.38 [0.48, 0.42]           Mean Difference           -0.35 [-4.68, 0.24]           -0.35 [-4.68, 0.24]           -0.35 [-4.68, 0.24]           -0.36 [-4.64, 0.24]           -0.37 [-0.85, 0.29]           -0.37 [-0.85, 0.29]           -0.37 [-0.85, 0.29]           -0.46 [-4.02, 0.44, 0.01]           -0.46 [-4.02, 0.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01]           -0.25 [-4.44, 0.01] <td>Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V. Random V.</td> <td>i 95% Cl </td> <td></td>	Lifestyle modification C V. Random V. Random V. Random V. Random V. Random V. Random V. Random Lifestyle modification C V. Random V.	i 95% Cl 	
f	Lifestyle Maan -5 -3, 7 -2 -4, 12 -4, 1	modifica SD 9 9 7,456 (1) 10 7,4 4,37, df = (2) 0,67 0	Total           265           151           311           61           46           834           47           675           675           675           675           675           676           677           676           677           675           676           677           675           676           677           675           676           677           7041           152           61           675           676           677           675           676           677           676           677           7041           152           615           311           616           834	Maan -3 -0.4 -0.4 -1 -2 0.36); F C Mean 0.06 0.08 -0.19 -0.29; F C C Mean -0.29; F C C Mean -0.49 -0.55 0.38 -0.4 -0.4 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	$\frac{\text{SD}}{\text{P}} = 7.42$ 100 8.2 9.98 and and a set of the set of	257 150 330 60 42 839 701 50 152 60 42 661 84% 700 152 60 152 60 42 661 5 757 150 152 60 42 661 5 757 150 152 60 42 839	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 100.0% Weight 31.1% S 5.5%	IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [-3.06, -1.24]           Mean Difference           IV. Random. 95% CI           0.28 [0.39, 0.17]           -0.38 [0.49, 0.11]           0.20 [0.30, 3.7]           0.21 [0.42, 0.01]           0.21 [0.42, 0.01]           0.21 [0.52, 0.00]           -0.17 [-0.38, 0.04]           Mean Difference           IV. Random. 95% CI           0.95 [-163, 0.20]           -0.57 [-0.85, -0.29]           0.56 [-163, 0.20]           -0.57 [-0.85, -0.29]           0.57 [-0.85, -0.29]           10.40 [-0.21, 0.14]           -0.25 [-0.30, 0.37]           -0.57 [-0.85, -0.29]           0.57 [-0.85, -0.29]           0.57 [-0.85, -0.29]           0.51 [-0.31, 0.00]           0.77 [-0.18, 0.32]           0.25 [-0.11 [-0.53, 0.31]	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Mean Diffe U. Randem Lifestyle modification C Std. Mean D U. Randem	i 95% Cl 	
f         Study or Subgroup.           DPS 2001         DPS 2001           DPS 2001         State 2019           Satio 2019         State 2019           Satio 2012         Total (95% CI)           Telest (or overall effect:         State 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Jondahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           DPS 2001         Contact (95% CI)           Heterogeneity: Tau <sup>2</sup> =         Teat (1000           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup         DPS 2001           Indahl 2009         Sakoto 2011           Study 2001         Study 2001           Indahl 2003         Sakoto 2011           Study 2001         Study 2001           Study 2001         Study 2001           Study 2002         Study 2001	Lifestyle Maan -5 -3, 7 -2 -4, 12 -4, 1	modifica SD 9 9 7,456 (1) 10 7,4 4,37, df = (2) 0,67 0	Total           265           151           311           61           46           834           47           675           675           675           675           675           676           677           676           677           675           676           677           675           676           677           