Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1 PRISMA flowchart



Study and country	Intervention	Provider	Delivery and Intensity	Duration	Comparison
Dong, 2016, China	Diet: 25-30kcal/kg/d if at least overweight, avoid greasy food Exercise: advice for aerobic 3-4x 30-60min/wk	Dietitian and exercise physiologist	Phone, 10minutes thi-monthly	2 years	Usual care
Sun, 2012, China	Diet: 25kcal/kg/day, low-fat, low-sugar, optimized mixed diet Exercise: advice to increase PA (23METs/h/wk) and exercise therapy (4METs/h/wk)	Physicians, hygienists, dietitians and nurses	Unclear	1 year	Basic healthy eating/exercise/weight loss advice
Wong, 2013, Hong Kong	Diet: hypoenergetic, low-fat, low-GI, varied, meal plans, and booklets Exercise: advice for 3-5x 30min/wk	Dietitian and exercise instructor	Face-to-face, individual, weekly for months 0-4 and monthly for months 5-12	1 year	Basic healthy eating/exercise/weight loss advice (Advice to reduce carbohydrate and fat intake and exercise 3x 30min/wk)
Cheng, 2017, China	Diet: 300-500kcal deficit/day if at least with overweight, low-carbohydrate with prepared meals Exercise: aerobic 2-3 times/wk, progressively increased	Nutritionist and exercise researcher	Face-to-face, 3x nutrition meetings, 2-3 exercise classes/week	8.6 months	Usual care: Maintain ordinary lifestyle
Abenavoli, 2017, Italy	Diet: 1400-1600kcal/d, Mediterranean Exercise: advice for daily physical activity	Unclear	Telephone, monthly	6 months	Usual care: Only monitored with the medical indication for weight loss
Axley, 2017, USA	Diet and exercise	Automated	Text messaging. 6x weekly	6 months	Basic healthy lifestyle/weight loss instructions
Eckard, 2013, USA	Arm 1: Diet: low-fat Arm 2: Diet: moderate-fat and low-processed- carbohydrate	Dietitian and exercise physiologist	Face-to-face, bi- monthly (diet)	6 months	Basic healthy eating/exercise/weight loss advice

eTable 1 Characteristics of the interventions of the included studies

	Diet (both arms): 500kcal deficit/day, received measuring cups and spoons and booklets Exercise (both arms): 1 class, log, pedometer and advice for -4-7x 20-60min/wk				
Promrat, 2010, USA	Diet: 1000-1500kcal/day, low-fat, meal replacements, meal plan, based on DPP Exercise: pedometer, log, advice for ≥200min/wk or 10,000steps/day	Nutritionist or health educator	Face to face, group, weekly for months 0-6 and biweekly for months 7-12	1 year (48 wk's)	Basic healthy lifestyle/weight loss instructions
Katsagoni, 2018, Greece	Diet: 1500-1800kcal/day, Mediterranean Exercise (for exercise group only): advice for 30min/day (also: advice for optimal sleep duration, and mid-day rest)	Dietitian	Face-to-face, group, fortnightly for months 0-2 and monthly for months 3-6	6 months	Minimal intervention
AbdEl-Kader, 2016, Saudi Arabia	Diet: 1200kcal/d, balanced Exercise: aerobic 3x 30min/wk on treadmill	Dietitians	Unclear	3 months	Usual care: Maintain ordinary lifestyle
Al-Jiffri, 2013, Saudi Arabia	Diet: 1200kcal/d, balanced Exercise: aerobic 3x30min/wk on treadmill	Dietitians	Unclear	Diet: 2 months Exercise: 3 months	Usual care: No intervention
Asghari, 2018, Iran	Diet: 500-1000kcal deficit/day, healthy	Nutritionist	Face to face, biweekly	3 months	Placebo Basic healthy lifestyle/weight loss instructions
St. George, 2009, Australia	Diet: 400-570kcal deficit/day, low in saturated fat and processed food, high in n-3 and fiber Exercise: advice for (mainly walking) ≥200min/wk	Dietitians and exercise physiologists	Face-to-face, individual, Low-intensity arm: 3x fortnightly	3 months	Basic healthy lifestyle/weight loss instructions

			Moderate-intensity arm: 6x fortnightly		
Lim, 2018, Singapore	Diet and exercise counselling for weight loss plus mobile app	Mobile app (unclear for counselling	Unclear	Unclear	Diet and exercise counselling
Selezneva, 2014, Russia	Diet: 1600-1700kcal/day	Unclear	Unclear	1 month	Isocaloric diet: 2500- 2700kcal/day
Armstrong, 2016, UK	Liraglutide: 1.8mg Standard recommendations for lifestyle modification	N/A	Subcutaneous injections, daily	12 months (48 wk's)	Placebo Standard recommendations for lifestyle modification
Khoo, 2017, Singapore	Liraglutide: 0.6mg and progressively increased to 3mg by 4 th week	N/A	Subcutaneous injections, daily	6 months	Diet: 400kcal deficit/day Exercise: advice for moderate-intensity 5-7x 30-60min/wk
Harrison, 2007, USA	Orlistat: 120mg Diet: 1400kcal/day Exercise: non-specific advice to increase PA	Research nurse and physician	Orlistat: 3x daily Diet: Face-to-face	Orlistat: 9 months (36 wk's) Diet: 1 month	Diet (as per the intervention group)
Ye, 2017, NR	Orlistat: 120mg	N/A	3x daily	6 months	Placebo
Zelber-Sagi, 2004, Israel	Orlistat: 120mg Diet: 25kcal/kg/day, low-fat, low in simple carbohydrates, balanced Exercise: advice for walking 3-4x 40min/wk	Nutritionist	Orlistat: 3x daily Diet: Face-to-face, individual, monthly	6 months	Placebo Diet and exercise (as per the intervention group)

Bahmanadabi,	Sibutramine: 15mg	Unclear	Sibutramine: daily	3 months	Diet: low-calorie
2011, Iran					
	Diet: low-calorie		Diet: Unclear		
Lee, 2012,	Gastric balloon	Dietitian and	Monthly	6 months	Sham surgery
Singapore		physiotherapist			
	Diet: 1200-1500kcal/day				Diet and exercise (as per
					the intervention group)
	Exercise: advice for walking/jogging 30min/day				
PA: physical activ	vity, wk: week				

eTable 2 Additional study characteristics

Study and country	Age (years)	BMI (kg/m ²)	Type 2 Diabetes	Hypertension
Dong, 2016, China	57 ± 6	25.8 ± 2.7	0%	NR
Sun, 2012, China	39 ± 15	37.9 ± 14.3	6%	NR
Wong, 2013, Hong Kong	51 ± 9	25.4 ± 3.6	8%	29%
Cheng, 2017, China	60 ± 4	26.7 ± 2.8	0%	NR
Abenavoli, 2017, Italy	45 ± 13	30.3 ± 3.1	0%	0%
Axley, 2017, USA	53 ± 9	37.3 ± 8.2	33%	NR
Eckard, 2013, USA	50 ± 10	35.7 ± 6.6	19%	56%
Promrat, 2010, USA	48 ± 11	33.6 ± 5	48%	NR
Katsagoni, 2018, Greece	46 ± 14	31.4 ± 4.4	0%	NR
AbdEl-Kader, 2016, Saudi Arabia	51 ± 6	32.1 ± 2.7	NR	NR
Al-Jiffri, 2013, Saudi Arabia	NR	32.2 ± 3.7	100%	0%
Asghari, 2018, Iran	40 ± 6	30.9 ± 3.4	0%	NR
StGeorge, 2009, Australia	48 ± 11	31.7 ± 5.3	19%	66%
Lim, 2018, Singapore	NR	NR	NR	NR
Selezneva, 2014, Russia	41 ± 2	37.1 ± 1.8	NR	NR
Armstrong, 2016, UK	51 ± 11	36 ± 5.7	33%	56%
Khoo, 2017, Singapore	41 ± 9	33.1 ± 3.5	0%	0%
Harrison, 2007, USA	47 ± 9	36.4 ± 6.2	10%	NR
Ye, 2017, NR	NR	28.9 ± 3.8	NR	NR
Zelber-Sagi, 2004, Israel	48 ± 10	33.1 ± 5.6	8%	NR
Bahmanadabi, 2011, Iran	38 ± 7	35.1 ± 7.3	0%	0%
Lee, 2012, Singapore	45 ± 17	31.5 ± 7.6	11%	NR
Data are reported as mean ± SD or pro	oportion of total I	N. NR: Not repor	ted.	

eTable 3 Handing of missing data in each study

Study	Year	Total N randomized	N analyzed	Missing data handling
Dong	2016	280	260	Complete case analysis
Sun	2012	1087	1006	Complete case analysis
Wong	2013	154	154	Missing data - last observation carried forward
Cheng ¹	2017	86	86	Missing data - multiple imputation and reporting of marginal means
Abenavoli ¹	2017	30	30	No missing data
Axley	2017	30	22	Missing data - no information on imputation – assumed complete case analysis
Eckard	2013	32	32	Complete case analysis
Promrat	2008	31	30	Complete case analysis
Katsagoni	2018	63	63	Missing data - multiple imputation
AbdEl-Kader	2016	100	100	No information – assumed 100% follow-up rate
Al-Jiffri	2013	100	100	No missing data
Asghari ¹	2018	60	60	Missing data – imputation (personal communication)
StGeorge	2009	152	143	Complete case analysis
Lim	2018	86	86	Complete case analysis - INTERIM
Selezneva	2014	174	174	No information – assumed 100% follow-up rate
Armstrong	2016	52	45	Complete case analysis
Khoo	2017	30	24	Complete case analysis
Harrison	2007	41	41	Complete case analysis
Ye	2017	30	30	Complete case analysis - INTERIM
Zelber-Sagi	2004	52	44	Missing data – complete case analysis in tables but mentions last observation carried forward in the statistical section
Bahmanabadi	2011	40	40	Unclear followed up rate – manuscript mentions that those with low adherence were excluded but unclear how many these were – assumed 100% follow-up
Lee	2009	18	18	Complete case analysis
¹ Numbers exclu	de particip	pants in trial arms that we	re not included i	n the current review

eTable 4 Reported adverse events

Study and country	Adverse events in the	Adverse events in the control
	Intervention group	group
Dong, 2016, China	None	None
Sun, 2012, China	Unclear	Unclear
Wong, 2013, Hong Kong	Unclear	Unclear
Cheng, 2017, China	Unclear	Unclear
Abenavoli, 2017, Italy	None	None
Axley, 2017, USA	None	None
Eckard, 2013, USA	Unclear	Unclear
Promrat, 2010, USA	None	None
Katsagoni, 2018, Greece	None	None
AbdEl-Kader, 2016, Saudi	Unclear	Unclear
Arabia		
Al-Jiffri, 2013, Saudi Arabia	None	None
Asghari, 2018, Iran	None	None
St. George, 2009, Australia	Unclear	Unclear
Lim, 2018, Singapore	Unclear	Unclear
Selezneva, 2014, Russia	Unclear	Unclear
Armstrong, 2016, UK	% serious AEs: 8%	% serious AEs: 8%
	% any AE: 88%	% any AE: 92%
	AEs included: gastrointestinal	AEs included: gastrointestinal
	disorders, nausea, diarrhea,	disorders, nausea, diarrhea,
	abdominal pain, vomiting,	abdominal pain, vomiting,
	constipation, dyspepsia,	dyspepsia, eye disorders,
	flatulence, bloating, eye	cardiac disorders, general
	disorders, cardiac disorders,	disorders and administration site
	general disorders and	conditions, injection site
	administration site conditions,	reaction, fatigue, influenza-like
	injection site reaction, fatigue,	symptoms, peripheral edema,
	influenza-like symptoms,	non-specific pain, infections and
	peripheral edema, chills, non-	infestations, chest infection,
	specific pain, infections and	urinary tract infection,
	infestations, investigations,	investigations, increased γ-
	increased aspartate	glutamyl transferase, increased
	aminotransferase, metabolism	aspartate aminotransferase,
	and nutrition disorders, anorexia	metabolism and nutrition
	(loss of appetite),	disorders, anorexia (loss of
	musculoskeletal and connective	appetite), musculoskeletal and
	disorders 8, back pain,	connective disorders 8, back
	arthralgia, nervous system	pain, arthralgia, muscle cramps,
	disorders, dizziness, headaches	nervous system disorders,
	or migraines, psychiatric	dizziness, headaches or
	disorders, depression, renal and	migraines, psychiatric disorders,
	urinary disorders, respiratory,	depression, renal and urinary
	thoracic, and mediastinal	disorders, respiratory, thoracic,
	disorders, cough, skin and soft	and mediastinal disorders,
	tissue disorders	cough, skin and soft tissue
		disorders
Knoo, 2017, Singapore	AEs included: Nausea, transient	None
	abdominal discomfort and	
	bioating, injection site reaction	
Harrison, 2007, USA	Unclear	Unclear
Ye, 2017, NR	Unclear	Unclear
Zelber-Sagi, 2004, Israel	AEs included: Gastrointestinal	AEs included: Gastrointestinal
	disorders	disorders
Bahmanadabi, 2011, Iran	Unclear	Unclear

Lee, 2012, Singapore	AEs included: Epigastric	AEs included: Epigastric
	discomfort, vomiting	discomfort, vomiting

1 Additional outcomes for the main analysis

eFigure 1.1 Glucose (mmol/L)

	more in	tensive	e WL	less int	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.6	0.8	20	-1.7	3	10	1.2%	1.10 [-0.79, 2.99]		
d. Sun 2012	-1.6	0.7	674	-0.2	1	332	6.9%	-1.40 [-1.52, -1.28]	-	+ ? + +
f. Abenavoli 2017	-0.2	0.2	20	0	0.1	10	6.9%	-0.20 [-0.31, -0.09]	-	●? ++
g. Wong 2013	0	0.6	77	0.1	0.6	77	6.7%	-0.10 [-0.29, 0.09]	-+	++ +
h. Armstrong 2016	-1	1.5	23	0.7	2.3	23	2.6%	-1.70 [-2.82, -0.58]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	0.2	0.2	30	0.1	0.1	30	7.0%	0.10 [0.02, 0.18]	-	$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
l. Katsagoni 2018 (D)	0	0.2	21	0.1	0.1	11	6.9%	-0.10 [-0.20, 0.00]	-	
n. StGeorge 2009 (M)	-0.2	0.7	73	0	0.7	17	5.9%	-0.20 [-0.57, 0.17]		?? 🕂 🛑
o. Katsagoni 2018 (D+E)	-0.1	0.1	21	0.1	0.1	10	7.0%	-0.20 [-0.28, -0.12]	-	
p. Zelber–Sagi 2004	-7.1	0.9	21	-5.1	0.3	23	5.8%	-2.00 [-2.40, -1.60]		
q. Harrison 2007	-0.4	0.2	23	-0.7	1.8	18	3.6%	0.30 [-0.54, 1.14]		? • • • • •
r. Cheng 2017 (D+E)	0.1	0.2	29	0.2	0.2	15	6.9%	-0.10 [-0.22, 0.02]	-	$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$
s. Dong 2016	0	0.5	130	0.2	0.5	130	6.9%	-0.20 [-0.32, -0.08]	-	♀ ? ♀♀●
t. StGeorge 2009 (L)	-0.3	0.6	36	0	0.7	17	5.9%	-0.30 [-0.69, 0.09]		?? 🕂 🛑
u. Cheng 2017 (D)	0.3	0.2	28	0.2	0.2	14	6.9%	0.10 [-0.03, 0.23]	<u>+</u> -	$\mathbf{++} \mathbf{++-}$
w. Eckard 2013 (MF)	-0.1	1.1	9	0.1	0.5	5	3.6%	-0.20 [-1.04, 0.64]		+ ? + +
x. Khoo 2017	-0.7	0.6	12	-0.6	0.5	12	5.6%	-0.10 [-0.54, 0.34]	_	$\mathbf{++} \mathbf{++}$
y. Eckard 2013 (LF)	-0.5	1.3	12	0.1	0.5	6	3.6%	-0.60 [-1.44, 0.24]		₽? ₽₽
Total (95% CI)			1259			760	100.0%	-0.34 [-0.57, -0.12]	•	
Heterogeneity: $Tau^2 = 0.1$	9; $Chi^2 = 5$	554.22,	df = 17	7 (P < 0.0	0001);	$l^2 = 97$	'%			-
Test for overall effect: Z =	2.96 (P =	0.003)							-2 -1 U I 2 more intensive WI less intensive WI	

Risk of bias legend for all forest plots

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of subjective outcome assessment
 (E) Incomplete outcome data (attrition bias)

(F) Other bias

eFigure 1.2 HbA1c (%)

	more in	tensive	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.5	0.5	20	-0.7	1.5	10	0.8%	0.20 [-0.76, 1.16]		•• ••
h. Armstrong 2016	-0.5	0.6	22	0	0.8	21	4.0%	-0.50 [-0.92, -0.08]		$\bullet \bullet \bullet \bullet \bullet \bullet$
q. Harrison 2007	-0.2	0.2	23	-0.3	0.7	18	6.2%	0.10 [-0.23, 0.43]	-+	? • • • • •
r. Cheng 2017 (D+E)	-0.1	0.1	29	0	0.1	15	58.0%	-0.10 [-0.16, -0.04]		
u. Cheng 2017 (D)	-0.1	0.3	28	0	0.1	14	31.0%	-0.10 [-0.22, 0.02]		
Total (95% CI)			122			78	100.0%	-0.10 [-0.19, -0.01]	•	
Heterogeneity: Tau ² = Test for overall effect:	0.00; Chi ² Z = 2.29 ($e^2 = 5.18$ (P = 0.0	8, df = 4)2)	(P = 0.2)	27); I ² =	= 23%			-1 -0.5 0 0.5 1 more intensive WL less intensive WL	-

	more i	ntensive	WL	less ir	ntensive	WL	9	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
a. Al-Jiffri 2013	-1.4	1.6	50	0.1	0.6	50	5.6%	-1.23 [-1.66, -0.80]	-	?? 🕂
b. Promrat 2010	-2	3	20	0.1	2.3	10	5.5%	-0.73 [-1.52, 0.05]		++ ++
c. AbdEl-Kader 2016	-2	0.7	50	0.3	0.5	50	5.6%	-3.75 [-4.41, -3.09]		? 🕂 🛛 ?
d. Sun 2012	-1.5	0.3	674	0.5	0.3	332	5.6%	-6.66 [-6.98, -6.34]	-	+? ++
f. Abenavoli 2017	0.2	0.5	20	0.6	0.3	10	5.5%	-0.87 [-1.67, -0.08]		●? ++
h. Armstrong 2016	-1.8	3.7	23	0.7	9.5	22	5.6%	-0.34 [-0.93, 0.25]		$\mathbf{\mathbf{+++++}}$
i. Asghari 2018	-0.2	0.5	30	0.7	1.9	30	5.6%	-0.64 [-1.16, -0.12]		
l. Katsagoni 2018 (D)	-0.5	0.8	21	-0.3	0.6	11	5.5%	-0.26 [-1.00, 0.47]		++ ++
n. StGeorge 2009 (M)	-0.2	2.3	36	0	1.5	17	5.6%	-0.09 [-0.67, 0.48]		?? 🗧 🖶
o. Katsagoni 2018 (D+E)	-0.8	0.5	21	-0.3	0.6	10	5.5%	-0.91 [-1.70, -0.12]		++ ++
p. Zelber-Sagi 2004	-6.2	19.6	21	-0.8	3	23	5.6%	-0.39 [-0.98, 0.21]		
q. Harrison 2007	0.01	0.014	23	0.01	0.007	18	5.6%	0.00 [-0.62, 0.62]	+	? • • • • •
r. Cheng 2017 (D+E)	-0.1	0.5	29	0.2	0.6	15	5.6%	-0.55 [-1.19, 0.08]		
t. StGeorge 2009 (L)	-0.4	1	73	0	1.5	17	5.6%	-0.36 [-0.89, 0.17]		?? 🕂 🖶
u. Cheng 2017 (D)	0.2	0.5	28	0.2	0.6	14	5.6%	0.00 [-0.64, 0.64]	+	
w. Eckard 2013 (MF)	-0.008	0.019	9	0	0.03	5	5.4%	-0.32 [-1.42, 0.78]		₽? ₽₽
x. Khoo 2017	-2.9	2.3	12	-3.2	2.6	12	5.5%	0.12 [-0.68, 0.92]		
y. Eckard 2013 (LF)	0.02	0.02	12	0	0.03	6	5.4%	0.81 [-0.22, 1.83]	—	+? ++
Total (95% CI)			1152			652	100.0%	-0.91 [-2.11, 0.30]	•	
Heterogeneity: $Tau^2 = 6.7$	0; Chi ² =	1219.38	, $df = 1$	7 (P < 0	.00001)	; I ² = 9	9%			_
Test for overall effect: Z =	1.47 (P =	0.14)							more intensive WL less intensive WL	

