HUNTER, E., AVENELL, A., MAHESHWARI, A., STADLER, G. and BEST, D. 2021. The effectiveness of weight-loss lifestyle interventions for improving fertility in women and men with overweight or obesity and infertility: a systematic review update of evidence from randomized controlled trials. [Dataset]. Obesity reviews [online], 22(12), article e13325. Available from: <u>https://tinyurl.com/4kpcrzv6</u>

# The effectiveness of weight-loss lifestyle interventions for improving fertility in women and men with overweight or obesity and infertility: a systematic review update of evidence from randomized controlled trials. [Dataset]

HUNTER, E., AVENELL, A., MAHESHWARI, A., STADLER, G. and BEST, D.

2021

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The effectiveness of weight-loss lifestyle interventions for improving fertility in women and men with overweight or obesity and infertility: a systematic review update of evidence from randomized controlled trials

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# Supplementary Data

## Supplementary data S1: Intervention Characteristics

Study	Country/	Intervention Length	ntervention Intervention details Sa ength Si	Sample Size/	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group)	Weight (kg) BMI	Weight change (kg):	Weight change (kg):
	Diet & Exercise			Sex			Mean yrs (SD)	(intervention group) Mean (SD)	<b>group</b> Mean (SD)	<b>group</b> Mean (SD)
Diet & Exe	rcise									
Duval et al.,2015 <sup>55</sup>	Canada	24 weeks	Intervention group: 24- week interdisciplinary lifestyle intervention involving individual meetings with dietician and kinesiologist plus 12 weekly group meetings. Nutritional counselling provided following 'Healthy Plate'. Participants were encouraged to increase physical activity levels. Control group: Standard fertility treatment. Participants followed up for 18 months or until the end of pregnancy	105 F	24	Primary outcomes: Pregnancy rate Secondary outcome: Live birth rates, Change in weight	30.5 ( <u>+</u> 4.8)	Details unavailable	Details unavailable	Details unavailable

Study	Country/	Intervention Length	Intervention details	Sample Size/	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group)	Weight (kg) BMI	Weight change (kg):	Weight change (kg):
	Setting			Sex			Mean yrs (SD)	(intervention group) Mean (SD)	<b>group</b> Mean (SD)	<b>group</b> Mean (SD)
Espinos et al., 2017 <sup>44</sup>	Spain Fertility Unit, Hospital de la Santa Creu i Sant Pau	12 weeks	Intervention group: 12- week, tailored diet, provided by dietician, reducing kcal intake by 500-800kcal per day. Encouraged 3 main meals and 2 snacks Self-reported food intake every 15 days. Diet readjusted if no weight loss achieved at follow up. 60 minutes of physical activity on stationary bike or treadmill, three times per week, monitored by trained staff. Control group: Straight to IVF. Participants followed up for 12 months	41 F	21	Primary outcome: Pregnancy rates Secondary outcomes: Change in weight, oocytes retrieved, miscarriage rate, live birth rate	32.0 ( <u>+</u> 3.2)	91.7 ( <u>+</u> 11.8) 34.6 ( <u>+</u> 3.0)	-6.4 ( <u>+</u> 7.72)	0.0 ( <u>+</u> 5.195)
Guzick et al., 1994 <sup>53</sup>	USA Magee Women's Hospital, University of Pittsburgh Medical Centre	12 weeks	Intervention group: 8 weeks VLCD, lean meat, fish or fowl and liquid meal replacements providing 400 kcal/day. Followed by gradual food reintroduction for 4 weeks until participants consumed around 1200 kcal/day. Training in behaviour modification to aid long- term changes to eating habits. Advised to gradually increase physical activity levels; walking was encouraged. Advised to gradually increase	12 F	6	Primary outcome: Hormonal and insulin level changes Secondary outcome: change in weight, ovulation	32.2 ( <u>+</u> 4.9)*	108.0 ( <u>+</u> 13.0)*	-16.2kg ( <u>+</u> 10.5)	0.0 ( <u>+</u> 5.195)