675           676           677           7041           152           61           675           676           677           675           676           677           676           677           7041           152           615           311           616           834	Maan -3 -0.4 -0.4 -1 -2 0.36); F C Mean 0.06 0.08 -0.19 -0.29; F C C Mean -0.29; F C C Mean -0.49 -0.55 0.38 -0.4 -0.4 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	$\frac{\text{SD}}{\text{P}} = 7.42$ 100 8.2 9.98 and and a set of the set of	257 150 330 60 42 839 701 50 152 60 42 661 84% 700 152 60 152 60 42 661 5 757 150 152 60 42 661 5 757 150 152 60 42 839	30.1% 25.6% 29.9% 10.2% 4.1% 100.0% Weight 23.1% 21.5% 100.0% Weight 31.1% S 5.5%	IV. Random. 95% CI           2.00 [3.4, 0.46]           -3.00 [4.49, 9.1, 61]           -1.00 [2.55, 0.55]           -3.10 [5.88, 0.32]           -2.17 [6.62, 2.28]           -2.15 [3.06, -1.24]           Mean Difference           IV. Random. 95% CI           0.28 [0.39, 0.17]           0.20 [0.30, 3.7]           0.20 [0.30, 3.7]           0.21 [0.48, 0.11]           0.20 [0.30, 0.37]           0.21 [0.48, 0.11]           0.20 [0.30, 0.37]           0.21 [0.52, 0.00]           -0.17 [-0.38, 0.04]           Mean Difference           IV. Random. 95% CI           0.35 [-105, 0.01]           0.35 [-105, 0.01]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-1048, -0.21]           0.35 [-103, 0.20]           0.35 [-103, 0.20]           0.35 [-1048, -0.21]           0.35 [-1048, -0.22]           0.4 [-164,	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	i 95% Cl 	+2
f         Study or Subgroup.           DPS 2001         DPS 2001           Study or Subgroup.         Study or Subgroup.           Study or Subgroup.         Total (9% C1)           Helenogoneity. Tau* =         Test for overall effect:           Study or Subgroup.         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup.         DPS 2001           Indahl 2009         Sakane 2011           Study or Subgroup.         DPS 2001           Jest for overall effect:         DPS 2001           Jest for overall effect.         Study or Subgroup.           DPS 2001         Sakane 2011           Study or Subgroup.         DPS 2001           Jest for overall effect.         Study or Subgroup.           DPS 2001         Jest for overall effect.           Study or Subgroup.         DPS 2001           Jest for overall effect.         Study 2005           Study 2012         Total (95% C1)           Heterogeneity. Tou* =         Total (95% C1)           Heterogeneity. Tou* =         Total (95% C1)           Heterogeneity. Tou* =         Total (95% C1)	Lifestyle Maanue Maanue Maanue 2 2 2 2 2 2 2 2 2 2 2 2 2	modificat SD SD SD SD SD SD SD SD SD SD	$\begin{array}{c} \hline { Total } \\ \hline \\$	Maan -0.4 -0.4 -1 -1 -2 0.36); F C C Mean 0.55 0.38 -0.19 0.55 0.38 -0.18 -0.55 0.38 -0.18 -0.55 0.38 -0.48 -0.48 -0.48 -0.48 -0.48 -0.48 -0.55 0.38 -0.45 -0.28 -0.28 -0.28 -0.28 -0.29); F C C Mean -0.28 -0.28 -0.29); F -0.28 -0.29); F -0.29); F -0.29	$\frac{\text{SD}}{\text{SD}} = \frac{9}{2}$	257 150 330 60 42 839 <b>Total</b> 257 150 42 60 42 661 5 7 150 42 661 5 7 150 330 42 839	30.1% 25.6% 29.9% 4.1% 100.2% 4.1% 100.0% Weight 33.1% 21.5% 100.0% Weight 13.6% 2.1% 100.0% S S S S S S S S S S S S S S S S S S S	IV. Random. 95% CI           -2.00 [3-4, -0.46]           -3.00 [4-99, -1.61]           -1.00 [2-55, 0.55]           -3.10 [5-88, -0.32]           -2.17 [5-68, -0.32]           -2.17 [5-68, -0.42]           -2.17 [5-68, -0.42]           -2.17 [5-62, 2.28]           -2.17 [5-62, 2.28]           -0.28 [0-39, -0.17]           -0.30 [0-40, -0.18]           -0.20 [0-32, 0.16]           -0.21 [0-32, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.26 [-0.52, 0.06]           -0.27 [-0.38, 0.04]           Mean Difference           IV. Random, 95% CI           -0.55 [-10.9, 0.20]           -0.57 [-0.85, -0.28]           -0.54 [-1.64, 0.10]           -0.54 [-1.64, 0.27]           -0.57 [-0.85, -0.28]           td. Mean Difference           IV. Random .95% CI           -0.54 [-1.64, 0.27]           -0.57 [-0.85, -0.28]           -0.51 [-0.31, 0.00]           0.71 [-0.38, 0.03]           0.71 [-0.43, 0.03]           0.71 [-0.53, 0.31]           0.71 [-0.53, 0.31]           0.71 [-0.53, 0.31]           0.71 [-0.58, 0.02]	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