eFigure 1.3 Insulin resistance index (HOMA-IR, QUICKI, or Matsuda)

eFigure 1.4 Insulin (pmol/L)

	more intensive WL			less intensive WL			Mean Difference		Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-31.2	58.8	20	18	30.6	10	5.8%	-49.20 [-81.20, -17.20]	(•• ••
d. Sun 2012	-27	31.8	674	22.2	25.2	332	8.2%	-49.20 [-52.82, -45.58]	*	+ ? + +
f. Abenavoli 2017	4.8	10.8	20	10.2	9	10	8.1%	-5.40 [-12.72, 1.92]	-	●? ++
h. Armstrong 2016	-15.9	54.7	23	-34.7	164.1	22	2.7%	18.80 [-53.32, 90.92]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	-7.8	12	30	16.8	52.8	30	7.2%	-24.60 [-43.98, -5.22]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
l. Katsagoni 2018 (D)	-30.8	16.6	21	-6.5	14	11	7.9%	-24.30 [-35.20, -13.40]	-	
n. StGeorge 2009 (M)	4.2	25.2	36	-1.8	27	17	7.5%	6.00 [-9.25, 21.25]		?? 🗧 🖶 🛑
o. Katsagoni 2018 (D+E)	-14.3	18.7	21	-6.5	14	10	7.8%	-7.80 [-19.60, 4.00]		+ + ++
p. Zelber-Sagi 2004	-81	235.8	21	-18.6	74.4	23	1.5%	-62.40 [-167.74, 42.94]		
q. Harrison 2007	-24	69.6	23	-6	16.8	18	6.1%	-18.00 [-47.48, 11.48]		? • • • • •
r. Cheng 2017 (D+E)	-4.2	24	29	0.6	35.4	15	7.1%	-4.80 [-24.73, 15.13]		$\mathbf{++} \mathbf{++=}$
t. StGeorge 2009 (L)	-9	22.2	73	-1.8	27	17	7.7%	-7.20 [-21.01, 6.61]		?? 🕂 🖶
u. Cheng 2017 (D)	-0.6	19.2	28	0.6	35.4	14	7.1%	-1.20 [-21.06, 18.66]	- + -	$\mathbf{++} \mathbf{++=}$
w. Eckard 2013 (MF)	15.6	36	9	-6.6	41.4	5	4.7%	22.20 [-21.04, 65.44]		+ ? + +
x. Khoo 2017	-54.6	45.6	12	-56.4	37.2	12	5.7%	1.80 [-31.50, 35.10]		+++++
y. Eckard 2013 (LF)	-31.2	44.4	12	-6.6	41.4	6	4.9%	-24.60 [-66.17, 16.97]		+ ? + +
Total (95% CI)			1052			552	100.0%	-13.75 [-28.04, 0.53]	•	
Heterogeneity: Tau ² = 643 Test for overall effect: Z =	.40; Chi ² 1.89 (P =	² = 222.9 = 0.06)	99, df =	15 (P <	0.0000	1); I ² =	93%		-100 -50 0 50 100 more intensive WL less intensive WL	

eFigure 1.5 Aspartate transaminase – AST (U/L)

	more intensive W					e WL	Mean Difference		Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
a. Al-Jiffri 2013	-11.6	2.2	50	0.7	1.8	50	7.2%	-12.30 [-13.09, -11.51]	•	?? 🕂
b. Promrat 2010	-20.2	14.1	20	-18	30.8	10	1.3%	-2.20 [-22.26, 17.86]		$\mathbf{++} \mathbf{++}$
c. AbdEl-Kader 2016	-9.5	1.6	50	0.4	1.4	50	7.2%	-9.90 [-10.49, -9.31]	•	? 🕂 🤅 ?
d. Sun 2012	-5.7	15.2	674	-0.5	5.7	332	7.1%	-5.20 [-6.50, -3.90]	•	+ ? + +
e. Bahmanabadi 2011	4.4	6.7	20	-1.7	7.9	20	5.8%	6.10 [1.56, 10.64]		?? 🗧 ? ?
f. Abenavoli 2017	2.8	6.3	20	12.4	15.2	10	3.4%	-9.60 [-19.42, 0.22]		●? ++
g. Wong 2013	-4	6.2	77	-3	5.4	77	7.0%	-1.00 [-2.84, 0.84]	-	+++
h. Armstrong 2016	-15.8	21.8	23	-8.6	28.3	22	2.0%	-7.20 [-22.01, 7.61]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	-4.1	3.6	30	4.4	11.8	30	5.9%	-8.50 [-12.91, -4.09]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
j. Axley 2017	-9	2.2	8	0	2	14	7.0%	-9.00 [-10.85, -7.15]	+	-
k. Selezneva 2014	0.1	13.7	58	-11	16.4	116	5.8%	11.10 [6.48, 15.72]		?? 🕂
m. Lim 2018	-19.3	26.1	43	-5.1	13.7	43	3.8%	-14.20 [-23.01, -5.39]		?? ?●
n. StGeorge 2009 (M)	-6.9	18.3	36	-2.6	14.7	17	3.6%	-4.30 [-13.50, 4.90]		?? + 🖶
p. Zelber-Sagi 2004	-18.9	33	21	-8.8	17.2	23	1.8%	-10.10 [-25.87, 5.67]		
q. Harrison 2007	-28	23.2	23	-29	18.4	18	2.5%	1.00 [-11.73, 13.73]		? • • • • •
r. Cheng 2017 (D+E)	-4.9	2.4	29	4	2.3	14	7.1%	-8.90 [-10.39, -7.41]	÷	$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
s. Dong 2016	-1	3.5	130	0.4	4.9	130	7.2%	-1.40 [-2.44, -0.36]	-	- ? ---
t. StGeorge 2009 (L)	-8.3	16.1	73	-2.6	14.7	17	4.2%	-5.70 [-13.60, 2.20]	+	?? + 🖶
u. Cheng 2017 (D)	0.4	2.6	28	4	2.3	15	7.1%	-3.60 [-5.11, -2.09]	-	$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
w. Eckard 2013 (MF)	-19.6	47.9	9	-2.9	25.8	5	0.4%	-16.70 [-55.31, 21.91]		+ ? + +
x. Khoo 2017	-18	15	12	-23	24	12	1.8%	5.00 [-11.01, 21.01]		
y. Eckard 2013 (LF)	-15.9	19.1	12	-2.9	25.8	6	1.0%	-13.00 [-36.30, 10.30]		₽? ₽₽
Total (95% CI)			1446			1031	100.0%	-4.84 [-7.31, -2.38]	◆	
Heterogeneity: $Tau^2 = 2$	21.83; Chi	$i^2 = 530$).14, df	= 21 (P	< 0.000	001); I ²	= 96%			
Test for overall effect: Z	2 = 3.85 (P = 0.00	001)						-50 -25 0 25 50	

eFigure 1.6 Alkaline phosphatase – ALP (U/L)

	more ii	ntensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
a. Al-Jiffri 2013	-15.9	2.7	50	0.4	2.2	50	35.3%	-16.30 [-17.27, -15.33]	•	?? 🕂
h. Armstrong 2016	-5.1	11.7	23	-1.2	19.1	22	31.1%	-3.90 [-13.20, 5.40]	-	
q. Harrison 2007	-4	9.6	23	-8	9.3	18	33.6%	4.00 [-1.82, 9.82]	+■-	? • • • • •
Total (95% CI)			96			90	100.0%	-5.63 [-20.48, 9.22]		
Heterogeneity: Tau ² = Test for overall effect	= 162.14; : Z = 0.74	$Chi^2 = \frac{1}{2}$	51.69, d 46)	df = 2 (P	< 0.00	001); I ²	= 96%		-50 -25 0 25 more intensive WL less intensive W	 50 /L

eFigure 1.7 γ-glutamyl transferase – GGT (U/L)

	more i	ntensive	ive WL less intensive WL					Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
h. Armstrong 2016	-33.7	42.5	21	-7.2	28.3	21	2.0%	-26.50 [-48.34, -4.66]		$\bullet \bullet \bullet \bullet \bullet$
o. Katsagoni 2018 (D+E)	-27.5	37.2	21	-5.8	27.8	10	1.8%	-21.70 [-45.15, 1.75]	_	+++++++++++++
I. Katsagoni 2018 (D)	-18	13.5	21	-5.8	27.8	11	2.9%	-12.20 [-29.61, 5.21]		
d. Sun 2012	-11.3	10.9	674	0.3	8.5	332	15.4%	-11.60 [-12.83, -10.37]	-	
p. Zelber-Sagi 2004	-22.3	42.2	21	-10.7	34.6	23	1.8%	-11.60 [-34.53, 11.33]		
a. Al–Jiffri 2013	-7.1	0.9	50	0.7	0.9	50	15.7%	-7.80 [-8.15, -7.45]	•	?? 🕂
t. StGeorge 2009 (L)	-16.1	35.3	73	-10.6	27	17	3.7%	-5.50 [-20.68, 9.68]		?? 🗣 🛑
s. Dong 2016	-2.3	15	130	1	12.6	130	13.5%	-3.30 [-6.67, 0.07]		🕂 ? 🛛 🕂 🖨
n. StGeorge 2009 (M)	-13	29.1	36	-10.6	27	17	3.4%	-2.40 [-18.37, 13.57]		?? 🗣 🛑
f. Abenavoli 2017	4.4	2.1	20	5	5.4	10	13.4%	-0.60 [-4.07, 2.87]	+	9 ? 9
r. Cheng 2017 (D+E)	0.3	5.9	29	-2.6	5.5	15	13.4%	2.90 [-0.62, 6.42]		$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$
u. Cheng 2017 (D)	1.8	6.9	28	-2.6	5.5	14	13.0%	4.40 [0.55, 8.25]		♀ ♀ ♀♀●
Total (95% CI)			1124			650	100.0%	-4.35 [-7.67, -1.04]	•	
Heterogeneity: $Tau^2 = 18$.	20; Chi² =	= 139.22	2, df = 3							
Test for overall effect: Z =	2.57 (P =	= 0.01)	-50 -25 0 25 more intensive WI less intensive W	50 /I						

eFigure 1.8 NAFLD Fibrosis score

	more in	tensive	e WL	less int	ensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
I. Katsagoni 2018 (D)	0	0.4	21	0	0.4	10	31.3%	0.00 [-0.30, 0.30]		
o. Katsagoni 2018 (D+E)	0	0.4	21	0	0.4	11	32.0%	0.00 [-0.29, 0.29]	_	++++++
s. Dong 2016	-4.7	1.1	130	-5.1	0.8	130	36.6%	0.40 [0.17, 0.63]		₽? ₽₽₽
Total (95% CI)			172			151	100.0%	0.15 [-0.13, 0.43]	-	
Heterogeneity: Tau ² = 0.04 Test for overall effect: Z =	4; Chi ² = 6 1.03 (P =	5.23, df 0.31)	^F = 2 (P	= 0.04); I	$ ^2 = 68$	%			-1 -0.5 0 0.5 more intensive WL less intensive W	+ 1 L

eFigure 1.9 Fatty liver index

	more i	ntensiv	e WL	less int	tensive	e WL	9	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
f. Abenavoli 2017	-18	6.8	20	3	2.3	10	48.3%	-3.55 [-4.78, -2.33]		- ? - +
s. Dong 2016	0	10.8	130	2.4	9	130	51.7%	-0.24 [-0.48, 0.00]	•	.
Total (95% CI)			150			140	100.0%	-1.84 [-5.08, 1.40]		
Heterogeneity: Tau ² =	= 5.28; Cł	$ni^2 = 26$.91, df =		-10 -5 0 5	10				
Test for overall effect.	Z = 1.11	$\Gamma(F = 0.$.27)						more intensive WL less intensive W	VL

eFigure 1.10 Enhanced liver fibrosis (ELF) score

	more in	tensive	e WL	less int	tensive	WL	Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI	IV, Fixed, 95% Cl	ABCDEF
h. Armstrong 2016	-0.3	0.8	23	0.1	0.8	22	-0.40 [-0.87, 0.07]		+++ ++
								-4 -2 0 2 4	—

eFigure 1.11 Liver stiffness (kPa)

	more in	tensiv	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
f. Abenavoli 2017	-1.7	0.6	20	0.4	0.6	10	24.0%	-2.10 [-2.56, -1.64]		●? -
g. Wong 2013	-0.5	0.9	77	0.2	0.7	77	25.4%	-0.70 [-0.95, -0.45]	+	++ +
l. Katsagoni 2018 (D)	-1.8	4.3	21	0.2	1.8	11	9.1%	-2.00 [-4.12, 0.12]		++ +=
o. Katsagoni 2018 (D+E)	-1.2	1.3	21	0.2	1.8	10	15.9%	-1.40 [-2.65, -0.15]		++ +=
x. Khoo 2017	-0.3	0.3	12	-0.2	0.2	12	25.6%	-0.10 [-0.30, 0.10]	4	
Total (95% CI)	2		151			120	100.0%	-1.11 [-1.91, -0.32]	•	
Heterogeneity: Tau ² = 0.63 Test for overall effect: Z =	3; Chi ² = 6 2.75 (P =	58.09, (0.006)	df = 4 (F	P < 0.000	001); I ²	= 94%			-4 -2 0 2 4 more intensive WL less intensive WL	_

eFigure 1.12 Presence of definite NASH (Yes/No)

	more intens	ive WL	less intensi	ve WL		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEF
b. Promrat 2010	6	18	8	10	45.6%	0.13 [0.02, 0.78]		•• ••
h. Armstrong 2016	14	23	20	22	54.4%	0.16 [0.03, 0.83]		$\bigcirc \bigcirc $
Total (95% CI)		41		32	100.0%	0.14 [0.04, 0.49]		
Total events	20		28					
Heterogeneity: Tau ² =	$= 0.00; Chi^2 =$	0.03, df	= 1 (P = 0.86)); $I^2 = 0\%$	6		+ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$ $+$	100
rest for overall effect	L Z = 3.10 (P =	0.002)					more intensive WL less intensive	WL

eFigure 1.13 Inflammation (score 0-3)



eFigure 1.14 Ballooning (score 0-2)

	more in	tensiv	e WL	less	intensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.9	0.2	18	-0.7	0.2	10	36.8%	-0.20 [-0.35, -0.05]		$\mathbf{++} \mathbf{++}$
h. Armstrong 2016	-0.5	0.7	23	-0.2	0.6	22	12.0%	-0.30 [-0.68, 0.08]		$\bullet \bullet \bullet \bullet \bullet \bullet$
q. Harrison 2007	0	0.2	23	0	0.2	18	43.3%	0.00 [-0.12, 0.12]		? • • • • •
v. Lee 2012	0	0.7	8	0	0.00001	10	7.9%	0.00 [-0.49, 0.49]		₽ ? ₽ ? ₽
Total (95% CI)			72			60	100.0%	-0.11 [-0.26, 0.04]	-	
Heterogeneity: Tau ² = Test for overall effect:	0.01; Chi Z = 1.47	$e^{2} = 5.2$ (P = 0.	29, df = .14)	-1 -0.5 0 0.5 more intensive WL less intensive WL	+ 1					

eFigure 1.15 Fibrosis (stage F0-F4)

	more in	tensive	e WL	less int	ensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	0	0.5	18	-0.3	0.6	10	19.8%	0.30 [-0.14, 0.74]		
h. Armstrong 2016	-0.2	0.8	23	0.2	1	22	17.9%	-0.40 [-0.93, 0.13]		+++ +
p. Zelber–Sagi 2004	-0.7	0.6	11	-0.5	0.4	11	20.1%	-0.20 [-0.63, 0.23]		
v. Lee 2012	0.5	0.8	8	0	0.3	10	16.8%	0.50 [-0.08, 1.08]		-+ ? -+ ? -+
w. Eckard 2013 (MF)	-0.1	1.5	9	0.1	0.5	5	9.1%	-0.20 [-1.27, 0.87]		-+? -++
y. Eckard 2013 (LF)	-0.8	0.8	12	0.1	0.5	6	16.4%	-0.90 [-1.50, -0.30]		₽? ₽₽
Total (95% CI)			81			64	100.0%	-0.13 [-0.54, 0.27]	-	
Heterogeneity: Tau ² =	0.16; Chi ²	² = 15.4	46, df =	5 (P = 0)	.009);	$I^2 = 689$	%			<u></u>
Test for overall effect:	Z = 0.65 (P = 0.5	52)						more intensive WL less intensive W	_

2 Effect of the weight loss interventions with long-term follow-up

eFigure 2.1 Weight (kg) (long-term)



eFigure 2.2 Glucose (mmol/L) (long-term)



eFigure 2.3 HOMA-IR (long-term)



eFigure 2.4 Alanine aminotransferase – ALT (U/L) (long-term)

	more ir	ntensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
g. Wong 2013	-9.1	33	68	-5.7	21.2	57	83.6%	-3.40 [-12.98, 6.18]		++ +
x. Khoo 2017	-22	43.6	13	-41.4	54.3	13	16.4%	19.40 [-18.45, 57.25]		++++++
Total (95% CI)			81			70	100.0%	0.34 [-16.21, 16.90]		
Heterogeneity: Tau ² = Test for overall effect:	61.45; C Z = 0.04	$hi^2 = 1$ (P = 0.	.31, df = 97)	-50 -25 0 25 50 more intensive WL less intensive WL	_					

eFigure 2.5 Fatty liver index (long-term)

	more intensive WL less intensive WL						9	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
g. Wong 2013	36.5	31.5	68	38.5	29.6	57	100.0%	-0.06 [-0.42, 0.29]		••••
Total (95% CI)			68			57	100.0%	-0.06 [-0.42, 0.29]	•	
Heterogeneity: Not ap Test for overall effect:	plicable Z = 0.36	(P = 0.	72)						-2 -1 0 1 2 more intensive WL less intensive WI	<u>-</u> 2 -

3 Risk of bias within and across studies

eFigure 3.1 Risk of bias within studies





eFigure 3.2 Funnel plot of studies reporting (a) alanine aminotransferase (ALT) and (b) aspartate transaminase (AST)