Study	Country/	Intervention Length	Intervention details	Sample Size/	<b>n</b> (interv	Outcomes	Age (intervention	<b>Weight</b> (kg) <i>BMI</i>	Weight change (kg):	Weight change (kg):
	Setting			Sex	ention)		group) Mean yrs (SD)	at start (intervention group) Mean (SD)	<b>intervention</b> <b>group</b> Mean (SD)	<b>control</b> group Mean (SD)
			distance walked to achieve around 3km, 5 days a week.					(50)		
			Control group: Waitlist control.							
			8-week screening period involving regular blood tests before and after the 12-week intervention for both groups.							
Hoeger et al., 2004 <sup>49</sup>	USA	48 weeks	Intervention group: Comprised of 2 groups	38	11	Primary outcome: Return of ovulation	28.6 (+5.0)	Details unavailable	-7.75** (+3.4)	-2.59** (+4.2)
	Reproductive Endocrinology Clinic, University of Rochester		metformin: 24-week intensive phase followed by 24-week maintenance phase. Individualised meal plan provided for each participant. 500-1000 kcal/day deficit. Encouraged participants to eat low GI foods. Weekly group meetings in the intensive phase, to educate and monitor progress. Fortnightly group meetings in the maintenance stage for support and to monitor progress. Participants were encouraged to participate in 150 minutes of exercise each week.	F		Secondary outcomes: Success of weight-reduction regimen, preliminary differences on outcome measurements	()		()	()
			Group 2, Lifestyle (as above) plus placebo							

Study	Country/ Setting	Intervention Length	Intervention details	Sample Size/ Sex	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group) Mean yrs (SD)	Weight (kg) BMI at start (intervention group) Mean (SD)	Weight change (kg): intervention group Mean (SD)	Weight change (kg): control group Mean (SD)
			Control group: Comprised of 2 groups Group 1, Metformin only							
Legro et al., 2015 <sup>56</sup>	USA Department of Obstetrics and Gynecology, University of Pennsylvania Penn State College of Medicine Multi-centre trial	16 weeks	Group 2, Placebo only Intervention group: Lifestyle plus Oral Contraceptive Pill (OCP): Reducing diet incorporating liquid meal replacements, prepared meals, snacks. Caloric deficiency calculated from each individual's body weight. Encouraged to gradually increase walking or similar aerobic exercise building to 30-35 mins on 5 days of the week Behavioural modification lessons were delivered by trained study coordinators.	149 F	50	Primary outcome: Live birth rate Secondary outcomes: Ovulation rates, change in weight	28.6 ( <u>+</u> 3.4)	96.0 ( <u>+</u> 15.8) 35.1 ( <u>+</u> 4.6)	-6.1 ( <u>+</u> 3.2)	-1.1 ( <u>+</u> 3.1)
			Recruited from October							

2008 until December 2012, follow up until March 2014.

Study	Country/ Setting	Intervention Length	Intervention details	Sample Size/	<b>n</b> (interv ention)	Outcomes	Age (intervention group)	<b>Weight</b> (kg) <i>BMI</i> at start	Weight change (kg): intervention	Weight change (kg): control
	Ū			Sex			Mean yrs (SD)	(intervention group) Mean (SD)	<b>group</b> Mean (SD)	<b>group</b> Mean (SD)
Moran et al., 2011 <sup>57</sup>	Australia Repromed		Intervention group: Reducing diet to around 1,200 kcal/day. 1 meal a day replaced with a liquid	46 F	18	Primary outcome: Pregnancy and live birth rates	33.8 (± 3.5)	93.0 (± 16.0)	-3.8 ( <u>+</u> 3.0)	-0.5 ( <u>+</u> 1.2)
	Infertility Clinic		meal replacement. 5-9 week intervention depending on when oocyte pick up and embryo transfer occurred. Prescribed a home-based conditioning and walking exercise programme. Diet and exercise advice provided by a qualified dietician.			Secondary outcomes: Change in weight, change in waist circumference		34.0 ( <u>+</u> 4.5)		
			<b>Control group:</b> Standard dietary and lifestyle advice, provided face to face, focusing on factors influencing fertility. No follow up							
Mutsaerts	The Netherlands	24 weeks	Intervention group: 24 week reducing diet by 600kcal/day but not lower	577	236	Primary outcome: Live birth rate	29.7 ( <u>+</u> 4.5)	Details	-4.4 ( <u>+</u> 5.8)	-1.1 ( <u>+</u> 4.3)
et al., 2016 <sup>41</sup>	6 University Medical Centres & 17 General Hospitals Multi-centre trial		than 1,200kcal/day. Advised to increase physical activity to achieve 30 minutes of moderate exercise 2-3 times a week. Provided with pedometer, encouraged to take 10,000 steps daily. Motivational counselling was provided to promote awareness of a healthy lifestyle and to formulate individualised goals. Led by trained coaches, purpose and distingen	F		Secondary outcomes: Change in weight, ongoing pregnancy rates, clinical pregnancy rates, miscarriage, fertility treatments, complications from treatments, gestational diabetes				