f	$eq:linear_line$	modifica SD 9 9 7,456 50 0,67	$\begin{array}{c} \hline { Total } \\ \hline { 1 \\ 265 \\ 151 \\ 311 \\ 61 \\ 61 \\ 834 \\ 834 \\ 834 \\ 44 \\ (P = 1 \\ 101 \\ 265 \\ 151 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\ 15$	Mean -3 -3 -3 -3 -3 -3 -3 -3 -3 -3	SD         9           9         7.42           100         8.2           9.98         8           8         9.98           0         8.2           9.98         0.50           0.067         0.86           0.58         0.58           0.58         0.58           1); i² =         2.22           2.34         1.9           5.57         2.22           2.41         1.9           5.57         2.80           2.80         2.66           0.58         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9           9.98         3.9	257 150 330 60 42 839 <b>Total</b> 257 152 60 42 661 84% <b>Total</b> 257 152 60 42 661 52 661 52 839 839 839	30.1% 25.6% 29.9% 4.1% 100.2% 4.1% 100.0% Weight 100.0% Weight 100.0% S Weight	IV. Random. 95% CI           -2.00 (3.4, -0.46)           -3.00 (4.99, -1.61)           -1.00 (2.55, 0.55)           -3.10 (5.88, -0.32)           -2.17 (5.62, 2.38)           -2.15 (-3.06, -1.24)           Mean Difference           IV. Random. 95% CI           -0.28 (-0.39, -0.17)           -0.28 (-0.39, -0.17)           -0.29 (-0.39, -0.17)           -0.20 (-0.39, -0.17)           -0.21 (-0.39, -0.17)           -0.25 (-0.30, -0.37)           -0.25 (-0.30, -0.20)           -0.21 (-0.39, -0.21)           -0.25 (-0.30, -0.20)           -0.21 (-0.49, -0.11)           -0.25 (-0.30, -0.20)           -0.27 (-0.48, -0.42)           -0.26 (-0.39, -0.20)           -0.37 (-0.85, -0.29)           -0.37 (-0.85, -0.29)           -0.40 (-0.21, -0.44, -0.01)           -0.26 (-0.44, -0.01)           -0.27 (-0.44, -0.01)           -0.28 (-0.40, -0.30)           -0.37 (-0.85, -0.29)           -0.41 (-0.53, -0.31)           -0.30 (-0.74, -0.30)           -0.10 (-0.20, -0.00]           -0.10 (-0.20, -0.01)           -0.10 (-0.20, -0.02)           td. Mean Difference           U. Random. 95% CI <td>Lifestyle modification C</td> <td>serve cell     serve celll     serve celll     serve celll     serve cell     serve cell</td> <td>+2</td>	Lifestyle modification C	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
f         Study or Subgroup.           DPS 2001         DPS 2001           DPS 2001         Study or Subgroup.           Satio 2012         Total (9% C1)           Total (9% C1)         Teleforgenetity. Tau* =           Test for overall effect:         3           Study or Subgroup.         DPS 2001           Inidahl 2009         Sakane 2011           Study or Subgroup.         DPS 2001           Inidahl 2009         Sakane 2011           Study or Subgroup.         DPS 2001           DPS 2001         Sakane 2011           Study or Subgroup.         DPS 2001           Total (9% C1)         Teleterogeneity. Tau* =           Test for overall effect:         3           Study or Subgroup.         DPS 2001           Inidahl 2009         Sakane 2011           Study or Subgroup.         DPS 2001           Inidahl 2009         Saloto 2011           Study or Subgroup.         DPS 2001           Inidahl 2009         Saloto 2011           Study or Subgroup.         Test for overall effect:           j         Study or Subgroup.           