4 Sensitivity analysis including only the studies with low risk of bias

eFigure 4.1 Weight (kg) (sensitivity analysis)

	more ir	ntensive	e WL	less int	ensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-8.7	12.4	20	-0.5	7.4	10	3.3%	-8.20 [-15.31, -1.09]		$\bullet \bullet \bullet \bullet \bullet$
g. Wong 2013	-5.6	5.7	77	-0.6	3.7	77	72.9%	-5.00 [-6.52, -3.48]		•• •
h. Armstrong 2016	-5.3	4.7	23	-0.6	4.4	22	23.8%	-4.70 [-7.36, -2.04]		$\bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			120			109	100.0%	-5.04 [-6.33, -3.74]	•	
Heterogeneity: Tau ² =	0.00; Ch	$i^2 = 0.8$	2, df =	2 (P = 0.1)	56); I ²	= 0%				
Test for overall effect:	Z = 7.61	(P < 0.	00001)						more intensive WI less intensive WI	

eFigure 4.2 HOMA-IR (sensitivity analysis)

	more in	tensive	e WL	less int	ensive	e WL		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-2	3	20	0.1	2.3	10	36.1%	-0.73 [-1.52, 0.05]		$\mathbf{++} \mathbf{++}$
h. Armstrong 2016	-1.8	3.7	23	0.7	9.5	22	63.9%	-0.34 [-0.93, 0.25]		$\bullet \bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			43			32	100.0%	-0.48 [-0.95, -0.01]	•	
Heterogeneity: Tau ² =	0.00; Chi	$^{2} = 0.6$	0, df =	1 (P = 0.1)	44); I ²	= 0%			-4 -2 0 2	4
lest for overall effect:	Z = 2.01	(P=0.	04)						more intensive WL less intensive WL	_

eFigure 4.3 Glucose (mmol/L) (sensitivity analysis)

	more in	tensive	e WL	less int	ensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.6	0.8	20	-1.7	3	10	22.2%	1.10 [-0.79, 2.99]		
g. Wong 2013	0	0.6	77	0.1	0.6	77	44.7%	-0.10 [-0.29, 0.09]	•	$\begin{array}{c} \bullet \bullet \\ \bullet \end{array} \bullet \\ \end{array}$
h. Armstrong 2016	-1	1.5	23	0.7	2.3	23	33.1%	-1.70 [-2.82, -0.58]		$\bigcirc \bigcirc $
Total (95% CI)			120			110	100.0%	-0.36 [-1.62, 0.89]		
Heterogeneity: Tau ² =	= 0.90; Chi : 7 = 0 57	$^{2} = 9.2$ (P = 0	24, df =	2 ($P = 0$.	010); I	$^{2} = 78\%$,)		-4 -2 0 2 4	
reserver over an encet.	0.57	· - 0.	,						more intensive WL less intensive WL	

eFigure 4.4 Insulin (pmol/L) (sensitivity analysis)

	more in	ntensive	e WL	less ir	ntensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEF
b. Promrat 2010	-31.2	58.8	20	18	30.6	10	61.8%	-49.20 [-81.20, -17.20]		•• ••
h. Armstrong 2016	-15.9	54.7	23	-34.7	164.1	22	38.2%	18.80 [-53.32, 90.92]		$\bullet \bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			43			32	100.0%	-23.20 [-87.97, 41.57]		
Heterogeneity: Tau ² =	= 1501.68	3; Chi ² =	2.85, c	lf = 1 (P	9 = 0.09)); $I^2 = 6$	5%			-
Test for overall effect	Z = 0.70	(P = 0.)	48)						more intensive WL less intensive WL	

Figure 4.5 HbA1c (%) (sensitivity analysis)

	more in	tensive	e WL	less int	ensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.5	0.5	20	-0.7	1.5	10	30.5%	0.20 [-0.76, 1.16]		$\mathbf{++} \mathbf{++}$
h. Armstrong 2016	-0.5	0.6	22	0	0.8	21	69.5%	-0.50 [-0.92, -0.08]		
Total (95% CI)			42			31	100.0%	-0.29 [-0.92, 0.35]		
Heterogeneity: Tau ² = Test for overall effect	= 0.10; Chi : Z = 0.89	$^{2} = 1.7$ (P = 0.	2, df = 37)	1 (P = 0.	19); I ²	= 42%			-2 -1 0 1 more intensive WL less intensive W	+ 2 L

eFigure 4.6 Alanine aminotransferase – ALT (U/L) (sensitivity analysis)

	more ir	ntensivo	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-42.4	23	20	-16.5	14.2	10	30.4%	-25.90 [-39.28, -12.52]		+++++
g. Wong 2013	-17	17.7	77	-7	9.5	77	50.8%	-10.00 [-14.49, -5.51]	•	••
h. Armstrong 2016	-26.6	34.4	23	-10.2	35.8	22	18.9%	-16.40 [-36.93, 4.13]		$\bullet \bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			120			109	100.0%	-16.04 [-27.01, -5.07]	•	
Heterogeneity: Tau ² =	56.48; C	$hi^2 = 5$.08, df =	= 2 (P =	0.08); I	$^{2} = 61\%$				-
Test for overall effect:	Z = 2.87	'(P = 0.)	004)						more intensive WL less intensive WL	

eFigure 4.7 Liver stiffness (kPa) (sensitivity analysis)

	more in	tensive	e WL	less int	ensive	e WL	Mean Difference	N	lean Differe	ence	Risk	of Bias
Study or Subgroup	Mean	Mean SD Total Mean SD Tota					IV, Random, 95% CI	IV,	Random, 95	5% CI	АВС	DEF
g. Wong 2013	-0.5	0.9	77	0.2	0.7	77	-0.70 [-0.95, -0.45]		+-		••	÷
								-2 -1	0	1	2	
								more intens	sive WL less	intensive	WL	

eFigure 4.8 Steatosis – Standardized Mean Difference as Assessed by Histologic Examination or MRI (Sensitivity Analysis)

	more in	tensive V	WL	less int	ensive	WL	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD T	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-1.1	0.4	18	-0.3	0.4	10	28.3%	-1.94 [-2.89, -0.99]		$\mathbf{++} \mathbf{++}$
g. Wong 2013	-6.8	3.1	77	-2.1	2.5	77	37.4%	-1.66 [-2.03, -1.29]	•	++ +
h. Armstrong 2016	-0.7	0.8	23	-0.4	0.8	22	34.3%	-0.37 [-0.96, 0.22]		$\bullet \bullet \bullet \bullet \bullet \bullet$
Total (95% CI)		_	118			109	100.0%	-1.30 [-2.24, -0.35]	•	
Heterogeneity: Tau ² = Test for overall effect	ogeneity: Tau ² = 0.58; Chi ² = 14.87, df = 2 (P = 0.0006); I ² = 87 or overall effect: Z = 2.70 (P = 0.007)								-4 -2 0 2 4 more intensive WL less intensive WL	-

eFigure 4.9 NAFLD activity score (NAS) (sensitivity analysis)

	more in	tensive	e WL	less int	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-2.4	0.7	18	-1.4	0.9	10	62.0%	-1.00 [-1.64, -0.36]		++ ++
h. Armstrong 2016	-1.3	1.6	23	-0.8	1.2	22	38.0%	-0.50 [-1.32, 0.32]		$\bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			41			32	100.0%	-0.81 [-1.32, -0.30]	•	
Heterogeneity: Tau ² = Test for overall effect	= 0.00; Chi :: Z = 3.13	$^{2} = 0.8$ (P = 0.	8, df = 002)	1 (P = 0.	35); I ²	= 0%			-2 -1 0 1 2 more intensive WL less intensive WL	-

eFigure 4.10 Inflammation (score 0-3) (sensitivity analysis)

	more in	tensive	e WL	less int	ensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.5	0.3	18	-0.4	0.3	10	65.9%	-0.10 [-0.33, 0.13]		$\mathbf{++} \mathbf{++}$
h. Armstrong 2016	-0.2	0.6	23	-0.2	0.5	22	34.1%	0.00 [-0.32, 0.32]		
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect	= 0.00; Chi : Z = 0.69	$P^{2} = 0.2$ (P = 0.	41 4, df = 49)	1 (P = 0.	62); I ²	32 = 0%	100.0%	-0.07 [-0.25, 0.12]	-1 -0.5 0 0.5 more intensive WL less intensive WL	+ 1

eFigure 4.11 Ballooning (score 0-2) (sensitivity analysis)

	more int	tensive	WL	less int	ensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
b. Promrat 2010	-0.9	0.2	18	-0.7	0.2	10	85.8%	-0.20 [-0.35, -0.05]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
h. Armstrong 2016	-0.5	0.7	23	-0.2	0.6	22	14.2%	-0.30 [-0.68, 0.08]		$\bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			41			32	100.0%	-0.21 [-0.36, -0.07]	•	
Heterogeneity: Tau ² =	0.00; Chi ²	$^{2} = 0.2$	3, df =	1 (P = 0.	63); I ²	= 0%				+
Test for overall effect:	Z = 2.93	(P=0.	003)						more intensive WL less intensive WI	L

eFigure 4.12 Fibrosis (scale F0-F4) (sensitivity analysis)

	more in	tensiv	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
h. Armstrong 2016	-0.2	0.8	23	0.2	1	22	47.6%	-0.40 [-0.93, 0.13]		+++ +
b. Promrat 2010	0	0.5	18	-0.3	0.6	10	52.4%	0.30 [-0.14, 0.74]	+	$\mathbf{\mathbf{+}} \mathbf{\mathbf{+}} \mathbf{\mathbf{+}} \mathbf{\mathbf{+}}$
Total (95% CI)			41			32	100.0%	-0.03 [-0.72, 0.65]		
Heterogeneity: Tau ² = Test for overall effect	= 0.18; Chi : Z = 0.10	$^{2} = 3.9$ (P = 0.	98, df = .92)	1 (P = 0.	.05); I ²	= 75%			-2 -1 0 1 more intensive WL less intensive W	+ 2 VL

eFigure 4.13 Aspartate transaminase – AST (U/L) (sensitivity analysis)



eFigure 4.14 Alkaline phosphatase - ALP (U/L) (sensitivity analysis)



eFigure 4.15 γ-glutamyl transferase – GGT (U/L) (sensitivity analysis)



5 Subgroup analysis by the type of intervention (behavioral, pharmacotherapy, surgery)

eFigure 5.1 Weight (kg) (subgroup analysis by the type of intervention)

	more i	ntensive	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.6.1 Behavioural progra	mmes									
a. Al-Jiffri 2013	-13.7	3.4	50	0.8	3	50	4.7%	-14.50 [-15.76, -13.24]		?? 🕂
b. Promrat 2010	-8.7	12.4	20	-0.5	7.4	10	2.4%	-8.20 [-15.31, -1.09]		$\mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi}$
c. AbdEl-Kader 2016	-5.9	2.2	50	2.1	2.9	50	4.8%	-8.00 [-9.01, -6.99]	-	? 🕂 🦷 ?
d. Sun 2012	-6.1	9.2	674	1.3	9.2	332	4.7%	-7.40 [-8.61, -6.19]		••
f. Abenavoli 2017	-5.1	3.4	20	0.4	2.3	10	4.5%	-5.50 [-7.56, -3.44]		●? -
g. Wong 2013	-5.6	5.7	77	-0.6	3.7	77	4.6%	-5.00 [-6.52, -3.48]		+++
i. Asghari 2018	-4.1	4	30	0	2.7	30	4.6%	-4.10 [-5.83, -2.37]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
j. Axley 2017	-2.7	5	8	0.9	6	14	3.3%	-3.60 [-8.28, 1.08]		-
k. Selezneva 2014	-9.3	1.8	58	-6.2	1.7	116	4.8%	-3.10 [-3.66, -2.54]	÷	?? 🕂
l. Katsagoni 2018 (D)	-5.6	4.1	21	-2.8	3.9	11	4.1%	-2.80 [-5.70, 0.10]		.
m. Lim 2018	-3.2	2.5	43	-0.9	2	43	4.8%	-2.30 [-3.26, -1.34]	-	???
n. StGeorge 2009 (M)	-2.8	3.4	73	-0.5	3.7	17	4.5%	-2.30 [-4.22, -0.38]		?? 🔒 🖶
o. Katsagoni 2018 (D+E)	-4.9	4.1	21	-2.8	3.9	10	4.1%	-2.10 [-5.09, 0.89]	+	
r. Cheng 2017 (D+E)	-1.5	3.2	29	0.2	3.3	15	4.5%	-1.70 [-3.74, 0.34]		
s. Dong 2016	-1.4	4.9	130	0.1	4.1	130	4.7%	-1.50 [-2.60, -0.40]		₽ ? ₽₽
t. StGeorge 2009 (L)	-1.9	3.7	36	-0.5	3.7	17	4.4%	-1.40 [-3.53, 0.73]	+	?? 🔒 🖶
u. Cheng 2017 (D)	-0.8	3.1	28	0.2	3.3	14	4.5%	-1.00 [-3.08, 1.08]		
w. Eckard 2013 (MF)	-3	4.7	9	-2.5	5.3	5	3.0%	-0.50 [-6.07, 5.07]		₽? ₽₽
y. Eckard 2013 (LF)	-0.2	5.4	12	-2.5	5.3	6	3.1%	2.30 [-2.93, 7.53]		+ ? + +
Subtotal (95% CI)			1389			957	80.2%	-3.93 [-5.67, -2.20]	◆	
Heterogeneity: $Tau^2 = 12$.	99; Chi ² =	= 430.74	4, df = 1	18 (P < 0	.00001); $ ^2 = 9$	6%			
Test for overall effect: Z =	4.44 (P <	0.000)1)							
4.6.2 Pharmacotherapy										
e. Bahmanabadi 2011	-13	10	20	-6.1	3	20	3.4%	-6.90 [-11.48, -2.32]		?? 🗧 ??
h. Armstrong 2016	-5.3	4.7	23	-0.6	4.4	22	4.2%	-4.70 [-7.36, -2.04]		
p. Zelber-Sagi 2004	-7.7	6.8	21	-5.9	5.9	23	3.8%	-1.80 [-5.58, 1.98]		
q. Harrison 2007	-8.2	5	23	-6.4	5.2	18	4.0%	-1.80 [-4.95, 1.35]		? • • • • •
x. Khoo 2017	-3.5	2.1	12	-3.5	3.3	12	4.4%	0.00 [-2.21, 2.21]		
Subtotal (95% CI)			99			95	19.8%	-2.75 [-5.10, -0.40]		
Heterogeneity: $Tau^2 = 4.5$	0; Chi ² =	11.33, a	df = 4 (I	P = 0.02)	; $I^2 = 6$	5%				
Test for overall effect: Z =	2.29 (P =	= 0.02)								
Total (95% CI)			1488			1052	100.0%	-3.73 [-5.26, -2.20]	◆	
Heterogeneity: $Tau^2 = 12$.	51; Chi ² =	= 451.09	9, df = 2	23 (P < 0	.00001); $I^2 = 9$	95%			_
Test for overall effect: Z =	4.78 (P <	0.0000)1)						-10 -5 0 5 10	
Test for subgroup differen	nces: Chi ²	= 0.63,	df = 1	(P = 0.43)	5), $ ^2 =$	0%			more intensive will less intensive wil	

eFigure 5.2 Glucose (mmol/L) (subgroup analysis by the type of intervention)

	more ir	ntensiv	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.4.1 Behavioural progra	mmes									
b. Promrat 2010	-0.6	0.8	20	-1.7	3	10	1.2%	1.10 [-0.79, 2.99]		
d. Sun 2012	-1.6	0.7	674	-0.2	1	332	6.9%	-1.40 [-1.52, -1.28]	÷	
f. Abenavoli 2017	-0.2	0.2	20	0	0.1	10	6.9%	-0.20 [-0.31, -0.09]	+	●? ++
g. Wong 2013	0	0.6	77	0.1	0.6	77	6.7%	-0.10 [-0.29, 0.09]		$\begin{array}{c} \bullet \bullet \\ \bullet \end{array} \bullet \\ \end{array}$
i. Asghari 2018	0.2	0.2	30	0.1	0.1	30	7.0%	0.10 [0.02, 0.18]	*	+ + + +
l. Katsagoni 2018 (D)	0	0.2	21	0.1	0.1	11	6.9%	-0.10 [-0.20, 0.00]	-	++ +=
n. StGeorge 2009 (M)	-0.2	0.7	73	0	0.7	17	5.9%	-0.20 [-0.57, 0.17]		?? 🕂 🛑
o. Katsagoni 2018 (D+E)	-0.1	0.1	21	0.1	0.1	10	7.0%	-0.20 [-0.28, -0.12]	-	++ +=
r. Cheng 2017 (D+E)	0.1	0.2	29	0.2	0.2	15	6.9%	-0.10 [-0.22, 0.02]	-	++ ++=
s. Dong 2016	0	0.5	130	0.2	0.5	130	6.9%	-0.20 [-0.32, -0.08]	+	+? +++
t. StGeorge 2009 (L)	-0.3	0.6	36	0	0.7	17	5.9%	-0.30 [-0.69, 0.09]		??
u. Cheng 2017 (D)	0.3	0.2	28	0.2	0.2	14	6.9%	0.10 [-0.03, 0.23]	-	••••
w. Eckard 2013 (MF)	-0.1	1.1	9	0.1	0.5	5	3.6%	-0.20 [-1.04, 0.64]		+ ? + +
y. Eckard 2013 (LF) Subtotal (95% CI)	-0.5	1.3	12 1180	0.1	0.5	6 684	3.6% 82.4%	-0.60 [-1.44, 0.24] - 0.23 [-0.47, 0.00]	•	₽ ? ₽ ₽
Heterogeneity: $Tau^2 = 0.1$	7; Chi ² = -	470.16	, df = 13	3 (P < 0.0	00001)	$ 1^2 = 97$	7%			
Test for overall effect: Z =	1.92 (P =	0.05)								
4.4.2 Pharmacotherapy										
h. Armstrong 2016	-1	1.5	23	0.7	2.3	23	2.6%	-1.70 [-2.82, -0.58]		$\bullet \bullet \bullet \bullet \bullet \bullet$
p. Zelber–Sagi 2004	-7.1	0.9	21	-5.1	0.3	23	5.8%	-2.00 [-2.40, -1.60]		
q. Harrison 2007	-0.4	0.2	23	-0.7	1.8	18	3.6%	0.30 [-0.54, 1.14]		? • • • • •
x. Khoo 2017	-0.7	0.6	12	-0.6	0.5	12	5.6%	-0.10 [-0.54, 0.34]		
Subtotal (95% CI)			79			76	17.6%	-0.87 [-2.10, 0.37]		
Heterogeneity: $Tau^2 = 1.4$	4; Chi ² =	50.25,	df = 3 (I	P < 0.000	001); I ²	= 94%				
reschor overan enect. Z –	1.50 (1 -	0.17)								
Total (95% CI)			1259			760	100.0%	-0.34 [-0.57, -0.12]	\bullet	
Heterogeneity: $Tau^2 = 0.1$	9; Chi ² =	554.22	, df = 17	7 (P < 0.0	00001)	; I ² = 97	7%			-
Test for overall effect: Z =	2.96 (P =	0.003)							more intensive WI less intensive WI	
Test for subgroup differen	ices: Chi ²	= 0.99,	df = 1	(P = 0.32)	2), $I^2 =$	0%			more mensive we less mensive we	

eFigure 5.3 Insulin resistance index (HOMA-IR or other) (subgroup analysis by the type of intervention)