Study	Country/ Setting	Intervention Length	Intervention details Control group: Straight to standard fertility treatments Recruitment from June 2009 until June 2012, follow up for 24 months or until end of pregnancy.	Sample Size/ Sex	<b>n</b> (interv ention)	Outcomes	Age (intervention group) Mean yrs (SD)	Weight (kg) BMI at start (intervention group) Mean (SD)	Weight change (kg): intervention group Mean (SD)	Weight change (kg): control group Mean (SD)
Palomba et al., 2010 <sup>58</sup>	Italy Hospital Fertility Unit	6 weeks	Intervention group: Lifestyle plus Clomiphene Citrate (CC) Hypocaloric diet to achieve approximately 800kcal deficit per day (based on baseline caloric intake of individual) Interactive, educational group meetings held with the aim of improving adherence 3 structured exercise sessions per week involving 30 mins on stationary bike, intensity gradually increased until working at 60-70% VO2 max. Control group: CC (150mg daily) only Recruitment from February 2008 until August 2009, follow up for 6 weeks.	96 F	32	Primary outcome: Ovulation rate Secondary outcomes: other reproductive outcomes, changes in anthropometric and hormonal measures and compliance	28.43 (± 8.31)	86.21 (± 6.98) <i>31.05</i> (±2.98)	-4.42 ( <u>+</u> 9.22)	-0.69 ( <u>+</u> 9.47)

Study	Country/ Setting	Intervention Length	Intervention details	Sample Size/ Sex	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group) Mean yrs (SD)	Weight (kg) BMI at start (intervention group) Mean (SD)	Weight change (kg): intervention group Mean (SD)	Weight change (kg): control group Mean (SD)
Rothberg et al., 2016 <sup>52</sup>	USA Centre for Reproductive medicine, University of Michigan (UM) UM Weight Management Programme	16 weeks	Intervention group: 12- week VLCD, liquid meal replacements providing 800 kcal/day. Followed by 2 weeks partial meal replacement then 2-week transition to fully food- based plan. Met with dietician twice a month. Encouraged to increase exercise to 40 minutes per day. <b>Control group</b> : usual care in the centre. Conventional food-based diet recommended for 12 weeks;1200kcal/ daily, aiming for 0.45-1.8kg weight loss per week. One meeting with dietician at end, 3 optional follow up visits if the participant desired. Recruitment from October 2013 until March 2015. 12-month follow up for all but last participant who received 6-month follow up.	14 F	6	Primary outcomes: Feasibility of recruitment, randomisation, intervention implementation, retention Secondary outcomes: Change in weight, pregnancy rates, live birth rates, miscarriages, ovulation rates, BMI	33.0 ( <u>+</u> 5.0)	108.0 ( <u>+</u> 10.0) 41 ( <u>+</u> 4)	-14 ( <u>+</u> 6.0)	-5 ( <u>+</u> 5.0)