DPS 2001         Test for overall effect:           j         Study or Subgroup.           DPS 2001	Lifestyle Maanue Maanue Maanue 4. Maanue 2. 2 2. 2 2. 2 2. 2 4. 17 1. 0: Chi <sup>2</sup> = 4. 2. 2 4. 17 0. 10: Chi <sup>2</sup> = 4. 0. 0: Chi <sup>2</sup> = 2. 0. 12 0. 0: Chi <sup>2</sup> = 2. 0. 0: 2. 0: 2. 0. 0: 2. 0: 2. 0: 1. 0: 0: 2. 0: 2. 0: 1. 0: 0: 0: 2. 0: 2. 0: 1. 0: 0: 0: 0: 2. 0: 2. 0: 1. 0: 0: 0: 0: 0: 1. 2. 0: 0: 0: 0: 0: 1. 2. 0: 0: 0: 0: 0: 0: 0: 0: 0: 0: 0: 0: 0: 0	modificat SD 	$\begin{array}{c} \hline { Total } \\ \hline \\ 265 \\ 265 \\ 151 \\ 311 \\ 61 \\ 61 \\ 834 \\ 46 \\ (P = \\ 9) \\ \hline \\ 152 \\ 61 \\ 152 \\ 61 \\ 152 \\ 61 \\ 675 \\ 675 \\ 61 \\ 152 \\ 61 \\ 675 \\ 61 \\ 152 \\ 61 \\ 152 \\ 61 \\ 152 \\ 61 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\ 152 \\ 61 \\ 152 \\$	Maan. -3.1 -0.4 -1.1 -3.1 -2 0.36); F C Mean -0.19 -0.5 0.89 0.05 0.38 c 0.36); C Mean -0.1 0.55 0.38 c 0.36 0.55 0.38 c 0.36 0.55 0.38 c 0.36 0.55 0.38 c 0.36 0.55 0.38 c 0.36 0.55 0.38 c 0.36 0.39 1 1 0.65 0.39 0.29); F C C Mean -0.19 1 0.01 0.39); F   c C Mean -0.19 1 0.39); F	SD         9           9         7.42           10         8.2           9.98         8.2           8.2         9.98           * = 9%         0.10           SD         0.07           0.067         0.86           0.58         0.58           1);  2 =         0.0110           SD         2.32           2.34         2.11           9.5.57         2           2.34         2.31           2.54         2.66           2.6         2.6           2.6         2.6           2.8         3.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         3.8	257 150 330 60 42 839 <b>Total</b> 257 150 42 661 5 60 42 661 5 60 42 661 5 7 50 60 42 839 7 7 50 60 42 839 7 7 50 60 42 839 7 7 50 60 42 839 7 7 50 60 42 839 7 7 50 7 50 7 50 7 50 7 50 7 50 7 50 7	30.1% 22.5% 29.9% 4.1% 100.2% 4.1% 100.0% Weight 12.3.1% 100.0% Weight 17.9% 100.0% S S Weight 18.3% 5.5% 100.0% S S S S S S S S S S S S S	IV. Random. 95% CI           -2.00 [-3.4, -0.46]           -3.00 [-4.9, -1.61]           -3.01 [-4.9, -1.61]           -1.00 [-2.55, 0.55]           -3.10 [-5.81, -0.32]           -2.17 [-6.62, 2.28]           -2.17 [-6.62, 2.28]           -2.17 [-6.62, 2.28]           -2.17 [-6.62, 2.28]           -2.17 [-6.62, 2.28]           -2.17 [-6.62, 2.28]           -2.17 [-0.28, 0.36, -1.74]           -0.28 [-0.38, -0.17]           -0.28 [-0.38, -0.17]           -0.28 [-0.38, 0.04]           Mean Difference           IV. Random, 95% CI           -0.26 [-0.52, 0.00]           -0.17 [-0.38, 0.04]           Mean Difference           IV. Random, 95% CI           -0.55 [-1.05, 0.01]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.29]           -0.57 [-0.65, -0.20]           -0.51 [-0.02, -0.00]           -0.51 [-0.02, -0.00]           -0.51 [-0.02, -0.00]           0.51 [-0.02, -0.00]	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
f         Subgroup           PPS 2001         Incluit 2009           Incluit 2009         Suble 2009           Suble 2009         Suble 2009           Sakane 2011         Suble 2009           Suble 2009         Suble 2001           Suble 2001         Suble 2001           Suble	Lifestyle $\frac{Maan}{2}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{1}{3}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{3}$ $\frac$	modificat SD 9 9 7.3 4.37, df -1 11.33 4.37, df -1 35 0.68 0.7 4.33, df = 0.12 1.89 0.68 0.7 2.37 2.02 2.37 5.00, df = 0.23 2.00 2.00, df = 0.040 1.85 0.041 5.00, df = 0.041 7 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 1.89 0.85 0.8	$\begin{array}{c} \hline { Total } \\ 2 \\ 2 \\ 2 \\ 5 \\ 1 \\ 5 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1$	Maan -3 -0.4 -1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -2 -3.1 -3.1 -2 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1	SD         9           9         7.42           10         8.2           9.98         8           * = 9%         9.98           * = 9%         0.167           0.067         0.86           0.58         0.58           1);  * =         0.078           0.58         2.32           2.32         2.34           2.11         1           5.57         2.34           2.54         2.34           0.56         26           0.58         2.