	more i	ntensive	e WL	less ir	itensive	e WL	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.5.1 Behavioural progra	mmes									
a. Al-Jiffri 2013	-1.4	1.6	50	0.1	0.6	50	5.6%	-1.23 [-1.66, -0.80]	-	?? 🕂
b. Promrat 2010	-2	3	20	0.1	2.3	10	5.5%	-0.73 [-1.52, 0.05]		$\mathbf{++} \mathbf{++}$
c. AbdEl-Kader 2016	-2	0.7	50	0.3	0.5	50	5.6%	-3.75 [-4.41, -3.09]	- -	? 🕂 ?
d. Sun 2012	-1.5	0.3	674	0.5	0.3	332	5.6%	-6.66 [-6.98, -6.34]	· •	+ ? + +
f. Abenavoli 2017	0.2	0.5	20	0.6	0.3	10	5.5%	-0.87 [-1.67, -0.08]		●? ++
i. Asghari 2018	-0.2	0.5	30	0.7	1.9	30	5.6%	-0.64 [-1.16, -0.12]		+ + + + +
l. Katsagoni 2018 (D)	-0.5	0.8	21	-0.3	0.6	11	5.5%	-0.26 [-1.00, 0.47]		++ +=
n. StGeorge 2009 (M)	-0.2	2.3	36	0	1.5	17	5.6%	-0.09 [-0.67, 0.48]	-+-	?? 🕂 🖶
o. Katsagoni 2018 (D+E)	-0.8	0.5	21	-0.3	0.6	10	5.5%	-0.91 [-1.70, -0.12]		$\bigcirc \bigcirc $
r. Cheng 2017 (D+E)	-0.1	0.5	29	0.2	0.6	15	5.6%	-0.55 [-1.19, 0.08]		$\begin{array}{c} \bullet \bullet \\ \bullet \bullet \\ \bullet $
t. StGeorge 2009 (L)	-0.4	1	73	0	1.5	17	5.6%	-0.36 [-0.89, 0.17]		?? 🕂 🖶
u. Cheng 2017 (D)	0.2	0.5	28	0.2	0.6	14	5.6%	0.00 [-0.64, 0.64]	_ _ _	$\mathbf{++} \mathbf{++=}$
w. Eckard 2013 (MF)	-0.008	0.019	9	0	0.03	5	5.4%	-0.32 [-1.42, 0.78]	— 	
y. Eckard 2013 (LF) Subtotal (95% CI)	0.02	0.02	12 1073	0	0.03	6 577	5.4% 77.7%	0.81 [-0.22, 1.83] -1.12 [-2.59, 0.35]	•	₽? ₽₽
Heterogeneity: $Tau^2 = 7.7$ Test for overall effect: Z =	3; Chi ² = 1.50 (P =	1096.63 0.13)	s, df = 1	3 (P < 0	.00001)); $I^2 = 9$	9%			
4.5.2 Pharmacotherapy										
h. Armstrong 2016	-1.8	3.7	23	0.7	9.5	22	5.6%	-0.34 [-0.93, 0.25]		$\bullet \bullet \bullet \bullet \bullet \bullet$
p. Zelber–Sagi 2004	-6.2	19.6	21	-0.8	3	23	5.6%	-0.39 [-0.98, 0.21]		
q. Harrison 2007	0.01	0.014	23	0.01	0.007	18	5.6%	0.00 [-0.62, 0.62]	+	? • • • • •
x. Khoo 2017 Subtotal (95% CI)	-2.9	2.3	12 79	-3.2	2.6	12 75	5.5% 22.3%	0.12 [-0.68, 0.92] -0.19 [-0.51, 0.13]		····
Heterogeneity: $Tau^2 = 0.0$ Test for overall effect: Z =	0; Chi ² = 1.18 (P =	1.61, df : 0.24)	= 3 (P =	= 0.66);	$I^2 = 0\%$					
Total (95% Cl)			1152			652	100.0%	-0.91 [-2.11, 0.30]	•	
Heterogeneity: $Tau^2 = 6.7$ Test for overall effect: Z =	0; Chi ² = 1.47 (P =	1219.38 0.14)	8, df = 1	7 (P < 0	.00001)); $I^2 = 9$	9%		-4 -2 0 2 4	_
Test for subgroup differer	nces: Chi ²	= 1.47,	df = 1 (P = 0.23	3), $ ^2 = 3$	32.0%			more intensive wL less intensive WL	

eFigure 5.4 Insulin (pmol/L) (subgroup analysis by the type of intervention)

	more i	ntensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.25.1 Behavioural progra	ammes									
b. Promrat 2010	-31.2	58.8	20	18	30.6	10	5.8%	-49.20 [-81.20, -17.20]	_	$\begin{array}{c} \bullet \bullet \\ \bullet \bullet \\ \bullet \end{array}$
d. Sun 2012	-27	31.8	674	22.2	25.2	332	8.2%	-49.20 [-52.82, -45.58]	•	+ ? + +
f. Abenavoli 2017	4.8	10.8	20	10.2	9	10	8.1%	-5.40 [-12.72, 1.92]	-	●? ++
i. Asghari 2018	-7.8	12	30	16.8	52.8	30	7.2%	-24.60 [-43.98, -5.22]		$\mathbf{+} \mathbf{-} \mathbf{+} \mathbf{+} \mathbf{+}$
l. Katsagoni 2018 (D)	-30.8	16.6	21	-6.5	14	11	7.9%	-24.30 [-35.20, -13.40]	-	
n. StGeorge 2009 (M)	4.2	25.2	36	-1.8	27	17	7.5%	6.00 [-9.25, 21.25]	- -	??
o. Katsagoni 2018 (D+E)	-14.3	18.7	21	-6.5	14	10	7.8%	-7.80 [-19.60, 4.00]		
r. Cheng 2017 (D+E)	-4.2	24	29	0.6	35.4	15	7.1%	-4.80 [-24.73, 15.13]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
t. StGeorge 2009 (L)	-9	22.2	73	-1.8	27	17	7.7%	-7.20 [-21.01, 6.61]		?? 🚽 🖶
u. Cheng 2017 (D)	-0.6	19.2	28	0.6	35.4	14	7.1%	-1.20 [-21.06, 18.66]	- + -	
w. Eckard 2013 (MF)	15.6	36	9	-6.6	41.4	5	4.7%	22.20 [-21.04, 65.44]		.
y. Eckard 2013 (LF)	-31.2	44.4	12	-6.6	41.4	6	4.9%	-24.60 [-66.17, 16.97]		₽? ₽₽
Subtotal (95% CI)			973			4//	84.0%	-14.65 [-30.39, 1.09]		
Heterogeneity: $Tau^2 = 658$.12; Chi ²	= 215.7	71, df =	11 (P <	0.0000	1); l² =	95%			
lest for overall effect: $Z =$	1.82 (P =	= 0.07)								
4.25.2 Pharmacotherapy										
h. Armstrong 2016	-15.9	54.7	23	-34.7	164.1	22	2.7%	18.80 [-53.32, 90.92]		+++++++++++++
p. Zelber-Sagi 2004	-81	235.8	21	-18.6	74.4	23	1.5%	-62.40 [-167.74, 42.94]		
q. Harrison 2007	-24	69.6	23	-6	16.8	18	6.1%	-18.00 [-47.48, 11.48]		? • • • • •
x. Khoo 2017	-54.6	45.6	12	-56.4	37.2	12	5.7%	1.80 [-31.50, 35.10]	_	
Subtotal (95% CI)			79			75	16.0%	-9.03 [-29.73, 11.66]		
Heterogeneity: $Tau^2 = 0.00$	$0; Chi^2 =$	2.32, df	⁼ = 3 (P	= 0.51);	$I^2 = 0\%$					
Test for overall effect: Z =	0.86 (P =	= 0.39)								
Total (95% CI)			1052			552	100.0%	-13 75 [-28 04 0 53]		
Hotore geneity: T_{2} , C_{1}	40. Ch:2	222.0		1 F / D - 4	0 0000	1). 12	0.20/	15.75 [20.04, 0.55]		_
Test for overall offect: 7	1 20 (P	= 222.5	, ui =	1) (r <	0.0000	1), I =	ינצ/0		-100 -50 0 50 100	
Test for subgroup differen	$1.09 (P = Ch)^2$	- 0.00)	df _ 1	$(\mathbf{P} - \mathbf{O} \in$	7) 1 ² - (70/			more intensive WL less intensive WL	
rescrot subgroup differen	ces: chi-	= 0.18,	ui = 1	r = 0.6	(), 1 = 0	J 70				

	more ii	ntensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEF
4.1.1 Behavioural progra	mmes									
a. Al-Jiffri 2013	-13.6	1.6	50	0.7	1.7	50	6.7%	-14.30 [-14.95, -13.65]	•	?? 🕂
b. Promrat 2010	-42.4	23	20	-16.5	14.2	10	3.3%	-25.90 [-39.28, -12.52]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
c. AbdEl–Kader 2016	-11.7	1.3	50	0.4	1.1	50	6.7%	-12.10 [-12.57, -11.63]	•	? 🕂 🦳 ?
d. Sun 2012	-22.9	9.2	674	3.7	9.2	332	6.6%	-26.60 [-27.81, -25.39]	- ·	.
f. Abenavoli 2017	0.5	7.2	20	-0.3	8.9	10	5.4%	0.80 [-5.55, 7.15]	_ _	●? -
g. Wong 2013	-17	17.7	77	-7	9.5	77	6.0%	-10.00 [-14.49, -5.51]		+++
i. Asghari 2018	-4.3	7.5	30	7.2	10.3	30	6.0%	-11.50 [-16.06, -6.94]		
j. Axley 2017	-12	8.1	8	-6	10.4	14	4.9%	-6.00 [-13.82, 1.82]		
k. Selezneva 2014	4	22	58	-21.3	11.4	116	5.5%	25.30 [19.27, 31.33]		?? 🕂
I. Katsagoni 2018 (D)	-20	26.1	21	-2.6	10.5	11	3.4%	-17.40 [-30.17, -4.63]		↓↓↓●
m. Lim 2018	-35.3	39.3	43	-9.6	23.2	43	3.2%	-25.70 [-39.34, -12.06]		???
n. StGeorge 2009 (M)	-19.1	29.7	73	-7.3	18.5	17	3.9%	-11.80 [-22.92, -0.68]		?? 🕂 🖶
o. Katsagoni 2018 (D+E)	-22.2	9.7	21	-2.6	10.5	10	4.9%	-19.60 [-27.32, -11.88]		.
r. Cheng 2017 (D+E)	-1.5	4	29	1.5	3.3	15	6.5%	-3.00 [-5.22, -0.78]	-	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
s. Dong 2016	-4.7	8.1	130	-1.6	8.5	130	6.5%	-3.10 [-5.12, -1.08]	-	₽? ₽₽₽
t. StGeorge 2009 (L)	-14.9	35.6	36	-7.3	18.5	17	3.0%	-7.60 [-22.18, 6.98]		?? 🕂 🖶
u. Cheng 2017 (D)	-4.4	4	28	1.5	3.3	14	6.5%	-5.90 [-8.18, -3.62]	+	
w. Eckard 2013 (MF)	-19.8	54.9	9	-4.3	38.7	5	0.4%	-15.50 [-64.87, 33.87]		₽? ₽₽
y. Eckard 2013 (LF)	-27.5	27.9	12	-4.3	38.7	6	0.8%	-23.20 [-57.96, 11.56]		
Subtotal (95% CI)			1389			957	90.1%	-9.55 [-13.10, -6.01]	◆	
Heterogeneity: $Tau^2 = 44$.	16; Chi ² =	= 912.46	5, df = 3	18 (P < 0	0.00001); $I^2 = 9$	8%			
Test for overall effect: Z =	5.28 (P <	0.000)1)							
4.1.2 Pharmacotherapy										
e. Bahmanabadi 2011	-7.5	10.9	20	-5.7	17.6	20	4.5%	-1.80 [-10.87, 7.27]	_	?? 🗧 ? ?
h. Armstrong 2016	-26.6	34.4	23	-10.2	35.8	22	1.9%	-16.40 [-36.93, 4.13]		$\bullet \bullet \bullet \bullet \bullet \bullet$
p. Zelber-Sagi 2004	-30.6	59	21	-12.7	26.6	23	1.2%	-17.90 [-45.38, 9.58]		
q. Harrison 2007	-55	58.8	23	-45	32.4	18	1.2%	-10.00 [-38.31, 18.31]		? • • • • •
x. Khoo 2017	-34	27	12	-42	46	12	1.0%	8.00 [-22.18, 38.18]		$\mathbf{+} \mathbf{+} \mathbf{-} \mathbf{+} \mathbf{+}$
Subtotal (95% CI)			99			95	9.9%	-4.85 [-12.26, 2.57]	\bullet	
Heterogeneity: $Tau^2 = 0.0$	0; Chi ² =	3.34, df	F = 4 (P)	= 0.50);	$l^2 = 0\%$					
Test for overall effect: Z =	1.28 (P =	- 0.20)								
Total (95% CI)			1488			1052	100.0%	-9.26 [-12.635.89]	•	
Heterogeneity: $Tau^2 - 44$	10 [.] Chi ² -	= 920 59	 	23 (P < 0	00001	$1^{2} = 9$	8%		<u> </u>	-
Test for overall effect: 7 –	5 39 (P -	· 0 0000)1)	(i < (,,	0/0		-50 -25 0 25 50	
	5.55 (1 <		df = 1	(P = 0.2)	6) I ² -	20 6%			more intensive WL less intensive WL	

eFigure 5.5 ALT (U/L) (subgroup analysis by type of intervention)

eFigure 5.6 Steatosis – Standardized Mean Difference as Assessed by Histologic Examination or MRI (Subgroup Analysis by the Type of Intervention)

	more in	tensiv	e WL	less in	tensiv	e WL		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.3.1 Behavioural pro	grammes									
b. Promrat 2010	-1.1	0.4	18	-0.3	0.4	10	8.9%	-1.94 [-2.89, -0.99]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
f. Abenavoli 2017	-1	0.2	20	0.1	0.2	10	7.2%	-5.35 [-6.99, -3.71]		●? ++
g. Wong 2013	-6.8	3.1	77	-2.1	2.5	77	9.9%	-1.66 [-2.03, -1.29]	-	++
i. Asghari 2018	-0.1	0.2	24	0	0.1	26	9.6%	-0.63 [-1.20, -0.06]		+ + + +
r. Cheng 2017 (D+E)	-7.6	3.6	29	2.8	2.7	15	8.9%	-3.07 [-3.99, -2.15]		++ ++=
s. Dong 2016	-1.1	0.4	130	0	0.4	130	9.9%	-2.74 [-3.08, -2.40]	-	+? +++
u. Cheng 2017 (D)	-5.4	3.3	28	2.8	2.7	14	9.0%	-2.58 [-3.45, -1.72]		$\mathbf{++} \mathbf{++=}$
Subtotal (95% CI)			326			282	63.3%	-2.40 [-3.17, -1.62]	◆	
Heterogeneity: Tau ² =	0.91; Chi ²	$^{2} = 65.$	41, df =	6 (P < 0	.00001	L); $I^2 = 9$	1%			
Test for overall effect:	Z = 6.07 ((P < 0.0)	00001)							
4.3.2 Pharmacothera	ру									
h. Armstrong 2016	-0.7	0.8	23	-0.4	0.8	22	9.6%	-0.37 [-0.96, 0.22]		+++++
p. Zelber-Sagi 2004	0.1	0.3	11	-0.6	0.4	12	8.7%	1.90 [0.88, 2.91]		
q. Harrison 2007	0	0.2	23	0	0.2	18	9.5%	0.00 [-0.62, 0.62]	+	? • • • • •
z. Ye 2017	-7.8	3.1	14	-1.9	2.4	16	8.9%	-2.09 [-3.00, -1.18]	_ _	??????
Subtotal (95% CI)			71			68	36.7%	-0.16 [-1.41, 1.10]	\bullet	
Heterogeneity: Tau ² =	1.47; Chi ²	$^{2} = 33.$	46, df =	3 (P < 0	.00001	L); $I^2 = 9$	1%			
Test for overall effect:	Z = 0.25 ((P=0.8)	81)							
Total (95% CI)			397			350	100.0%	-1.61 [-2.43, -0.80]	\bullet	
Heterogeneity: Tau ² =	1.72; Chi ²	$^{2} = 178$	3.92, df	= 10 (P <	< 0.000)01); I ² =	= 94%			-
Test for overall effect:	Z = 3.88 ((P = 0.0)	0001)						-4 -2 U Z 4	
Test for subgroup diff	erences: C	$hi^2 = 8$.88, df	= 1 (P =	0.003)	$l^2 = 88$.7%		more mensive we less mensive we	

	more i	ntensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
5.3.1 Behavioural prog	grammes									
a. Al-Jiffri 2013	-11.6	2.2	50	0.7	1.8	50	7.2%	-12.30 [-13.09, -11.51]	•	?? 🔒
b. Promrat 2010	-20.2	14.1	20	-18	30.8	10	1.3%	-2.20 [-22.26, 17.86]		$\mathbf{\mathbf{+}} \mathbf{\mathbf{+}} \mathbf{\mathbf{+}}$
c. AbdEl-Kader 2016	-9.5	1.6	50	0.4	1.4	50	7.2%	-9.90 [-10.49, -9.31]	•	? 🕂 🥐
d. Sun 2012	-5.7	15.2	674	-0.5	5.7	332	7.1%	-5.20 [-6.50, -3.90]	*	₽? ₽₽
f. Abenavoli 2017	2.8	6.3	20	12.4	15.2	10	3.4%	-9.60 [-19.42, 0.22]		●? ++
g. Wong 2013	-4	6.2	77	-3	5.4	77	7.0%	-1.00 [-2.84, 0.84]	-	••
i. Asghari 2018	-4.1	3.6	30	4.4	11.8	30	5.9%	-8.50 [-12.91, -4.09]	-	$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
j. Axley 2017	-9	2.2	8	0	2	14	7.0%	-9.00 [-10.85, -7.15]	-	++ +
k. Selezneva 2014	0.1	13.7	58	-11	16.4	116	5.8%	11.10 [6.48, 15.72]		?? 🕂
m. Lim 2018	-19.3	26.1	43	-5.1	13.7	43	3.8%	-14.20 [-23.01, -5.39]		???
n. StGeorge 2009 (M)	-6.9	18.3	36	-2.6	14.7	17	3.6%	-4.30 [-13.50, 4.90]		?? 🕂 🛑
r. Cheng 2017 (D+E)	-4.9	2.4	29	4	2.3	14	7.1%	-8.90 [-10.39, -7.41]	-	$\mathbf{++} \mathbf{++=}$
s. Dong 2016	-1	3.5	130	0.4	4.9	130	7.2%	-1.40 [-2.44, -0.36]	-	
t. StGeorge 2009 (L)	-8.3	16.1	73	-2.6	14.7	17	4.2%	-5.70 [-13.60, 2.20]	+	?? 🕂 🛑
u. Cheng 2017 (D)	0.4	2.6	28	4	2.3	15	7.1%	-3.60 [-5.11, -2.09]	-	$\mathbf{++} \mathbf{++=}$
w. Eckard 2013 (MF)	-19.6	47.9	9	-2.9	25.8	5	0.4%	-16.70 [-55.31, 21.91]		4 ? 44
y. Eckard 2013 (LF)	-15.9	19.1	12	-2.9	25.8	6	1.0%	-13.00 [-36.30, 10.30]		4 ? 44
Subtotal (95% CI)			1347			936	86.1%	-5.79 [-8.38, -3.19]	◆	
Heterogeneity: Tau ² = 2	20.54; Ch	$i^2 = 488$	8.52, df	= 16 (P	< 0.000	01); I ²	= 97%			
Test for overall effect: 2	Z = 4.38 (P < 0.00	001)							
5 2 2 Bharmacatharan	.,									
5.5.2 Fildi inacotherap	y A A	67	20	1 7	7.0	20	F 00/			
e. Banmanabadi 2011	4.4	6.7 21.0	20	-1.7	7.9	20	5.8%	6.10 [1.56, 10.64]		
n. Armstrong 2016	-15.8	21.8	23	-8.6	28.3	22	2.0%	-7.20 [-22.01, 7.61]		
p. Zeiber-Sagi 2004	-18.9	33	21	-8.8	17.2	23	1.8%	-10.10 [-25.87, 5.67]	·	
q. Harrison 2007	-28	23.2	23	-29	18.4	18	2.5%	1.00 [-11.73, 13.73]		
X. KNOO 2017 Subtotal (95% CI)	-18	12	99	-23	24	95	13 9%	1 14 [-5 28 7 56]	<u> </u>	
Heterogeneity: $T_{2}u^{2} = 1$	10 12. Ch	$i^2 - 6 2i$	_ 15_0	4 (R _ 0	10).12	_ 26%	13.570	1.14 [5.20, 7.50]		
Test for everall effect:	19.42, CH 7 - 0.25 (P = 0.5	0, u = 0	4 (P = 0.	10), 1 =	= 50%				
rest for overall effect.	2 - 0.33 (r – 0.7.)							
Total (95% CI)			1446			1031	100.0%	-4.84 [-7.31, -2.38]	♦	
Heterogeneity: Tau ² = 2	21.83; Ch	$i^2 = 530$).14, df	= 21 (P	< 0.000	01); I ²	= 96%			_
Test for overall effect: 2	Z = 3.85 (P = 0.00	001)						more intensive WI less intensive WI	
Test for subgroup diffe	rences: C	hi² = 3.8	84, df =	1 (P = 0)).05), l ²	= 74.0	%		more mensive we less mensive we	

eFigure 5.7 AST (U/L) (subgroup analysis by type of intervention)