Study	Country/ Setting	Intervention Length	Intervention details	Sample Size/ Sex	<b>n</b> (interv ention)	Outcomes	Age (intervention group) Mean yrs (SD)	Weight (kg) BMI at start (intervention group) Mean	Weight change (kg): intervention group Mean (SD)	Weight change (kg): control group Mean (SD)
Sim et al., 2014 <sup>59</sup>	Australia Fertility Unit, Royal Prince Alfred Hospital	12 weeks	Intervention group: 6- week VLCD incorporating liquid meal replacements providing around 600 kcal/day, followed by refeeding protocol involving mildly hypocaloric diet (600kcal daily deficit), individualised plan prescribed by a dietician Weekly group meetings involved dietary, exercise and psychological/behavioural advice relating to weight loss and infertility Encouraged to increase step count to 10,000 steps/ day over first 6 weeks and maintain that level for the remainder of the study. Control group: Standard care; advised to see GP for weight loss advice or referred to weight loss service if BMI >35kg/m <sup>2</sup> . Received same printed material as intervention group. Recruitment from February 2007 to February 2011, follow up for 12 months.	49 F	26	Primary Outcome: Clinical pregnancy rate Secondary outcomes: Changes in anthropometric measures, reproductive parameters, fertility treatment measures, miscarriage rates and compliance	32.9 (± 3.3)	(SD) 95.8 (±12.7) 35.1 ( <u>+</u> 3.8)	-6.6 ( <u>+</u> 4.6)	-1.6 ( <u>+</u> 3.6)

Study	Country/	Intervention Length	on Intervention details Sa Si Se	Sample Size/	<b>n</b> (interv	Outcomes	Age (intervention	<b>Weight</b> (kg) <i>BMI</i>	Weight change (kg):	Weight change (kg):
	Setting			Sex	ention)		group) Mean yrs (SD)	at start (intervention group) Mean (SD)	<b>intervention</b> <b>group</b> Mean (SD)	<b>control</b> group Mean (SD)
Diet Alone										
Becker et al., 2015 <sup>54</sup>	Brazil Obstetrics & Gynaecology Service, Hospital de Clinicas de Porto Alegre	12 weeks	Intervention group: 12- week intervention Low GI, hypocaloric diet Individualised diet for each participant with calorie content equivalent to 20kcals/kg of their current body weight. 3-day food diary completed at baseline, 6 and 12 weeks.	36 F	16	Primary outcomes: Anthropometric (change in weight, BMI) and metabolic changes. Secondary outcomes: Clinical pregnancy rate, live birth rate, oocyte retrieval, compliance to diet.	31.36 (± 0.89)*	77.03 (± 2.06)* 28.67 ( <u>+</u> 0.06)	-4.51 ( <u>+</u> 3.11)	0.72 ( <u>+</u> 2.6)
			<b>Control group:</b> 3-day food diary at baseline, 6 and 12 weeks. Recruitment and follow up from January 2012-							
Einarsson et al., 2017 <sup>48</sup>	Sweden, Denmark & Iceland 9 Infertility Clinics Multi-centre trial	16 weeks	December 2013. Intervention group: 12- week VLCD, liquid meal replacements providing 880kcal/ day. Followed by meetings with dietician for 2-5 weeks for reintroduction of solid food and weight stabilisation. Participants unable to complete VLCD were offered individualised weight loss counselling until start of IVF. Control group: Straight to IVF.	317 F	152	Primary outcome: Live birth. Secondary outcomes: Pregnancy rate, miscarriage rate, live birth after spontaneous pregnancy, oocyte retrieval, change in weight.	31.5 ( <u>+</u> 4.3)	92.4 ( <u>+</u> 8.0)	-9.1 ( <u>+</u> 6.83)	1.19 ( <u>+</u> 1.95)
			Recruitment from October 2010 until January 2016,							