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         8           0.58         8           0.58         8           0.14         5.14	257 150 330 60 42 839 Total 257 150 152 661 84% 70tal 257 150 152 661 42 661 50 42 661 50 42 661 50 42 839 70tal 839 70tal 839 70tal 839 70tal 839 70tal 839 70tal 839 70tal 839 70tal 700	30.1% 25.6% 29.9% 4.1% 100.2% 4.1% 100.0% Weight 23.1% 21.5% 21.5% 21.7% 23.7% 100.0% S S Weight 18.3% 5.5% 100.0% S S 31.1% 18.3% 5.5% 100.0%	IV. Random. 95%; CI           -2.00 [3-4; -0.46]           -3.00 [4-99, -1.61]           -1.00 [2-55, 0.55]           -3.10 [5-88, -0.32]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.28]           -2.17 [6.62, 2.38]           -2.17 [6.62, 2.38]           -2.17 [0.62, 0.28]           -0.28 [0.33, 0.17]           -0.39 [0.43, 0.17]           -0.30 [0.44]           -0.21 [0.43, 0.17]           -0.30 [0.43, 0.17]           -0.30 [0.44]           -0.26 [0.52, 0.00]           -0.27 [0.43, 0.04]           Mean Difference           IV. Random, 95%; CI           -0.55 [-1.05, 0.01]           -0.57 [-0.38, 0.04]           -0.57 [-0.38, 0.29]           -0.57 [-0.48, -0.29]           -0.57 [-0.85, -0.29]           -0.57 [-0.85, 0.31]           -0.37 [-0.85, 0.31]           -0.11 [-0.30, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.11 [-0.50, 0.31]           -0.15 [-0.02, 0.30]	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
f	$eq:linear_line$	modifica SD 9 9 7,556 30 4,37, df = (3,7, df = 50,065 0,65 0,65 0,65 0,65 0,65 0,65 0,65 0,65 24,80, df = 0,12) modifica SD 2,31 2,37 2,37 2,37 2,37 2,02 2,37 5,00, df = 0,65 2,2,37 5,00, df = 0,65 2,2,37 4,13, df = 0,65 2,2,37 4,13, df = 0,65 2,2,37 2,2,37 5,00, df = 0,65 2,2,37 2,2,37 5,00, df = 0,65 2,2,37 2,2,2 2,3,7 3,5,35 2,6,55 2,75	$\begin{array}{c} \hline { Total } \\ \hline \\$	Maan -3 -0.4 -1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -2 -3.1 -3.1 -2 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1	SD         9           9         7.42           100         8.2           9.98         8           2         9.98           0         0.10           SD         0.67           0.68         0.682           0.58         0.58           11); I* =            2.22         2.34           2.1         1.9           5.57            2.22         2.34           2.1         1.9           5.57            2.22         2.34           0.58            5.57            2.22         2.34           0.58            5.57            2.8         0.10           2.8         0.56           2.6         0.58           0.58            3.94         0.58           3.95            3.94         0.58           3.95            3.96            3.97            3.96	257 150 330 60 42 839 Total 257 150 152 60 42 661 84% Total 257 150 152 661 257 150 152 661 257 150 152 839	30.1% 22.5% 29.9% 4.1% 100.2% 4.1% 100.0% 20.6% 21.5% 100.0% Weight 10.0% Weight 13.1% 31.1% 5.5% 100.0% S S S S S S S S S S S S S	IV. Random. 95% CI           -2.00 (3.4, -0.46)           -3.00 (4.99, -1.61)           -1.00 (-2.55, 0.55)           -3.10 (-5.88, -0.32)           -2.17 (-5.68, -0.32)           -2.17 (-5.62, -2.83)           -2.15 (-3.06, -1.24)           Mean Difference           IV. Random, 95%, CI           -0.28 (-0.39, -0.77)           -0.30 (-0.49, -0.11)           -0.20 (-0.39, -0.72)           -0.21 (-0.39, -0.72)           -0.25 (-0.30, 0.37)           -0.26 (-0.39, -0.26)           -0.26 (-0.39, -0.27)           -0.37 (-0.48, -0.11)           -0.26 (-0.39, -0.26)           -0.27 (-0.48, 0.41)           Wean Difference           V.V. Random, 95%, CI           -0.35 (+0.30, -0.20)           -0.37 (-0.85, -0.29)           -0.47 (-0.48, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.21, -0.44, -0.41)           -0.40 (-0.22, -0.40)           -0.41 (-0.53, -0.31)	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