6 Subgroup analysis by the intensity of the comparator intervention

	more ir	tensive	e WL	less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	IV. Random, 95% CI	ABCDEF
5.15.1 Comparator: usual	care/mi	nimal ir	nterven	tion	_			,, ,		
a. Al-Iiffri 2013	-13.7	3.4	50	0.8	3	50	4.5%	-14.50 [-15.76, -13.24]	-	?? 🗣
b. Promrat 2010	-8.7	12.4	20	-0.5	7.4	10	2.3%	-8.20 [-15.31, -1.09]		4444
c. AbdEl-Kader 2016	-5.9	2.2	50	2.1	2.9	50	4.6%	-8.00 [-9.01, -6.99]	-	? + ?
d. Sun 2012	-6.1	9.2	674	1.3	9.2	332	4.5%	-7.40 [-8.61, -6.19]	-	A ? AA
f. Abenavoli 2017	-5.1	3.4	20	0.4	2.3	10	4.3%	-5.50 [-7.56, -3.44]		e ? e
g. Wong 2013	-5.6	5.7	77	-0.6	3.7	77	4.5%	-5.00 [-6.52, -3.48]	- - -	44 4
h. Armstrong 2016	-5.3	4.7	23	-0.6	4.4	22	4.1%	-4.70 [-7.36, -2.04]		ÖÖ O O O
i. Asghari 2018	-4.1	4	30	0	2.7	30	4.4%	-4.10 [-5.83, -2.37]		
j. Axley 2017	-2.7	5	8	0.9	6	14	3.2%	-3.60 [-8.28, 1.08]	+	••
l. Katsagoni 2018 (D)	-5.6	4.1	21	-2.8	3.9	11	4.0%	-2.80 [-5.70, 0.10]		+++++
n. StGeorge 2009 (M)	-2.8	3.4	73	-0.5	3.7	17	4.3%	-2.30 [-4.22, -0.38]		?? 🗣 🖶
o. Katsagoni 2018 (D+E)	-4.9	4.1	21	-2.8	3.9	10	3.9%	-2.10 [-5.09, 0.89]	+	+++++
r. Cheng 2017 (D+E)	-1.5	3.2	29	0.2	3.3	15	4.3%	-1.70 [-3.74, 0.34]		++ ++
s. Dong 2016	-1.4	4.9	130	0.1	4.1	130	4.6%	-1.50 [-2.60, -0.40]	-	₽? ₽₽₽
t. StGeorge 2009 (L)	-1.9	3.7	36	-0.5	3.7	17	4.3%	-1.40 [-3.53, 0.73]	+	?? 🕂 🛑
u. Cheng 2017 (D)	-0.8	3.1	28	0.2	3.3	14	4.3%	-1.00 [-3.08, 1.08]	+	++ +++
w. Eckard 2013 (MF)	-3	4.7	9	-2.5	5.3	5	2.8%	-0.50 [-6.07, 5.07]		🕂 ? 🗣 🕂
y. Eckard 2013 (LF) Subtotal (95% CI)	-0.2	5.4	12 1311	-2.5	5.3	6 820	3.0% 71.7%	2.30 [-2.93, 7.53] - 4.10 [-6.17, -2.03]	•	₽? ₽₽
Heterogeneity: $Tau^2 = 17.8$	80; Chi ² =	361.58	8, df = 1	L7 (P < 0	.00001); $I^2 = 9$	5%			
Test for overall effect: $Z =$	3.88 (P =	0.0001	L)							
5.15.2 Comparator: lower	intensity	/ interv	ention							
e. Bahmanabadi 2011	-13	10	20	-6.1	3	20	3.2%	-6.90 [-11.48, -2.32]		?? 🗣 ? ?
k. Selezneva 2014	-9.3	1.8	58	-6.2	1.7	116	4.6%	-3.10 [-3.66, -2.54]	-	?? 🕂
m. Lim 2018	-3.2	2.5	43	-0.9	2	43	4.6%	-2.30 [-3.26, -1.34]	-	???
p. Zelber–Sagi 2004	-7.7	6.8	21	-5.9	5.9	23	3.6%	-1.80 [-5.58, 1.98]		
q. Harrison 2007	-8.2	5	23	-6.4	5.2	18	3.9%	-1.80 [-4.95, 1.35]		? • • • •
v. Lee 2012	-1.6	3.1	8	-0.8	2.3	10	4.1%	-0.80 [-3.38, 1.78]		🕂 ? 🕂 ? 🕂
x. Khoo 2017	-3.5	2.1	12	-3.5	3.3	12	4.2%	0.00 [-2.21, 2.21]		
Subtotal (95% CI)			185			242	28.3%	-2.21 [-3.25, -1.16]	◆	
Heterogeneity: Tau ² = 0.86 Test for overall effect: Z =	5; Chi ² = 4.13 (P <	14.22, d 0.0001	df = 6 (F L)	P = 0.03)	; I ² = 5	8%				
Total (95% CI)			1496			1062	100.0%	-3.61 [-5.11, -2.12]	•	
Heterogeneity: Tau ² = 12.4	45; Chi ² =	458.04	4, df = 2	24 (P < 0)	.00001); $I^2 = 9$	5%			-
Test for overall effect: Z =	4.74 (P <	0.0000)1)						-10 -5 U 5 IU more intensive WI less intensive WI	
Test for subgroup differen	ces: Chi²	= 2.56,	df = 1	(P = 0.11)), I ² =	61.0%			more mensive we less mensive we	

eFigure 6.1 Weight change (kg) by the intensity of the comparator intervention

eFigure 6.2 Glucose (mmol/L) by the intensity of the comparator intervention

	more in	itensive	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
5.13.1 Comparator: usua	l care/mir	nimal ir	nterven	tion						
b. Promrat 2010	-0.6	0.8	20	-1.7	3	10	1.2%	1.10 [-0.79, 2.99]		- •••
d. Sun 2012	-1.6	0.7	674	-0.2	1	332	6.9%	-1.40 [-1.52, -1.28]	-	
f. Abenavoli 2017	-0.2	0.2	20	0	0.1	10	6.9%	-0.20 [-0.31, -0.09]	-	●? ++
g. Wong 2013	0	0.6	77	0.1	0.6	77	6.7%	-0.10 [-0.29, 0.09]		$\begin{array}{c} \bullet \bullet \\ \bullet \end{array} \bullet \\ \end{array}$
h. Armstrong 2016	-1	1.5	23	0.7	2.3	23	2.6%	-1.70 [-2.82, -0.58]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	0.2	0.2	30	0.1	0.1	30	7.0%	0.10 [0.02, 0.18]	*	
I. Katsagoni 2018 (D)	0	0.2	21	0.1	0.1	11	6.9%	-0.10 [-0.20, 0.00]	*	+++++++++++++
n. StGeorge 2009 (M)	-0.2	0.7	73	0	0.7	17	5.9%	-0.20 [-0.57, 0.17]		?? 🕂 🖶
o. Katsagoni 2018 (D+E)	-0.1	0.1	21	0.1	0.1	10	7.0%	-0.20 [-0.28, -0.12]	-	++++++
q. Harrison 2007	-0.4	0.2	23	-0.7	1.8	18	3.6%	0.30 [-0.54, 1.14]		? • • • • •
r. Cheng 2017 (D+E)	0.1	0.2	29	0.2	0.2	15	6.9%	-0.10 [-0.22, 0.02]	-	++++++
s. Dong 2016	0	0.5	130	0.2	0.5	130	6.9%	-0.20 [-0.32, -0.08]	-	
t. StGeorge 2009 (L)	-0.3	0.6	36	0	0.7	17	5.9%	-0.30 [-0.69, 0.09]		?? 🕂 🖶
u. Cheng 2017 (D)	0.3	0.2	28	0.2	0.2	14	6.9%	0.10 [-0.03, 0.23]	-	
w. Eckard 2013 (MF)	-0.1	1.1	9	0.1	0.5	5	3.6%	-0.20 [-1.04, 0.64]		• • • •
y. Eckard 2013 (LF)	-0.5	1.3	12	0.1	0.5	6	3.6%	-0.60 [-1.44, 0.24]		.
Subtotal (95% CI)			1226			725	88.7%	-0.25 [-0.48, -0.02]	\blacklozenge	
Heterogeneity: $Tau^2 = 0.1$	7; Chi ² = 4	478.40,	df = 15	5 (P < 0.0)0001)	$ I^2 = 97$	' %			
Test for overall effect: Z =	2.15 (P =	0.03)								
- 12 2 6 1										
5.13.2 Comparator: lower	r intensity	/ interv	ention							
p. Zelber–Sagi 2004	-7.1	0.9	21	-5.1	0.3	23	5.8%	-2.00 [-2.40, -1.60]		
x. Khoo 2017	-0.7	0.6	12	-0.6	0.5	12	5.6%	-0.10 [-0.54, 0.34]		
Subtotal (95% CI)	2		33		-	35	11.3%	-1.05 [-2.91, 0.81]		
Heterogeneity: $Tau^2 = 1.7$	6; Chi ² = 3	38.69, c	df = 1 (F	P < 0.000	001); I ²	= 97%				
Test for overall effect: Z =	1.11 (P =	0.27)								
Total (95% CI)			1259			760	100.0%	-0.34 [-0.57, -0.12]	◆	
Heterogeneity: $Tau^2 = 0.1$	9; Chi ² = 5	554.22,	df = 17	7 (P < 0.0)0001)	$ 1^2 = 97$	7%			-
Test for overall effect: $Z =$	2.96 (P =	0.003)							-2 -1 0 1 2	
Test for subgroup differen	nces: Chi ² :	= 0.70,	df = 1	(P = 0.40))), $ ^2 =$	0%			more intensive we less intensive we	

eFigure 6.3 Insulin resistance indices by the intensity of the comparator intervention

	more i	ntensive	e WL	less ir	ntensive	WL	9	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
5.14.1 Comparator: usua	l care/mi	nimal in	tervent	ion						
a. Al-Jiffri 2013	-1.4	1.6	50	0.1	0.6	50	5.6%	-1.23 [-1.66, -0.80]	-	?? 🕂
b. Promrat 2010	-2	3	20	0.1	2.3	10	5.5%	-0.73 [-1.52, 0.05]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
c. AbdEl-Kader 2016	-2	0.7	50	0.3	0.5	50	5.6%	-3.75 [-4.41, -3.09]		? 🕂 ?
d. Sun 2012	-1.5	0.3	674	0.5	0.3	332	5.6%	-6.66 [-6.98, -6.34]	÷	+ ? + +
f. Abenavoli 2017	0.2	0.5	20	0.6	0.3	10	5.5%	-0.87 [-1.67, -0.08]		😑 ? 🛛 🕂 🕂
h. Armstrong 2016	-1.8	3.7	23	0.7	9.5	22	5.6%	-0.34 [-0.93, 0.25]		$\mathbf{+++++}$
i. Asghari 2018	-0.2	0.5	30	0.7	1.9	30	5.6%	-0.64 [-1.16, -0.12]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
l. Katsagoni 2018 (D)	-0.5	0.8	21	-0.3	0.6	11	5.5%	-0.26 [-1.00, 0.47]		++ +−
n. StGeorge 2009 (M)	-0.2	2.3	36	0	1.5	17	5.6%	-0.09 [-0.67, 0.48]	-+-	?? 🕂 🛑
o. Katsagoni 2018 (D+E)	-0.8	0.5	21	-0.3	0.6	10	5.5%	-0.91 [-1.70, -0.12]		++ +−
r. Cheng 2017 (D+E)	-0.1	0.5	29	0.2	0.6	15	5.6%	-0.55 [-1.19, 0.08]		$\mathbf{++} \mathbf{++=}$
t. StGeorge 2009 (L)	-0.4	1	73	0	1.5	17	5.6%	-0.36 [-0.89, 0.17]	+	?? 🕂 🛑
u. Cheng 2017 (D)	0.2	0.5	28	0.2	0.6	14	5.6%	0.00 [-0.64, 0.64]	- + -	++ ++=
w. Eckard 2013 (MF)	-0.008	0.019	9	0	0.03	5	5.4%	-0.32 [-1.42, 0.78]		+ ? + +
y. Eckard 2013 (LF)	0.02	0.02	12	0	0.03	6	5.4%	0.81 [-0.22, 1.83]	_ 	+ ? + +
Subtotal (95% CI)			1096			599	83.3%	-1.07 [-2.46, 0.32]	\bullet	
Heterogeneity: $Tau^2 = 7.3$	7; Chi ² =	1131.59), df = 1	4 (P < 0	.00001)	; $I^2 = 9$	9%			
Test for overall effect: Z =	1.51 (P =	0.13)								
5.14.2 Comparator: lower	r intensit	y interv	ention							
p. Zelber–Sagi 2004	-6.2	. 19.6	21	-0.8	3	23	5.6%	-0.39 [-0.98, 0.21]	+	
g. Harrison 2007	0.01	0.014	23	0.01	0.007	18	5.6%	0.00 [-0.62, 0.62]	- -	? • • • •
x. Khoo 2017	-2.9	2.3	12	-3.2	2.6	12	5.5%	0.12 [-0.68, 0.92]		
Subtotal (95% CI)			56			53	16.7%	-0.13 [-0.51, 0.25]		
Heterogeneity: $Tau^2 = 0.0$	0: $Chi^2 =$	1.25. df	= 2 (P =	= 0.54):	$ ^2 = 0\%$					
Test for overall effect: Z =	0.67 (P =	• 0.50)								
Total (95% CI)			1152			652	100.0%	-0.91 [-2.11, 0.30]		
Heterogeneity: $Tau^2 = 6.7$	0; Chi ² =	1219.38	s, df = 1	7 (P < 0	.00001)	$; I^2 = 9$	9%			-
Test for overall effect: Z =	1.47 (P =	0.14)		,	,				-4 -2 0 2 4	
Test for subgroup differen	nces: Chi ²	= 1.65,	df = 1 (P = 0.20)), $I^2 = 3$	89.3%			more intensive wL less intensive wL	

eFigure 6.4 Insulin (pmol/L) by the intensity of the comparator intervention

	more i	ntensiv	e WL	less ir	ntensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEF
5.25.1 Comparator: usua	l care/mi	nimal ii	nterven	tion						
b. Promrat 2010	-31.2	58.8	20	18	30.6	10	5.8%	-49.20 [-81.20, -17.20]	_	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
d. Sun 2012	-27	31.8	674	22.2	25.2	332	8.2%	-49.20 [-52.82, -45.58]	÷	+ ? + +
f. Abenavoli 2017	4.8	10.8	20	10.2	9	10	8.1%	-5.40 [-12.72, 1.92]		●? ++
h. Armstrong 2016	-15.9	54.7	23	-34.7	164.1	22	2.7%	18.80 [-53.32, 90.92]		+++++
i. Asghari 2018	-7.8	12	30	16.8	52.8	30	7.2%	-24.60 [-43.98, -5.22]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
l. Katsagoni 2018 (D)	-30.8	16.6	21	-6.5	14	11	7.9%	-24.30 [-35.20, -13.40]	-	++ ++
n. StGeorge 2009 (M)	4.2	25.2	36	-1.8	27	17	7.5%	6.00 [-9.25, 21.25]	+	?? 🕂 🖶
o. Katsagoni 2018 (D+E)	-14.3	18.7	21	-6.5	14	10	7.8%	-7.80 [-19.60, 4.00]		++ +=
r. Cheng 2017 (D+E)	-4.2	24	29	0.6	35.4	15	7.1%	-4.80 [-24.73, 15.13]		
t. StGeorge 2009 (L)	-9	22.2	73	-1.8	27	17	7.7%	-7.20 [-21.01, 6.61]		?? 🗣 🖶
u. Cheng 2017 (D)	-0.6	19.2	28	0.6	35.4	14	7.1%	-1.20 [-21.06, 18.66]	-+-	$\bigcirc \bigcirc $
w. Eckard 2013 (MF)	15.6	36	9	-6.6	41.4	5	4.7%	22.20 [-21.04, 65.44]		
y. Eckard 2013 (LF)	-31.2	44.4	12	-6.6	41.4	6	4.9%	-24.60 [-66.17, 16.97]		₽? ₽₽
Subtotal (95% CI)			996			499	86.7%	-13.61 [-29.12, 1.89]	\blacklozenge	
Heterogeneity: $Tau^2 = 659$	9.06; Chi ²	= 217.	57, df =	12 (P <	0.0000	1); I ² =	94%			
Test for overall effect: Z =	1.72 (P =	= 0.09)								
5.25.2 Comparator: lower	r intensit	y interv	ention							
p. Zelber–Sagi 2004	-81	235.8	21	-18.6	74.4	23	1.5%	-62.40 [-167.74, 42.94]		
q. Harrison 2007	-24	69.6	23	-6	16.8	18	6.1%	-18.00 [-47.48, 11.48]		? • • • • •
x. Khoo 2017	-54.6	45.6	12	-56.4	37.2	12	5.7%	1.80 [-31.50, 35.10]		
Subtotal (95% CI)			56			53	13.3%	-11.53 [-33.14, 10.07]	•	
Heterogeneity: $Tau^2 = 0.0$	0; $Chi^2 =$	1.70, dt	⁼ = 2 (P	= 0.43)	$l^2 = 0\%$					
Test for overall effect: Z =	1.05 (P =	= 0.30)								
Total (95% CI)			1052			552	100.0%	-13.75 [-28.04, 0.53]	•	
Heterogeneity: $Tau^2 = 643$	3.40; Chi ²	= 222.9	99. df =	15 (P <	0.0000	1); $ ^2 =$	93%			-
Test for overall effect: $Z =$	1.89 (P =	= 0.06)	,			<i>,,</i> -				
Test for subgroup differen	ices: Chi ²	= 0.02.	df = 1	(P = 0.8)	8) $I^2 = 1$	0%			more intensive WL less intensive WL	