f         Subgroup           PPS 2001         Incluit 2009           Incluit 2009         Suble 2009           Suble 2009         Suble 2009           Sakane 2011         Suble 2009           Suble 2009         Suble 2001           Suble 2001         Suble 2001           Suble	Lifestyle $\frac{Maan}{2}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{4}{3}$ $\frac{1}{3}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{2}$ $\frac{1}{3}$ $\frac$	modificat SD 9 9 7.3 4.37, df -1 11.33 4.37, df -1 35 0.68 0.7 4.33, df = 0.12 1.89 0.68 0.7 2.37 2.02 2.37 5.00, df = 0.23 2.00 2.00, df = 0.040 1.85 0.041 5.00, df = 0.041 7 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 8 0.77 1.89 0.85 0.8	$\begin{array}{c} \hline { Total } \\ 2 \\ 2 \\ 2 \\ 5 \\ 1 \\ 5 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1$	Maan -3 -0.4 -1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -3.1 -2 -2 -3.1 -3.1 -2 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1 -3.1	SD         9           9         7.42           10         8.2           9.98         8           * = 9%         9.98           * = 9%         0.167           0.067         0.86           0.58         0.58           1);  * =         0.078           0.58         2.32           2.32         2.34           2.11         1           5.57         2.34           2.54         2.34           0.56         26           0.58         2.8           0.58         3.8           0.58         3.8           0.58         3.8           0.58         8           0.58         8           0.58         8           0.14         5.14	257 150 330 60 42 839 Total 257 150 152 661 84% <b>Total</b> 257 150 152 661 42 661 5 7 839 839 <b>Total</b> 257 150 152 60 42 839	30.1% 25.6% 29.9% 4.1% 100.2% 4.1% 100.0% Weight 23.1% 21.5% 21.5% 21.7% 23.7% 100.0% S S Weight 18.3% 5.5% 100.0% S S 31.1% 18.3% 5.5% 100.0%	IV. Random. 95% CI           -2.00 (53.4, -0.46)           -3.00 (14.99, -1.61)           -1.00 (25.56, 0.55)           -3.10 (5.88, -0.32)           -2.17 (56.82, -0.32)           -2.17 (56.82, -0.32)           -2.17 (56.82, -0.32)           -2.17 (56.82, -0.32)           -0.28 (-0.33, -0.17)           -0.38 (-0.43, -0.17)           -0.39 (-0.43, -0.17)           -0.31 (-0.43, -0.17)           -0.28 (-0.33, -0.17)           -0.28 (-0.32, 0.01)           -0.28 (-0.32, 0.02)           -0.17 (-0.38, 0.04)           Mean Difference           IV. Random, 95% CI           -0.55 (-10.50, 0.01)           -0.55 (-10.50, 0.01)           -0.55 (-10.60, 0.01)           -0.57 (-0.85, -0.29)           -0.57 (-0.85, -0.29)           -0.57 (-0.85, -0.29)           -0.57 (-0.85, -0.29)           -0.57 (-0.85, -0.29)           -0.51 (-0.20, -0.00)           -0.71 (-0.19, 0.52)           -0.11 (-0.53, 0.31)           -0.10 (-0.20, -0.00]           10.15 (-0.20, 0.20)           11.10 (-0.20, 0.20)           10.15 (-0.20, 0.20)           10.15 (-0.20, 0.20)           10.15 (-0.20, 0.20)	Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Lifestyle modification C Std. Mean Diffe	serve cell     serve celll     serve celll     serve celll     serve cell     serve cell	+2
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FIGURE 4 | Traditional meta-analysis of the effect on physical conditions: Lifestyle modification vs. Control. (a–j) BMI (kg/m<sup>2</sup>), body weight (kg), waist circumference (cm), hip circumference (cm), systolic pressure (mmHg), diastolic pressure (mmHg), fasting blood glucose (mg/dL), 2 h postprandial blood glucose (mg/dL), total cholesterol (mmol/L, mg/dL), HDL (mmol/L, mg/dL).