eFigure 6.5 ALT (U/L) by the intensity of the comparator intervention

	more ii	ntensive	e WL	less ir	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEI
5.1.1 Comparator: usual	care/min	imal int	erventi	on						
a. Al-Jiffri 2013	-13.6	1.6	50	0.7	1.7	50	6.4%	-14.30 [-14.95, -13.65]	•	?? 🕂
b. Promrat 2010	-42.4	23	20	-16.5	14.2	10	3.1%	-25.90 [-39.28, -12.52]		$\mathbf{++} \mathbf{++}$
c. AbdEl-Kader 2016	-11.7	1.3	50	0.4	1.1	50	6.5%	-12.10 [-12.57, -11.63]	•	? 🕂 ?
d. Sun 2012	-22.9	9.2	674	3.7	9.2	332	6.4%	-26.60 [-27.81, -25.39]	+	+? ++
f. Abenavoli 2017	0.5	7.2	20	-0.3	8.9	10	5.2%	0.80 [-5.55, 7.15]	- - -	-? ++
g. Wong 2013	-17	17.7	77	-7	9.5	77	5.8%	-10.00 [-14.49, -5.51]	-	++ +
h. Armstrong 2016	-26.6	34.4	23	-10.2	35.8	22	1.9%	-16.40 [-36.93, 4.13]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	-4.3	7.5	30	7.2	10.3	30	5.8%	-11.50 [-16.06, -6.94]		$\bullet \bullet \bullet \bullet \bullet \bullet$
j. Axley 2017	-12	8.1	8	-6	10.4	14	4.7%	-6.00 [-13.82, 1.82]		++ +
I. Katsagoni 2018 (D)	-20	26.1	21	-2.6	10.5	11	3.3%	-17.40 [-30.17, -4.63]		
n. StGeorge 2009 (M)	-19.1	29.7	73	-7.3	18.5	17	3.7%	-11.80 [-22.92, -0.68]		?? 🕂
o. Katsagoni 2018 (D+E)	-22.2	9.7	21	-2.6	10.5	10	4.8%	-19.60 [-27.32, -11.88]		$\mathbf{++} \mathbf{++}$
r. Cheng 2017 (D+E)	-1.5	4	29	1.5	3.3	15	6.3%	-3.00 [-5.22, -0.78]	-	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
s. Dong 2016	-4.7	8.1	130	-1.6	8.5	130	6.3%	-3.10 [-5.12, -1.08]	-	
t. StGeorge 2009 (L)	-14.9	35.6	36	-7.3	18.5	17	2.9%	-7.60 [-22.18, 6.98]		?? 🕂
u. Cheng 2017 (D)	-4.4	4	28	1.5	3.3	14	6.3%	-5.90 [-8.18, -3.62]	+	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
w. Eckard 2013 (MF)	-19.8	54.9	9	-4.3	38.7	5	0.4%	-15.50 [-64.87, 33.87]		₽? ₽₽
y. Eckard 2013 (LF)	-27.5	27.9	12	-4.3	38.7	6	0.8%	-23.20 [-57.96, 11.56]		+ ? + +
Subtotal (95% CI)			1311			820	80.5%	-11.32 [-14.74, -7.91]	•	
Heterogeneity: $Tau^2 = 36$.	62; Chi ² =	= 752.85	5, df = 1	17 (P < (0.00001	.); $I^2 = 9$	8%			
lest for overall effect: Z =	6.50 (P <	: 0.0000)1)							
5.1.2 Comparator: lower	intensity	interve	ntion							
e. Bahmanabadi 2011	-7.5	10.9	20	-5.7	17.6	20	4.3%	-1.80 [-10.87, 7.27]	_ _	?? 🗧 ? ?
k. Selezneva 2014	4	22	58	-21.3	11.4	116	5.3%	25.30 [19.27, 31.33]		?? +
m. Lim 2018	-35.3	39.3	43	-9.6	23.2	43	3.1%	-25.70 [-39.34, -12.06]		?? ?
p. Zelber–Sagi 2004	-30.6	59	21	-12.7	26.6	23	1.2%	-17.90 [-45.38, 9.58]		
g. Harrison 2007	-55	58.8	23	-45	32.4	18	1.1%	-10.00 [-38.31, 18.31]		? • • • •
v. Lee 2012	-53	13.3	8	-27.5	13.3	10	3.4%	-25.50 [-37.86, -13.14]		.
x. Khoo 2017	-34	27	12	-42	46	12	1.0%	8.00 [-22.18, 38.18]		
Subtotal (95% CI)			185			242	19.5%	-6.59 [-26.11, 12.93]		
Heterogeneity: $Tau^2 = 597$	7.23; Chi ²	= 92.01	L, df = 6	5 (P < 0.	00001);	$1^2 = 93$	%			
Test for overall effect: Z =	0.66 (P =	0.51)								
Total (95% CI)			1496			1062	100.0%	-9.81 [-13.12, -6.50]	•	
Heterogeneity: $Tau^2 = 44$.	17; Chi ² =	= 924.44	1, df = 2	24 (P < 0	0.00001); $I^2 = 9$	7%	-		-
Test for overall effect: $7 =$	5.81 (P <	: 0.0000)1)			,,. J			-50 -25 0 25 50	
Test for subgroup differen	nces: Chi ²	= 0.22	df = 1	(P = 0.6)	4). $I^2 =$	0%			more intensive WL less intensive WL	

eFigure 6.6 AST (U/L) by the intensity of the comparator intervention

	more i	ntensive	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEI
5.2.1 Comparator: usu	al care/n	nınimal	interve	ntion				_		-
a. Al–Jiffri 2013	-11.6	2.2	50	0.7	1.8	50	7.2%	-12.30 [-13.09, -11.51]	•	?? +
b. Promrat 2010	-20.2	14.1	20	-18	30.8	10	1.3%	-2.20 [-22.26, 17.86]		
c. AbdEl-Kader 2016	-9.5	1.6	50	0.4	1.4	50	7.2%	-9.90 [-10.49, -9.31]	•	? 🕂 ?
d. Sun 2012	-5.7	15.2	674	-0.5	5.7	332	7.1%	-5.20 [-6.50, -3.90]	T	+ ? + +
f. Abenavoli 2017	2.8	6.3	20	12.4	15.2	10	3.4%	-9.60 [-19.42, 0.22]		
g. Wong 2013	-4	6.2	77	-3	5.4	77	7.0%	-1.00 [-2.84, 0.84]	4	$\mathbf{++} \mathbf{+}$
h. Armstrong 2016	-15.8	21.8	23	-8.6	28.3	22	2.0%	-7.20 [-22.01, 7.61]		
i. Asghari 2018	-4.1	3.6	30	4.4	11.8	30	5.9%	-8.50 [-12.91, -4.09]		$\mathbf{\mathbf{+-+++}}$
j. Axley 2017	-9	2.2	8	0	2	14	7.0%	-9.00 [-10.85, -7.15]	+	++ -
n. StGeorge 2009 (M)	-6.9	18.3	36	-2.6	14.7	17	3.6%	-4.30 [-13.50, 4.90]		??
r. Cheng 2017 (D+E)	-4.9	2.4	29	4	2.3	14	7.1%	-8.90 [-10.39, -7.41]		++ ++
s. Dong 2016	-1	3.5	130	0.4	4.9	130	7.2%	-1.40 [-2.44, -0.36]	•	+? ++
t. StGeorge 2009 (L)	-8.3	16.1	73	-2.6	14.7	17	4.2%	-5.70 [-13.60, 2.20]		?? 🕂
u. Cheng 2017 (D)	0.4	2.6	28	4	2.3	15	7.1%	-3.60 [-5.11, -2.09]	-	++ ++
w. Eckard 2013 (MF)	-19.6	47.9	9	-2.9	25.8	5	0.4%	-16.70 [-55.31, 21.91]		+ ? + +
y. Eckard 2013 (LF) Subtotal (95% CI)	-15.9	19.1	12 1269	-2.9	25.8	6 799	1.0% 78.5%	-13.00 [-36.30, 10.30] - 6.66 [-9.21, -4.10]	· · · · · · · · · · · · · · · · · · ·	₽? ₽₽
Heterogeneity: Tau ² = 1 Test for overall effect: 2	17.81; Ch Z = 5.11 (i ² = 420 P < 0.00).27, df)001)	= 15 (P	< 0.000	001); I ²	= 96%			
5.2.2 Comparator: low	er intens	ity inter	ventior	ı						
e. Bahmanabadi 2011	4.4	6.7	20	-1.7	7.9	20	5.8%	6.10 [1.56, 10.64]		?? 🗧 ? ?
k. Selezneva 2014	0.1	13.7	58	-11	16.4	116	5.8%	11.10 [6.48, 15.72]		?? +
m. Lim 2018	-19.3	26.1	43	-5.1	13.7	43	3.8%	-14.20 [-23.01, -5.39]		?? ?
p. Zelber–Sagi 2004	-18.9	33	21	-8.8	17.2	23	1.8%	-10.10 [-25.87, 5.67]		
g. Harrison 2007	-28	23.2	23	-29	18.4	18	2.5%	1.00 [-11.73, 13.73]		? • • • •
x. Khoo 2017	-18	15	12	-23	24	12	1.8%	5.00 [-11.01, 21.01]		$\mathbf{\dot{+}}$
Subtotal (95% CI)	-	-	177	-	-	232	21.5%	0.62 [-7.52, 8.76]	•	
Heterogeneity: Tau ² = 1	75.27; Ch	$i^2 = 29.0$	07, df =	5 (P < 0).0001)	$; I^2 = 83$	3%			
Test for overall effect: 2	Z = 0.15 (P=0.88	3)							
Total (95% CI)			1446			1031	100.0%	-4.84 [-7.31, -2.38]	•	
Heterogeneity: $Tau^2 = 3$	21.83: Ch	$i^2 = 530$.14. df	= 21 (P	< 0.000	001): I ²	= 96%		-++++++++	
Test for overall effect.	7 = 3.85 (P = 0.00	001)	(/, /	20/0		-50 -25 0 25 50	
Test for subaroun diffe	rences: C	$hi^2 = 2.2$	79. df =	1 (P = 0)).09). I ²	= 64.2	%		more intensive WL less intensive WL	

eFigure 6.7 Steatosis by the intensity of the comparator intervention

	more in	tensiv	e WL	less in	tensive	e WL		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
4.3.1 Behavioural pro	grammes									
b. Promrat 2010	-1.1	0.4	18	-0.3	0.4	10	8.9%	-1.94 [-2.89, -0.99]		$\mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi} \mathbf{\Phi}$
f. Abenavoli 2017	-1	0.2	20	0.1	0.2	10	7.2%	-5.35 [-6.99, -3.71]		●? -
g. Wong 2013	-6.8	3.1	77	-2.1	2.5	77	9.9%	-1.66 [-2.03, -1.29]	-	++ +
i. Asghari 2018	-0.1	0.2	24	0	0.1	26	9.6%	-0.63 [-1.20, -0.06]		+ + + + +
r. Cheng 2017 (D+E)	-7.6	3.6	29	2.8	2.7	15	8.9%	-3.07 [-3.99, -2.15]		$\mathbf{++} \mathbf{++}$
s. Dong 2016	-1.1	0.4	130	0	0.4	130	9.9%	-2.74 [-3.08, -2.40]	-	+? ++
u. Cheng 2017 (D) Subtotal (95% Cl)	-5.4	3.3	28 326	2.8	2.7	14 282	9.0% 63.3%	-2.58 [-3.45, -1.72] - 2.40 [-3.17, -1.62]	•	••
4.3.2 Pharmacotherap	ру									
h. Armstrong 2016	-0.7	0.8	23	-0.4	0.8	22	9.6%	-0.37 [-0.96, 0.22]		$\mathbf{++++++}$
p. Zelber–Sagi 2004	0.1	0.3	11	-0.6	0.4	12	8.7%	1.90 [0.88, 2.91]		
q. Harrison 2007	0	0.2	23	0	0.2	18	9.5%	0.00 [-0.62, 0.62]	-+-	? • • • •
z. Ye 2017 Subtotal (95% CI)	-7.8	3.1	14 71	-1.9	2.4	16 68	8.9% 36.7%	-2.09 [-3.00, -1.18] - 0.16 [-1.41, 1.10]		??????
Heterogeneity: $Tau^2 =$	1.47: Chi ²	$^{2} = 33.4$	46. df =	3 (P < 0	.00001); $ ^2 = 9$	91%			
Test for overall effect:	Z = 0.25 ((P = 0.8)	31)			.,				
Total (95% CI)			397			350	100.0%	-1.61 [-2.43, -0.80]	•	
Heterogeneity: $Tau^2 =$	1.72; Chi ²	$^{2} = 178$.92, df	= 10 (P <	< 0.000	01); I ² :	= 94%			
Test for overall effect:	Z = 3.88 ((P = 0.0))001)						-4 -2 0 2 4	
Test for subgroup diffe	erences: C	$hi^2 = 8$.88, df	= 1 (P =)	0.003),	$l^2 = 88$.7%		more milensive will less milensive wil	

7 Subgroup analysis by the presence/absence of a minimum cut-off in the eligibility criteria for including only people with overweight/obesity

eFigure 7.1 Weight loss by the presence of a minimum overweight/obesity cut-off

	more intensive WL		less in	tensive	WL		Mean Difference	Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
6.24.1 With minimum BM	l cut-off									
a. Al-Jiffri 2013	-13.7	3.4	50	0.8	3	50	4.5%	-14.50 [-15.76, -13.24]		?? 🕂
b. Promrat 2010	-8.7	12.4	20	-0.5	7.4	10	2.3%	-8.20 [-15.31, -1.09]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
c. AbdEl-Kader 2016	-5.9	2.2	50	2.1	2.9	50	4.6%	-8.00 [-9.01, -6.99]	-	? 🕂 🥐
d. Sun 2012	-6.1	9.2	674	1.3	9.2	332	4.5%	-7.40 [-8.61, -6.19]	-	
e. Bahmanabadi 2011	-13	10	20	-6.1	3	20	3.2%	-6.90 [-11.48, -2.32]		?? 🗧 ? ?
f. Abenavoli 2017	-5.1	3.4	20	0.4	2.3	10	4.3%	-5.50 [-7.56, -3.44]		●? -
h. Armstrong 2016	-5.3	4.7	23	-0.6	4.4	22	4.1%	-4.70 [-7.36, -2.04]		$\bullet \bullet \bullet \bullet \bullet \bullet$
i. Asghari 2018	-4.1	4	30	0	2.7	30	4.4%	-4.10 [-5.83, -2.37]		
j. Axley 2017	-2.7	5	8	0.9	6	14	3.2%	-3.60 [-8.28, 1.08]	+	++ -
I. Katsagoni 2018 (D)	-5.6	4.1	21	-2.8	3.9	11	4.0%	-2.80 [-5.70, 0.10]		++++++
m. Lim 2018	-3.2	2.5	43	-0.9	2	43	4.6%	-2.30 [-3.26, -1.34]	-	???
o. Katsagoni 2018 (D+E)	-4.9	4.1	21	-2.8	3.9	10	3.9%	-2.10 [-5.09, 0.89]	+	.
q. Harrison 2007	-8.2	5	23	-6.4	5.2	18	3.9%	-1.80 [-4.95, 1.35]	+	? • • • • •
v. Lee 2012	-1.6	3.1	8	-0.8	2.3	10	4.1%	-0.80 [-3.38, 1.78]	-+	+?+?+
x. Khoo 2017	-3.5	2.1	12	-3.5	3.3	12	4.2%	0.00 [-2.21, 2.21]	_ + _	$\bigcirc \bigcirc $
Subtotal (95% CI)			1023			642	59.8%	-4.83 [-7.16, -2.49]	◆	
Heterogeneity: Tau ² = 19.0	01; Chi ² =	322.62	2, df = 1	L4 (P < 0	.00001); $I^2 = 9$	6%			
Test for overall effect: Z =	4.05 (P <	0.0001	.)							
6 24 2 No minimum BMI (ut-off									
a Wong 2012	E C	F 7	77	0.6	27	77	4 50/			
g. wong 2013	- 3.0	1.0	// Е0	-0.0	3.7	116	4.3/0	-3.00[-0.32, -3.48]		
n StCoorgo 2009 (M)	-9.5	2.0	73	-0.2	2.7	17	4.0%	-3.10[-3.00, -2.34]		
n. Sideorge 2009 (M)	-2.0	5.4 6.9	75	-0.5	5.7	22	4.5%			
p. Zeiber-Sagi 2004 r. Chopg 2017 (D \downarrow E)	-7.7	2.0	21	-3.9	2.9	25	1 20/	-1.80 [-3.38, 1.98]		
$r_{\rm cherry 2017}(D+E)$	-1.5	3.2 4 0	120	0.2	J.J ⊿ 1	120	4.5%	-1.70[-3.74, 0.34]		
t StCoorgo 2009 (L)	-1.4	37	36	-0.5	37	17	4.0%	-1.00[-2.00, -0.40]		
L. Stdeorge 2009 (L) (L)	-0.8	3.7	20	-0.3	2.7	1/	4.3%	-1.40[-3.08, 1.08]		
w Eckard 2013 (ME)	-0.3	47	20	-2 5	5.3	14 5	7.5%			
w. Eckard 2013 (MF)	-3	4.7 5.4	12	-2.5	5.3	5	2.0%			
Subtotal (95% CI)	-0.2	5.4	473	-2.5	5.5	420	40.2%	-2.20 [-3.15, -1.25]		••
Heterogeneity: $Tau^2 - 1$ 1	7. Chi ² –	24.81 6	ייים. או בייט וו	- 0 003	2)· 1 ² -	64%			•	
Test for overall effect: Z =	4.53 (P <	0.0000	11 – 9 (r 1)	- 0.002	,, i =	U- T /0				
			1400			1002	100.00/			
			1496			1002	100.0%	-3.01 [-3.11, -2.12]		
Heterogeneity: $Tau^2 = 12.4$	45; Chi ² =	458.04	-10 -5 0 5 10	-						
Test for overall effect: $Z =$	4.74 (P <	0.0000	1)						more intensive WL less intensive WL	
Test for subgroup differen	ces: Chi ²	= 4.18,	df = 1	(P = 0.04)	ŀ), l⁴ =	76.1%				

eFigure 7.2 Glucose (mmol/L) by the presence of a minimum overweight/obesity cut-off