FIGURE 5 | Traditional meta-analysis of the effect on physical conditions: Medicine vs. Control. (a–f) BMI (kg/m<sup>2</sup>), systolic pressure (mmHg), diastolic pressure (mmHg), fasting blood glucose (mg/dL), 2 h postprandial blood glucose (mg/dL), total cholesterol (mmol/L, mg/dL).

expensive, researchers need to consider interventions beyond the optimal intervention. The order of interventions can be ranked according to the size of the SUCRA value. Because this article explores the adverse event rates of diabetes, the greater the value, the less prioritized is the intervention (**Figure 3**).

Consistent with the findings of previous studies (47), statins exposed participants to an incidence of diabetes greater than that of control and other intervention groups. The slight difference of LST, Lifestyle and LSM suggested a lack of evidence for supporting the superiority



of lifestyle modification and these two pharmacological combination therapies.

The results of GI, LSM and SU ( $I^2 = 72.5\%$ , 48.2%, 70.6%) exhibited high heterogeneity vs. control (**Supplementary Figure 1**). We suspect that each of GI, SU, or LSM contains two or more medicine or lifestyle interventions, possibly explaining the higher heterogeneity.

## **Physical Consequence of Interventions**

Traditional meta-analysis supported the benefits of both lifestyle modification and anti-diabetic medication. Lifestyle modification with a duration of at least 1 year decreases body mass index (BMI), body weight, waist and hip circumference, systolic and diastolic blood pressure, 2-h postprandial blood glucose, and increases serum HDL (**Figure 4**). BMI, body weight, waist and hip circumference, systolic pressure and fasting blood glucose exhibited high heterogeneity (I<sup>2</sup> value exceeded 50%, I<sup>2</sup> = 95, 87, 84, 56, 73, and 84% respectively); however, all these individual trials supported physical improvements except for fasting blood glucose. Anti-diabetic medication (including GLP-1RAs and insulin-sensitizing agents) decreased BMI, systolic blood pressure, fasting blood glucose and 2-h postprandial blood glucose (**Figure 5**).

## **Trial Sequential Analysis**

TSA was performed to evaluate random errors caused by limited data and repetitive testing of accumulating data. The cumulative z-curve crossed both the traditional boundary and the trial sequential monitoring boundary but not the futility boundary, suggesting firm evidence for an average of 20% relative risk reduction of diabetes with lifestyle modification (**Figure 6**). Similarly, TSA supported sufficient evidence for 20% relative increased risk of diabetes with statins and 20% relative risk reduction of diabetes with metformin (**Supplementary Figure 2A**). The lack of evidence for a 30%, 60% and 25% relative risk reduction in diabetes with GI, orlistat and sulfonylureas demands larger trials (**Supplementary Figure 2B**). Other intervention strategies failed to establish such an analysis for the limited information size.

## **Credibility Analysis**

We assessed several biases using Cochrane Collaboration's tool rating risk bias (**Figures 7A,B**). However, when trials assigned participants to undertake lifestyle modification, the potential allocation concealment were generated, increasing the likelihood of significant findings (48). Therefore, we should understand that the effects of lifestyle modification were at risk of exaggeration. Various definitions of the IFG, IGT, pre-diabetes and diabetes definitions in the trials may also interfere with the final results.

## DISCUSSION

A total of 32 RCTs with available data contributed to this trial analysis, including traditional and network meta-analyses, TSA of the incidence of diabetes and a traditional meta-analysis of physical conditions.

Compared to placebo (**Figure 2A**), GLP-1RAs (0.28, [0.15, 0.50]), TZM (0.33, [0.16, 0.63]), and TZD (0.39, [0.27, 0.53]) significantly delayed the progression of diabetes; however, the limited sample size and the small quantity of studies caused



FIGURE 7 | (A) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included 32 studies. (B) Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

instability of this inference. The data of both GLP-1RAs and orlistat were captured from severely obese people (mean BMI = 39 and 37 respectively), contributing to potential inconsistency. Metformin is less effective in people with lower baseline BMIs or lower FPG concentrations than in those with higher values for these variables; the drug works by inhibiting endogenous glucose production (49). It is not as flexible as lifestyle modifications that can be adjusted according to the specific physical conditions of the individual. Several studies reported that vitamin D supplementation reduced the incidence of diabetes in patients with both pre-diabetes and vitamin D deficiency (50); however, our review, similar to Angellotti and Pittas (51) showed the controversial result that vitamin D did not protect the prediabetic population without vitamin D deficiency from developing diabetes. There is evidence suggesting that obesity patients are susceptible to GLP-1RAs (32) and orlistat (25) on the progression of diabetic prevention. For population with prediabetes and other metabolic disturbances, including higher body weight or blood pressure or dyslipidemia, lifestyle modification should be a considerable intervening measure. Current researches support that patients are expected to benefit from GI (42) and statins for cardiovascular risk reduction (29, 37).