	more in	more intensive WL			tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
6.21.1 With minimum BM	ll cut-off									
b. Promrat 2010	-0.6	0.8	20	-1.7	3	10	1.2%	1.10 [-0.79, 2.99]		- •• ••
d. Sun 2012	-1.6	0.7	674	-0.2	1	332	6.9%	-1.40 [-1.52, -1.28]	-	₽? ₽₽
f. Abenavoli 2017	-0.2	0.2	20	0	0.1	10	6.9%	-0.20 [-0.31, -0.09]	-	😑 ? 🛛 🕂 🕂
h. Armstrong 2016	-1	1.5	23	0.7	2.3	23	2.6%	-1.70 [-2.82, -0.58]		+++++
i. Asghari 2018	0.2	0.2	30	0.1	0.1	30	7.0%	0.10 [0.02, 0.18]	-	+ + + + +
l. Katsagoni 2018 (D)	0	0.2	21	0.1	0.1	11	6.9%	-0.10 [-0.20, 0.00]	-	++ +=
o. Katsagoni 2018 (D+E)	-0.1	0.1	21	0.1	0.1	10	7.0%	-0.20 [-0.28, -0.12]	+	++ +=
q. Harrison 2007	-0.4	0.2	23	-0.7	1.8	18	3.6%	0.30 [-0.54, 1.14]		? • • • • •
x. Khoo 2017	-0.7	0.6	12	-0.6	0.5	12	5.6%	-0.10 [-0.54, 0.34]		+++++
Subtotal (95% CI)			844			456	47.8%	-0.31 [-0.68, 0.06]	\bullet	
Heterogeneity: $Tau^2 = 0.2$	5; Chi ² = 4	448.16,	, df = 8	(P < 0.00)	0001);	$1^2 = 98\%$	6			
Test for overall effect: Z =	1.65 (P =	0.10)								
6.21.2 No minimum BMI	cut-off									
g. Wong 2013	0	0.6	77	0.1	0.6	77	6.7%	-0.10 [-0.29, 0.09]		++ +
n. StGeorge 2009 (M)	-0.2	0.7	73	0	0.7	17	5.9%	-0.20 [-0.57, 0.17]	+	?? 🗣 🖶
p. Zelber–Sagi 2004	-7.1	0.9	21	-5.1	0.3	23	5.8%	-2.00 [-2.40, -1.60]	_ _ _	
r. Cheng 2017 (D+E)	0.1	0.2	29	0.2	0.2	15	6.9%	-0.10 [-0.22, 0.02]	-	++ ++=
s. Dong 2016	0	0.5	130	0.2	0.5	130	6.9%	-0.20 [-0.32, -0.08]	-	
t. StGeorge 2009 (L)	-0.3	0.6	36	0	0.7	17	5.9%	-0.30 [-0.69, 0.09]	+	?? 🗣 🖶
u. Cheng 2017 (D)	0.3	0.2	28	0.2	0.2	14	6.9%	0.10 [-0.03, 0.23]	-	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
w. Eckard 2013 (MF)	-0.1	1.1	9	0.1	0.5	5	3.6%	-0.20 [-1.04, 0.64]		+ ? ++
y. Eckard 2013 (LF)	-0.5	1.3	12	0.1	0.5	6	3.6%	-0.60 [-1.44, 0.24]		
Subtotal (95% CI)			415			304	52.2%	-0.36 [-0.62, -0.10]	\blacklozenge	
Heterogeneity: $Tau^2 = 0.1$	2; Chi ² = 9	98.31, 0	df = 8 (I	P < 0.000	001); I ²	= 92%				
Test for overall effect: Z =	2.68 (P =	0.007)	1							
Total (95% CI)			1259			760	100.0%	-0.34 [-0.57, -0.12]	\bullet	
Heterogeneity: $Tau^2 = 0.1$	9; Chi ² = 5	554.22,	, df = 17	7 (P < 0.0	00001)	$; I^2 = 97$	7%			_
Test for overall effect: Z =	2.96 (P =	0.003)	1						-2 -1 U I Z	
Test for subgroup differen	ices: Chi ² =	= 0.04,	df = 1	(P = 0.84)	1), $ ^2 =$	0%			more miterisive will less miterisive will	

eFigure 7.3 Insulin resistance index (HOMA-IR or other) by the presence of a minimum overweight/obesity cut-off

	more intensive WL			less intensive WL			9	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
6.22.1 With minimum BM	l cut-off									
a. Al-Jiffri 2013	-1.4	1.6	50	0.1	0.6	50	5.6%	-1.23 [-1.66, -0.80]		?? 🕂
b. Promrat 2010	-2	3	20	0.1	2.3	10	5.5%	-0.73 [-1.52, 0.05]		$\mathbf{++} \mathbf{++}$
c. AbdEl-Kader 2016	-2	0.7	50	0.3	0.5	50	5.6%	-3.75 [-4.41, -3.09]		? 🕂 🛛 ?
d. Sun 2012	-1.5	0.3	674	0.5	0.3	332	5.6%	-6.66 [-6.98, -6.34]	-	••
f. Abenavoli 2017	0.2	0.5	20	0.6	0.3	10	5.5%	-0.87 [-1.67, -0.08]		●? ++
h. Armstrong 2016	-1.8	3.7	23	0.7	9.5	22	5.6%	-0.34 [-0.93, 0.25]		$\mathbf{\mathbf{\Phi}} \mathbf{\mathbf{\Phi}} \mathbf{\mathbf{\Phi}} \mathbf{\mathbf{\Phi}} \mathbf{\mathbf{\Phi}}$
i. Asghari 2018	-0.2	0.5	30	0.7	1.9	30	5.6%	-0.64 [-1.16, -0.12]		
l. Katsagoni 2018 (D)	-0.5	0.8	21	-0.3	0.6	11	5.5%	-0.26 [-1.00, 0.47]		•• ••
o. Katsagoni 2018 (D+E)	-0.8	0.5	21	-0.3	0.6	10	5.5%	-0.91 [-1.70, -0.12]		.
q. Harrison 2007	0.01	0.014	23	0.01	0.007	18	5.6%	0.00 [-0.62, 0.62]	- -	? • • • • •
x. Khoo 2017	-2.9	2.3	12	-3.2	2.6	12	5.5%	0.12 [-0.68, 0.92]	-	+++++
Subtotal (95% CI)			944			555	61.2%	-1.40 [-3.13, 0.34]		
Test for overall effect: Z = 6.22.2 No minimum BMI of	1.58 (P =	= 0.11)		`	,,					
n. StGeorge 2009 (M)	-0.2	2.3	36	0	1.5	17	5.6%	-0.09 [-0.67, 0.48]	+	?? 🕂 🛑
p. Zelber-Sagi 2004	-6.2	19.6	21	-0.8	3	23	5.6%	-0.39 [-0.98, 0.21]		
r. Cheng 2017 (D+E)	-0.1	0.5	29	0.2	0.6	15	5.6%	-0.55 [-1.19, 0.08]		
t. StGeorge 2009 (L)	-0.4	1	73	0	1.5	17	5.6%	-0.36 [-0.89, 0.17]		?? 🕂 🖶
u. Cheng 2017 (D)	0.2	0.5	28	0.2	0.6	14	5.6%	0.00 [-0.64, 0.64]	-+-	$\mathbf{++} \mathbf{+++}$
w. Eckard 2013 (MF)	-0.008	0.019	9	0	0.03	5	5.4%	-0.32 [-1.42, 0.78]		 ,,,,,,,
y. Eckard 2013 (LF)	0.02	0.02	12	0	0.03	6	5.4%	0.81 [-0.22, 1.83]		
Subtotal (95% CI)			208			97	38.8%	-0.22 [-0.47, 0.04]	•	
Heterogeneity: Tau ² = 0.00 Test for overall effect: Z =	D; Chi ² = 1.68 (P =	6.13, df • 0.09)	= 6 (P =	= 0.41);	$l^2 = 2\%$					
Total (95% CI)			1152			652	100.0%	-0.91 [-2.11, 0.30]		
Heterogeneity: Tau ² = 6.70 Test for overall effect: Z = Test for subgroup differen); Chi ² = 1.47 (P = ces: Chi ²	1219.38 = 0.14) = 1.74,	df = 1	7 (P < C) P = 0.19	(0.00001)	; I ² = 9 2.5%	9%		-4 -2 0 2 4 more intensive WL less intensive WL	

eFigure 7.4 Insulin (pmol/L) by the presence of a minimum overweight/obesity cut-off

	more intensive WL			less ir	ntensive	WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEF
6.2.1 With minimum BMI	cut-off									
b. Promrat 2010	-31.2	58.8	20	18	30.6	10	5.8%	-49.20 [-81.20, -17.20]	_ -	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
d. Sun 2012	-27	31.8	674	22.2	25.2	332	8.2%	-49.20 [-52.82, -45.58]	+ I	• ? •
f. Abenavoli 2017	4.8	10.8	20	10.2	9	10	8.1%	-5.40 [-12.72, 1.92]		●? ++
h. Armstrong 2016	-15.9	54.7	23	-34.7	164.1	22	2.7%	18.80 [-53.32, 90.92]		$\mathbf{\dot{+}}\mathbf{\dot{+}}\mathbf{\dot{+}}\mathbf{\dot{+}}\mathbf{\dot{+}}\mathbf{\dot{+}}$
i. Asghari 2018	-7.8	12	30	16.8	52.8	30	7.2%	-24.60 [-43.98, -5.22]		
I. Katsagoni 2018 (D)	-30.8	16.6	21	-6.5	14	11	7.9%	-24.30 [-35.20, -13.40]		+++++
o. Katsagoni 2018 (D+E)	-14.3	18.7	21	-6.5	14	10	7.8%	-7.80 [-19.60, 4.00]		+++++
q. Harrison 2007	-24	69.6	23	-6	16.8	18	6.1%	-18.00 [-47.48, 11.48]	+	? • • • • •
x. Khoo 2017	-54.6	45.6	12	-56.4	37.2	12	5.7%	1.80 [-31.50, 35.10]		
Subtotal (95% CI)			844			455	59.5%	-20.46 [-38.62, -2.29]	\blacklozenge	
Heterogeneity: $Tau^2 = 61^2$	1.36; Chi ²	= 155.	12, df =	8 (P < 0	0.00001); $I^2 = 9$	95%			
Test for overall effect: Z =	2.21 (P =	= 0.03)								
6.2.2 No minimum BMI c	ut-off									
n. StGeorge 2009 (M)	4.2	25.2	36	-1.8	27	17	7.5%	6.00 [-9.25, 21.25]		?? 🕂 🖶
p. Zelber–Sagi 2004	-81	235.8	21	-18.6	74.4	23	1.5%	-62.40 [-167.74, 42.94]		
r. Cheng 2017 (D+E)	-4.2	24	29	0.6	35.4	15	7.1%	-4.80 [-24.73, 15.13]		$\mathbf{++} \mathbf{++-}$
t. StGeorge 2009 (L)	-9	22.2	73	-1.8	27	17	7.7%	-7.20 [-21.01, 6.61]	+	?? 🕂 🖶
u. Cheng 2017 (D)	-0.6	19.2	28	0.6	35.4	14	7.1%	-1.20 [-21.06, 18.66]	-+-	$\bullet \bullet $
w. Eckard 2013 (MF)	15.6	36	9	-6.6	41.4	5	4.7%	22.20 [-21.04, 65.44]		
y. Eckard 2013 (LF)	-31.2	44.4	12	-6.6	41.4	6	4.9%	-24.60 [-66.17, 16.97]	<u>+</u>	+ ? + +
Subtotal (95% CI)			208			97	40.5%	-2.22 [-10.17, 5.74]		
Heterogeneity: $Tau^2 = 0.0$	0; Chi ² =	5.28, df	f = 6 (P)	= 0.51);	$I^2 = 0\%$					
Test for overall effect: Z =	0.55 (P =	= 0.58)								
Total (95% CI)			1052			552	100.0%	-13.75 [-28.04, 0.53]	•	
Heterogeneity: $Tau^2 = 643$	3.40; Chi ²	= 222.9	99, df =	15 (P <	0.0000	1); $I^2 =$	93%			-
Test for overall effect: Z =	1.89 (P =	= 0.06)							-100 -50 0 50 100	
Test for subgroup differen	ices: Chi ²	= 3.25,	df = 1	(P = 0.0)	7), $ ^2 = 1$	69.2%			more intensive will less intensive will	

	more intensive WL		less intensive WL			Mean Difference		Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
6.1.1 With minimum BMI	cut-off									
a. Al-Jiffri 2013	-13.6	1.6	50	0.7	1.7	50	6.4%	-14.30 [-14.95, -13.65]	•	?? 🕂
b. Promrat 2010	-42.4	23	20	-16.5	14.2	10	3.1%	-25.90 [-39.28, -12.52]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{+}$
c. AbdEl-Kader 2016	-11.7	1.3	50	0.4	1.1	50	6.5%	-12.10 [-12.57, -11.63]	•	? 🕂 🦓
d. Sun 2012	-22.9	9.2	674	3.7	9.2	332	6.4%	-26.60 [-27.81, -25.39]	•	+ ? + +
e. Bahmanabadi 2011	-7.5	10.9	20	-5.7	17.6	20	4.3%	-1.80 [-10.87, 7.27]	—	?? 🗧 ? ?
f. Abenavoli 2017	0.5	7.2	20	-0.3	8.9	10	5.2%	0.80 [-5.55, 7.15]	_ _	●? ++
h. Armstrong 2016	-26.6	34.4	23	-10.2	35.8	22	1.9%	-16.40 [-36.93, 4.13]		$\mathbf{+++++}$
i. Asghari 2018	-4.3	7.5	30	7.2	10.3	30	5.8%	-11.50 [-16.06, -6.94]	-	+ + + +
j. Axley 2017	-12	8.1	8	-6	10.4	14	4.7%	-6.00 [-13.82, 1.82]		++ -
l. Katsagoni 2018 (D)	-20	26.1	21	-2.6	10.5	11	3.3%	-17.40 [-30.17, -4.63]		++ ++
m. Lim 2018	-35.3	39.3	43	-9.6	23.2	43	3.1%	-25.70 [-39.34, -12.06]		???
o. Katsagoni 2018 (D+E)	-22.2	9.7	21	-2.6	10.5	10	4.8%	-19.60 [-27.32, -11.88]		++ ++
q. Harrison 2007	-55	58.8	23	-45	32.4	18	1.1%	-10.00 [-38.31, 18.31]		? • • • •
v. Lee 2012	-53	13.3	8	-27.5	13.3	10	3.4%	-25.50 [-37.86, -13.14]		+ ? + ? +
x. Khoo 2017	-34	27	12	-42	46	12	1.0%	8.00 [-22.18, 38.18]		++++ +
Subtotal (95% CI)			1023			642	61.1%	-14.25 [-17.97, -10.53]	•	
Heterogeneity: $Tau^2 = 31.2$	10; Chi² =	= 526.84	4, df = 1	14 (P < C	0.00001); $I^2 = 9$	7%			
Test for overall effect: Z =	7.50 (P <	0.0000)1)							
6.1.2 No BMI cut-off										
g. Wong 2013	-17	17.7	77	-7	9.5	77	5.8%	-10.00 [-14.49, -5.51]		44 4
k. Selezneva 2014	4	22	58	-21.3	11.4	116	5.3%	25.30 [19.27, 31.33]		?? 🕂
n. StGeorge 2009 (M)	-19.1	29.7	73	-7.3	18.5	17	3.7%	-11.80 [-22.92, -0.68]		??
p. Zelber–Sagi 2004	-30.6	59	21	-12.7	26.6	23	1.2%	-17.90 [-45.38, 9.58]		
r. Cheng 2017 (D+E)	-1.5	4	29	1.5	3.3	15	6.3%	-3.00 [-5.22, -0.78]	+	
s. Dong 2016	-4.7	8.1	130	-1.6	8.5	130	6.3%	-3.10 [-5.12, -1.08]	-	4 ? 44
t. StGeorge 2009 (L)	-14.9	35.6	36	-7.3	18.5	17	2.9%	-7.60 [-22.18, 6.98]		?? •
u. Cheng 2017 (D)	-4.4	4	28	1.5	3.3	14	6.3%	-5.90 [-8.18, -3.62]	-	
w. Eckard 2013 (MF)	-19.8	54.9	9	-4.3	38.7	5	0.4%	-15.50 [-64.87, 33.87]		.
y. Eckard 2013 (LF)	-27.5	27.9	12	-4.3	38.7	6	0.8%	-23.20 [-57.96, 11.56]		••
Subtotal (95% CI)			473			420	38.9%	-2.88 [-8.29, 2.53]	\blacklozenge	
Heterogeneity: $Tau^2 = 46.3$	31; Chi ² =	= 105.23	3, df = 9	9 (P < 0.1)	00001);	$l^2 = 91$	%			
Test for overall effect: Z =	1.04 (P =	= 0.30)								
Total (95% CI)			1496			1062	100.0%	-9.81 [-13.12, -6.50]	•	
Heterogeneity: $Tau^2 = 44$	17: Chi ² =	= 924.44	4. df = 2	24 (P < 0	0.00001): $ ^2 = 9$	7%		· · · · · · · · · · · · · · · · · · ·	-
Test for overall effect: $7 =$	5.81 (P <	: 0.0000)1)			,,			-50 -25 0 25 50	
Test for subgroup differen	ces: Chi ²	= 11.52	2, df = 1	(P = 0.0)	0007), I	$^{2} = 91.3$	3%		more intensive WL less intensive WL	

eFigure 7.5 ALT (U/L) by the presence of a minimum overweight/obesity cut-off

eFigure 7.6 AST (U/L) by the presence of a minimum overweight/obesity cut-off

	more intensive WL			less intensive WL			Mean Difference		Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF	
6.3.1 With minimum B	MI cut-o	ff									
a. Al–Jiffri 2013	-11.6	2.2	50	0.7	1.8	50	7.2%	-12.30 [-13.09, -11.51]	•	?? 🕂	
b. Promrat 2010	-20.2	14.1	20	-18	30.8	10	1.3%	-2.20 [-22.26, 17.86]		$\begin{array}{c} \bullet \bullet \\ \bullet \bullet \\ \bullet \end{array}$	
c. AbdEl-Kader 2016	-9.5	1.6	50	0.4	1.4	50	7.2%	-9.90 [-10.49, -9.31]	•	? 🕂 ?	
d. Sun 2012	-5.7	15.2	674	-0.5	5.7	332	7.1%	-5.20 [-6.50, -3.90]	• •	₽? ₽₽	
e. Bahmanabadi 2011	4.4	6.7	20	-1.7	7.9	20	5.8%	6.10 [1.56, 10.64]		?? 🛑 ? ?	
f. Abenavoli 2017	2.8	6.3	20	12.4	15.2	10	3.4%	-9.60 [-19.42, 0.22]		●? ++	
h. Armstrong 2016	-15.8	21.8	23	-8.6	28.3	22	2.0%	-7.20 [-22.01, 7.61]		$\bullet \bullet \bullet \bullet \bullet \bullet$	
i. Asghari 2018	-4.1	3.6	30	4.4	11.8	30	5.9%	-8.50 [-12.91, -4.09]			
j. Axley 2017	-9	2.2	8	0	2	14	7.0%	-9.00 [-10.85, -7.15]	+	++ +	
m. Lim 2018	-19.3	26.1	43	-5.1	13.7	43	3.8%	-14.20 [-23.01, -5.39]		?? ? 🗧	
n. StGeorge 2009 (M)	-6.9	18.3	36	-2.6	14.7	17	3.6%	-4.30 [-13.50, 4.90]		?? 💡 🖶	
q. Harrison 2007	-28	23.2	23	-29	18.4	18	2.5%	1.00 [-11.73, 13.73]		? • • • • •	
x. Khoo 2017	-18	15	12	-23	24	12	1.8%	5.00 [-11.01, 21.01]			
Subtotal (95% CI)			1009			628	58.6%	-6.93 [-9.32, -4.53]	◆		
Heterogeneity: $Tau^2 = 9.88$; $Chi^2 = 143.94$, $df = 12$ (P < 0.00001); $I^2 = 92\%$											
Test for overall effect: 2	Z = 5.67 (P < 0.0	0001)								
622 No minimum PM	Lout off										
	r cut-on	6.2		2	- 4		7 00/	1 00 [2 04 0 04]			
g. wong 2013	-4	6.2	//	-3	5.4	110	7.0%	-1.00 [-2.84, 0.84]	1		
K. Selezneva 2014	0.1	13.7	58	-11	16.4	116	5.8%	11.10 [6.48, 15.72]			
p. Zeiber-Sagi 2004	-18.9	33	21	-8.8	17.2	23	1.8%	-10.10 [-25.87, 5.67]			
r. Cheng 2017 (D+E)	-4.9	2.4	120	4	2.3	14	7.1%	-8.90 [-10.39, -7.41]	•		
s. Dong 2016	-1	3.5	130	0.4	4.9	130	1.2%	-1.40 [-2.44, -0.36]			
t. StGeorge 2009 (L)	-8.3	16.1	73	-2.6	14.7	17	4.2%	-5.70 [-13.60, 2.20]			
u. Cheng 2017 (D)	0.4	2.6	28	4	2.3	12	7.1%	-3.60 [-5.11, -2.09]			
W. ECKard 2013 (MF)	-19.6	47.9	12	-2.9	25.8	5	0.4%	-16.70 [-55.31, 21.91]	•		
y. Eckard 2013 (LF)	-15.9	19.1	12	-2.9	25.8	402	1.0%				
	17 20. Ch	:2 11-	, oo he	0 (D)	0 0000		0.20/	-2.40 [-5.88, 1.08]	•		
Heterogeneity: $Tau^{-} = 1$	17.39; Cn 7 1 25 ($I^{-} = 112$	2.80, ar	= 8 (P <	0.0000)1); I [_] =	93%				
rest for overall effect: A	2 = 1.35 (r = 0.16	0)								
Total (95% CI)			1446			1031	100.0%	-4.84 [-7.31, -2.38]	•		
Heterogeneity: Tau ² = 2	21.83; Ch	$i^2 = 530$).14, df	= 21 (P	< 0.000	001); I ²	= 96%			_	
Test for overall effect: $Z = 3.85$ (P = 0.0001)									-50 -25 0 25 50		
Test for subgroup diffe	rences: C	hi² = 4.	41, df =	1 (P = 0)	0.04), I ²	= 77.3	%		more miterisive will less miterisive will		

eFigure 7.7 Steatosis (Standardized Mean Difference as Assessed by Histologic Examination, MRI, or Ultrasonography) by the Presence of a Minimum Overweight/Obesity Cut-off

	more in	tensiv	e WL	less in	tensive	WL	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
6.15.1 With minimum	BMI cut-	off								
b. Promrat 2010	-1.1	0.4	18	-0.3	0.4	10	8.1%	-1.94 [-2.89, -0.99]		$\begin{array}{c} \bullet \bullet \\ \bullet \bullet \\ \bullet \end{array}$
f. Abenavoli 2017	-1	0.2	20	0.1	0.2	10	6.6%	-5.35 [-6.99, -3.71]		●? ++
g. Wong 2013	-6.8	3.1	77	-2.1	2.5	77	9.0%	-1.66 [-2.03, -1.29]	-	$\mathbf{+}\mathbf{+} \mathbf{+}$
h. Armstrong 2016	-0.7	0.8	23	-0.4	0.8	22	8.8%	-0.37 [-0.96, 0.22]		$\mathbf{++++++}$
i. Asghari 2018	-0.1	0.2	24	0	0.1	26	8.8%	-0.63 [-1.20, -0.06]		$\mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+} \mathbf{+}$
q. Harrison 2007	0	0.2	23	0	0.2	18	8.7%	0.00 [-0.62, 0.62]	+	? • • • •
v. Lee 2012	-1	0.3	8	-1	0.3	10	8.2%	0.00 [-0.93, 0.93]	-+-	+?+?+
z. Ye 2017	-7.8	3.1	14	-1.9	2.4	16	8.2%	-2.09 [-3.00, -1.18]		??????
Subtotal (95% CI)			207			189	66.4%	-1.33 [-2.09, -0.57]	\bullet	
Heterogeneity: Tau ² =	1.02; Chi ²	$^{2} = 68.4$	42, df =	7 (P < 0	.00001	.); $I^2 = 9$	0%			
Test for overall effect:	Z = 3.42	(P=0.0)	0006)							
						10	0.00/	1 00 [0 00 0 01]		
p. Zelber-Sagi 2004	0.1	0.3	11	-0.6	0.4	12	8.0%	1.90 [0.88, 2.91]		
r. Cheng 2017 (D+E)	-7.6	3.6	29	2.8	2.7	15	8.2%	-3.07 [-3.99, -2.15]		
s. Dong 2016	-1.1	0.4	130	0	0.4	130	9.1%	-2.74 [-3.08, -2.40]		
u. Cheng 2017 (D)	-5.4	3.3	28	2.8	2.7	14 171	8.3%	-2.58[-3.45, -1.72]		
	2.21.61	2 - 4	130	2 (5 0		1/1	55.0%	-1.05 [-5.46, 0.16]		
Heterogeneity: I au ² =	3.31; Chi	$^{2} = /4.3$	82, df =	3 (P < 0	.00001	$(); 1^2 = 9$	6%			
lest for overall effect:	Z = 1.770	(P = 0.0)	(80							
Total (95% CI)			405			360	100.0%	-1.48 [-2.27, -0.70]	•	
Heterogeneity: Tau ² =	1.74: Chi ²	$^{2} = 190$.62. df	= 11 (P <	< 0.000)01): I ² =	= 94%			
Test for overall effect: $Z = 3.70$ (P = 0.0002)									-4 -2 0 2 4	
Test for subaroup diff	erences: C	$hi^2 = 0$.10. df -	= 1 (P =	0.75). I	$^{2} = 0\%$			more intensive wL less intensive WL	
		-	,		- ,, -					

8 Subgroup analysis by the severity of the disease (NAFLD vs NASH)

eFigure 8.1 Fibrosis (stage F0-F4)

	more in	tensive	e WL	less in	tensive	e WL		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
7.1.1 NAFLD										
p. Zelber–Sagi 2004	-0.7	0.6	11	-0.5	0.4	11	20.1%	-0.20 [-0.63, 0.23]		
w. Eckard 2013 (MF)	-0.1	1.5	9	0.1	0.5	5	9.1%	-0.20 [-1.27, 0.87]		
y. Eckard 2013 (LF) Subtotal (95% CI)	-0.8	0.8	12 32	0.1	0.5	6 22	16.4% 45.6%	-0.90 [-1.50, -0.30] - 0.45 [-0.94, 0.05]		•?•
Heterogeneity: Tau ² = Test for overall effect:	0.09; Chi Z = 1.77	$^{2} = 3.62$ (P = 0.0	1, df = 1 08)	2 (P = 0.	16); l ² =	= 45%				
7.1.2 NASH										
b. Promrat 2010	0	0.5	18	-0.3	0.6	10	19.8%	0.30 [-0.14, 0.74]	+	
h. Armstrong 2016	-0.2	0.8	23	0.2	1	22	17.9%	-0.40 [-0.93, 0.13]		+++ ++
v. Lee 2012 Subtotal (95% CI)	0.5	0.8	8 49	0	0.3	10 42	16.8% 54.4%	0.50 [-0.08, 1.08] 0.13 [-0.38, 0.64]		₽?₽?₽
Heterogeneity: Tau ² = Test for overall effect:	0.14; Chi Z = 0.50	$^{2} = 5.9!$ (P = 0.6	5, df = 1 51)	2 (P = 0.0)	05); l ² =	= 66%				
Total (95% CI)			81			64	100.0%	-0.13 [-0.54, 0.27]		
Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diff	0.16; Chi Z = 0.65 erences: C	$P^{2} = 15.4$ (P = 0.5 Chi ² = 2	46, df = 52) .54, df		-2 -1 0 1 more intensive WL less intensive W					

9 eMethods: Search strategy

Medline

	Searches
1	Non-alcoholic Fatty Liver Disease/
2	*Fatty Liver/
3	((nonalcoholic or non-alcoholic) adj5 (fatty liver or steatohepatitis)).ti,ab.
4	(fatty liver or steatohepatitis).ti.
5	(nafld or nash).ti,ab.
6	1 or 2 or 3 or 4 or 5
7	Weight Loss/
8	Weight Reduction Programs/
9	diet therapy/ or caloric restriction/ or diet, reducing/
10	exp Obesity/dh [Diet Therapy]
11	(weight adj3 (loss or lose or lost or losing or chang* or reduc* or manag*)).ti,ab.
12	((energy or calori*) adj2 (reduc* or restrict)).ti,ab.
13	((weight or overweight or obes*) adj5 (program* or service? or intervention?)).ti,ab.
14	exp Anti-Obesity Agents/
15	exp Obesity/dt, th [Drug Therapy, Therapy]
16	((weight or overweight or obes*) adj3 (therap* or treat* or drug? or agent?)).ti,ab.
17	exp OBESITY/su [Surgery]
18	exp Bariatric Surgery/
19	((weight loss or bariatric or obes*) adj5 surg*).ti,ab. or bariatric*.ti.
20	(((gastric or jejunoileal) adj3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio-pancreatic) adj2 diver*)).ti,ab.
21	obesity management/ or bariatrics/
22	((obes* or overweight) adj3 manage*).ti,ab.
23	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	randomized controlled trial.pt.
25	controlled clinical trial.pt.
26	randomized.ab.
27	placebo.ab.
28	drug therapy.fs.
29	randomly.ab.
30	trial.ab.
31	groups.ab.
32	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33	exp animals/ not humans.sh.
34	32 not 33
35	6 and 23 and 34

Embase

	Searches
1	nonalcoholic fatty liver/
2	*Fatty Liver/
3	((nonalcoholic or non-alcoholic) adj5 (fatty liver or steatohepatitis)).ti,ab.
4	(fatty liver or steatohepatitis).ti.
5	(nafld or nash).ti,ab.
6	1 or 2 or 3 or 4 or 5
7	weight reduction/
8	weight loss program/
9	diet therapy/ or exp diet restriction/ or low calory diet/ or low fat diet/
10	exp Obesity/dm
11	(weight adj3 (loss or lose or lost or losing or chang* or reduc* or manag*)).ti,ab.
12	((energy or calori*) adj2 (reduc* or restrict)).ti,ab.
13	((weight or overweight or obes*) adj5 (program* or service? or intervention?)).ti,ab.
14	exp antiobesity agent/
15	exp Obesity/dt, th
16	((weight or overweight or obes*) adj3 (therap* or treat* or drug? or agent?)).ti,ab.
17	exp OBESITY/su
18	exp Bariatric Surgery/
19	((weight loss or bariatric or obes*) adj5 surg*).ti,ab. or bariatric*.ti.
20	(((gastric or jejunoileal) adj3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio-pancreatic) adj2 diver*)).ti,ab.
21	obesity management/ or bariatrics/
22	((obes* or overweight) adj3 manage*).ti,ab.
23	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	6 and 23
25	randomized controlled trial/
26	single blind procedure/ or double blind procedure/
27	crossover procedure/
28	random*.tw.
29	(random or ((singl* or doubl*) adj (blind* or mask*)) or crossover or cross over or factorial* or latin square or assign* or allocat* or volunteer*).ti,ab.
30	25 or 26 or 27 or 28 or 29
31	(exp animals/ or nonhuman/) not human/
32	30 not 31
33	24 and 32

PsycINFO

	Searches
1	((nonalcoholic or non-alcoholic) adj5 (fatty liver or steatohepatitis)).ti,ab.
2	(fatty liver or steatohepatitis).ti.
3	(nafld or nash).ti,ab.
4	1 or 2 or 3
5	weight loss/ or weight control/
6	(weight adj3 (loss or lose or lost or losing or chang* or reduc* or manag*)).ti,ab.
7	((energy or calori*) adj2 (reduc* or restrict)).ti,ab.
8	((weight or overweight or obes*) adj5 (program* or service? or intervention?)).ti,ab.
9	((weight or overweight or obes*) adj3 (therap* or treat* or drug? or agent?)).ti,ab.
10	bariatric surgery/
11	((weight loss or bariatric or obes*) adj5 surg*).ti,ab. or bariatric*.ti.
12	(((gastric or jejunoileal) adj3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio-pancreatic) adj2 diver*)).ti,ab.
13	((obes* or overweight) adj3 manage*).ti,ab.
14	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15	4 and 14
16	random*.ti,ab,hw,id.
17	trial*.ti,ab,hw,id.
18	controlled stud*.ti,ab,hw,id.
19	placebo*.ti,ab,hw,id.
20	((singl* or doubl* or trebl* or tripl*) and (blind* or mask*)).ti,ab,hw,id.
21	(cross over or crossover or factorial* or latin square).ti,ab,hw,id.
22	(assign* or allocat* or volunteer*).ti,ab,hw,id.
23	treatment effectiveness evaluation/
24	mental health program evaluation/
25	exp experimental design/
26	(clinical trial or treatment outcome).md.
27	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28	15 and 27

Cinahl

#	Query
S14	S3 AND S12 Limiters - Clinical Queries: Therapy - Best Balance
S13	S3 AND S12
S12	S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S11	(MH "Obesity+/DH/DT/SU/TH")
S10	TI (((weight loss or bariatric or obes*) N5 surg*)) OR AB (((weight loss or bariatric or obes*) N5 surg*)) OR TI bariatric* OR TI ((((gastric or jejunoileal) N3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio-pancreatic) N2 diver*))) OR AB ((((gastric or jejunoileal) N3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or (biliopancreatic) N2 diver*)) or gastrectom* or gastroplast* or (biliopancreatic) N2 diver*)) or gastrectom* or gastroplast* or balloon* or diver*)) or gastrectom* or gastroplast* or (biliopancreatic) N2 diver*)))
S9	(MH "Bariatric Surgery+")
S8	TI (((weight or overweight or obes*) N3 (therap* or treat* or drug? or agent?))) AND AB (((weight or overweight or obes*) N3 (therap* or treat* or drug? or agent?)))
S7	(MH "Antiobesity Agents+")
S6	TI ((weight N3 (loss or lose or lost or losing or chang* or reduc* or manag*))) OR AB ((weight N3 (loss or lose or lost or losing or chang* or reduc* or manag*))) OR TI (((energy or calori*) N2 (reduc* or restrict))) OR AB (((energy or calori*) N2 (reduc* or restrict))) OR TI (((weight or overweight or obes*) N5 (program* or service? or intervention?))) OR AB (((weight or overweight or obes*) N5 (program* or service? or intervention?))) OR AB (((weight or overweight or obes*) N5 (program* or service? or intervention?)))
S5	(MH "Diet, Reducing") OR (MH "Diet Therapy")
S4	(MH "Weight Loss") OR (MH "Weight Reduction Programs")
S3	S1 OR S2
S2	TI ("fatty liver" or steatohepatitis) OR AB (((nonalcoholic or non-alcoholic) N5 ("fatty liver" or steatohepatitis))) OR TI (nafld or nash) OR AB (nafld or nash)
S1	(MM "Fatty Liver") OR (MH "Nonalcoholic Fatty Liver Disease")

Cochrane

ID	Search
#1	MeSH descriptor: [Non-alcoholic Fatty Liver Disease] explode all trees
#2	((nonalcoholic or non-alcoholic) near (fatty liver or steatohepatitis)):ti,ab,kw or fatty liver or steatohepatitis:ti or nafld or nash:ti,ab,kw (Word variations have been searched)
#3	#1 or #2
#4	weight or obes* or overweight or bariatric*:ti,ab,kw (Word variations have been searched)
#5	MeSH descriptor: [Weight Loss] this term only
#6	MeSH descriptor: [Weight Reduction Programs] explode all trees
#7	MeSH descriptor: [Diet Therapy] this term only
#8	MeSH descriptor: [Diet, Reducing] explode all trees
#9	MeSH descriptor: [Caloric Restriction] explode all trees
#10	(weight near/3 (loss or lose or lost or losing or chang* or reduc* or manag*)):ti,ab,kw or ((energy or calori*) near/2 (reduc* or restrict)):ti,ab,kw or ((weight or overweight or obes*) near (program* or service? or intervention?)):ti,ab,kw (Word variations have been searched)
#11	MeSH descriptor: [Anti-Obesity Agents] explode all trees
#12	((weight or overweight or obes*) near/3 (therap* or treat* or drug? or agent?)):ti,ab,kw (Word variations have been searched)
#13	MeSH descriptor: [Bariatric Surgery] explode all trees

#14	bariatric*:ti or ((weight loss or bariatric or obes*) near surg*):ti,ab,kw or (((gastric or jejunoileal) near/3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio- pancreatic) near/2 diver*)):ti,ab,kw or ((obes* or overweight) near/3 manage*):ti,ab,kw (Word variations have been searched)
#15	MeSH descriptor: [Obesity] explode all trees
#16	MeSH descriptor: [Obesity Management] explode all trees
#17	#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16
#18	#3 and #17

WoS

Set	Save search history and/or create an alertOpen a saved search history
#9	#8 AND #7
# 8	TOPIC: ((random* or blind* or allocat* or assign* or trial* or crossover* or cross-over*))
#7	#6 AND #1
#6	#5 OR #4 OR #3 OR #2
# 5	TOPIC: (((obes* or overweight) NEAR/3 manage*))
#4	TOPIC: (((weight loss or bariatric or obes*) NEAR5 surg*)) OR TOPIC: (bariatric*) OR TOPIC: ((((gastric or jejunoileal) NEAR/3 (band* or bypass* or balloon* or diver*)) or gastrectom* or gastroplast* or ((biliopancreatic or bilio-pancreatic) NEAR/2 diver*)))
#3	TOPIC: (((weight or overweight or obes*) NEAR/3 (therap* or treat* or drug? or agent?)))
#2	TOPIC: ((weight NEAR/3 (loss or lose or lost or losing or chang* or reduc* or manag*))) OR TOPIC: (((energy or calori*) NEAR/2 (reduc* or restrict))) OR TOPIC: (((weight or overweight or obes*) NEAR/5 (program* or service? or intervention?)))
# 1	TOPIC: (((nonalcoholic or non-alcoholic) NEAR/5 ("fatty liver" or steatohepatitis))) OR TITLE: ("fatty liver" or steatohepatitis) OR TOPIC: (nafld OR nash)

Trial Registers

ClinicalTrials.gov
Other terms=(obesity OR obesity OR weight OR overweight OR bariatric OR bariatrics) AND
Condition=("nonalcoholic fatty liver" OR "non alcoholic fatty liver" OR "nonalcoholic steatohepatitis" OR "non-
alcoholic steatohepatitis" OR nafld OR nash)
WHO ICTRP

nonalcoholic fatty liver AND obese OR non alcoholic fatty liver AND obese OR nonalcoholic steatohepatitis AND obese OR non-alcoholic steatohepatitis AND obese OR nafld AND obese OR nash AND obese

nonalcoholic fatty liver AND obesity OR non alcoholic fatty liver AND obesity OR nonalcoholic steatohepatitis AND obesity OR non-alcoholic steatohepatitis AND obesity OR nafld AND obesity OR nash AND obesity

nonalcoholic fatty liver AND overweight OR non alcoholic fatty liver AND overweight OR nonalcoholic steatohepatitis AND overweight OR non-alcoholic steatohepatitis AND overweight OR nafld AND overweight OR nash AND overweight

nonalcoholic fatty liver AND weight OR non alcoholic fatty liver AND weight OR nonalcoholic steatohepatitis AND weight OR nan-alcoholic steatohepatitis AND weight OR nafld AND weight OR nash AND weight

nonalcoholic fatty liver AND bariatric OR non alcoholic fatty liver AND bariatric OR nonalcoholic steatohepatitis AND bariatric OR non-alcoholic steatohepatitis AND bariatric OR nafld AND bariatric OR nash AND bariatric

nonalcoholic fatty liver AND bariatrics OR non alcoholic fatty liver AND bariatrics OR nonalcoholic steatohepatitis AND bariatrics OR non-alcoholic steatohepatitis AND bariatrics OR nafld AND bariatrics OR nash AND bariatrics