According to a review of collected trials, Haw et al. (11) suggested that lifestyle modification was a promising longterm diabetes prevention strategy; nevertheless, its sustained protective effects relied on maintenance interventions, even intermittent ones. This was consistent with prior results, to the effect that lifestyle interventions can somewhat prevent the conversion of pre-diabetes into diabetes. TSA can verify type I errors, thus avoiding more experiments to re-confirm this result, resulting in a waste of resources. Furthermore, reductions in BMI, body weight, waist and hip circumference induced by lifestyle intervention are expected to improve individual physical conditions, because weight loss appears to be the key factor associated with reduced diabetes progression (11). Their findings supported the use of pharmacological interventions (weight loss and insulin-sensitizing agents) to reduce diabetes incidence, and when the drug is eliminated from the body, its therapeutic effect will be weakened or even disappeared. It was suggested that the differences in insulin sensitivity and insulin secretion between IGT and IFG, and the greater severity of the abnormalities when both coexist might predict different rates of progression to diabetes, and different pharmacological agents might be needed to treat the pathophysiology. Recently, Pang et al. (52) reported multiple-treatment comparisons to discuss various diabetes preventing strategies in China, filling an investigative gap in traditional Chinese medicine. For the first time, we summarized the previous overview of pre-diabetes studies, and have found that medications and lifestyle interventions improve individual physical metabolism variously, permitting caregivers to individualize preventive care appropriate to individual clinical characteristics. The associated risk reduction of lifestyle modification, including healthy meals, increased physical exercise and weight loss is more pronounced than the effect of any single factor alone.

In order to distinguish unfinished and completed conclusions, avoid exceeding experimental waste of resources and therefore

guiding the next step of clinical research, the collected studies were tested using TSA.

Despite the fact that this review performed trial sequential analysis of intervention strategies, the diabetes incidence was reported only once for ACEI, GLP-1RAs, LST, TZM and vitamin D, creating potential bias. Complications of diabetes increase patient suffering and mortality. Effective interventions may also delay or prevent complications, thereby significantly reducing the personal and public health burden of diabetes. Therefore, more relevant trials are needed to reinforce or further complement this review, especially for endpoints of clinical complications, such as cardiovascular events/death and data on cost-effectiveness.

## CONCLUSIONS

In adults with pre-diabetes, firm evidence supports the notion that lifestyle modifications and metformin reduces the incidence of diabetes with an average of 20% relative risk reduction, while statins increase the relative risk 20%. We found that lifestyle modifications, promising long-term strategies involving three factors (nutrition, exercise and weight loss) contribute to health by reducing BMI, body weight, waist and hip circumference, systolic and diastolic pressure, fasting and 2-h postprandial blood glucose, total cholesterol and by increasing HDL. We made this determination using TSA, avoiding further waste of experimental resources.

## CONSENT FOR PUBLICATION

The corresponding author had final responsibility for the decision to submit for publication.

## **AUTHOR CONTRIBUTIONS**

ZS and J-YC contributed equally to this work, including the conception and design research, data extraction, data analysis, and drafted the composition. Y-CP, H-CX, and J-WC contributed to statistical analysis. J-HY, RW, C-SZ, and L-XW conducted the proofreading work. JD contributed to crucial revisal of the treatise for important intellectual content.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fendo. 2019.00455/full#supplementary-material

**Supplementary Figure 1** | Heterogeneity test in network meta-analysis using I2 in pair-wise and network pooled comparison.

**Supplementary Figure 2 | (A)** TSA of metformin and statins. Effect of metformin vs. control on diabetes using a required information size of 3,388 participants in order to detect or reject a 20% RRR with a power of 80%; effect of statins vs. control on diabetes using a required information size of 15,632 participants in

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order to detect or reject a 20% relative increased risk with a power of 80%. **(B)** TSA of GI, orlistat and sulphonylureas. Effect of GI vs. control on diabetes using a required information size of 11,993 participants in order to detect or reject a 30% RRR with a power of 80%; effect of orlistat vs. control on diabetes using a required information size of 368 participants in order to detect or reject a 60% RRR with a power of 80%; effect of sulphonylureas vs. control on diabetes using a required information size of 1,003 participants in order to detect or reject a 25% RRR with a power of 80%.

Supplementary Table 1 | Database-appropriate terms and the text words.

Supplementary Table 2 | Description of lifestyle modification.

Supplementary Table 3 | Baseline characteristics of excluded trials.

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**Conflict of Interest Statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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