Intervention Length	Intervention details followed up until February 2017.	Sample Size/ Sex	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group) Mean yrs (SD)	Weight (kg) BMI at start (intervention group) Mean (SD)	Weight change (kg): intervention group Mean (SD)	Weight change (kg): control group Mean (SD)
10 weeks f & c of tal	Intervention group: High intensity interval training (HIIT) performed 3 times a week. 2 sessions involved working at 85-95% max HR for 4 minutes repeated four times. 1 session involved working at 100% max HR for 1 minute repeated 10 times. All sessions were supervised until the participant was familiar with the protocol. Exercise regime continued until ovulation induction. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.	18 F	8	Primary outcome: Pregnancy rates Secondary outcomes: Insulin sensitivity, body composition	33.1 ( <u>+</u> 5.9)	85.7 ( <u>+</u> 3.5) 28.9 ( <u>+</u> 2.4)	-0.6 ( <u>+</u> 6.08)	-0.7 ( <u>+</u> 6.11)
	Intervention Length 10 weeks f & tof tal r	Intervention LengthIntervention detailsfollowed up until February 2017.10 weeksff&f&f&fafafafafafafafaafaafaaabaaabaababababbacbabbabbbbbcbabababababbbbbbbbbbbbbbbbbbbcbcbcbcbcbb <td< td=""><td>Intervention LengthIntervention details Size/Sample Size/Sexfollowed up until February 2017.10 weeksIntervention group: High intensity interval training (HIIT) performed 3 times a week. 2 sessions involved working at 85-95% max HR for 4 minutes repeated four times. 1 session involved working at 100% max HR for 1 minute repeated 10 times. All sessions were supervised until the participant was familiar with the protocol. Exercise regime continued until ovulation induction. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.18</td><td>Intervention LengthIntervention details size/Sample size/n (interv ention)Sexfollowed up until February 2017.10 weeksIntervention group: High intensity interval training (HIT) performed 3 times a week. 2 sessions involved working at 85-95% max HR for 4 minutes repeated four times. All sessions were supervised until the participant was familiar with the protocol. Exercise regime continued until outlation induction. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.188</td><td>Intervention Length       Intervention details       Sample Size/       n (intervention)       Outcomes         Sex       followed up until February 2017.       Sex       Sex       Sex         10 weeks       Intervention group: High intensity interval training (HIT) performed 3 times a week.2 sessions involved working at 85-95% max HR for 4 minutes repeated four times. 1 session involved working at 100% max HR for 1 minute sessions were supervised until the participant was familiar with the protocol. Exercise regime continued until ovulation induction. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.       18       8       Primary outcome: Pregnancy rates         f      </br></br></td><td>Intervention Length       Intervention details       Sample Size/       n (interv ention)       Outcomes       Age (intervention group) Mean yrs (SD)         10 weeks       Intervention group: High intensity interval training (HIT) performed 3 times a week, 2 sessions involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 100% max H R for 1 minute tail       18 F       8 F       Primary outcome: Pregnancy rates Insulin sensitivity, body composition       33.1 (±5-9)         6 r      </td><td>Intervention LengthIntervention details Size/Sample Size/n (interv ention)OutcomesAge (intervention group)Weight (kg) BM/ at start (intervention group) Mean10 weeksIntervention group: High intensity interval training (Intervention group)188Primary outcome: Pregnancy rates33.1 (±5.9)85.7 (±3.5)6Mitoria t85-96 weak week, 2 session simolutes to f at start moving at 85-96 weak HR for 4 minutes repeated 10 times. All session were supervised until the participant was functional advice weak and there to Norwegian diet repoated to admete to Nor</td><td>Intervention Length       Intervention (see )       Intervention (see )       Intervention (see )       Sample (see (see )       n (see (see )       Outcomes (see )       Age (intervention group) Mean (sc)       Weight (kg) (bill (kt) at start (sc)       Weight (kg) (ht) at start (sc)         10 weeks       Intervention group: High intensity interval training (HIT) performed 3 times a week. 2 seesions involved working at 85-9% (kt) of involved working at 100% mean tables but no doubles the participant was familiar with the protocol. Exercise regime continued until ovulation induction. 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Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.18	Intervention LengthIntervention details size/Sample size/n (interv ention)Sexfollowed up until February 2017.10 weeksIntervention group: High intensity interval training (HIT) performed 3 times a week. 2 sessions involved working at 85-95% max HR for 4 minutes repeated four times. All sessions were supervised until the participant was familiar with the protocol. Exercise regime continued until outlation induction. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.188	Intervention Length       Intervention details       Sample Size/       n (intervention)       Outcomes         Sex       followed up until February 2017.       Sex       Sex       Sex         10 weeks       Intervention group: High 	Intervention Length       Intervention details       Sample Size/       n (interv ention)       Outcomes       Age (intervention group) Mean yrs (SD)         10 weeks       Intervention group: High intensity interval training (HIT) performed 3 times a week, 2 sessions involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 85-95% max H for 4 minutes repeated four times. 1 session involved working at 100% max H R for 1 minute tail       18 F       8 F       Primary outcome: Pregnancy rates Insulin sensitivity, body composition       33.1 (±5-9)         6 r	Intervention LengthIntervention details Size/Sample Size/n (interv ention)OutcomesAge (intervention group)Weight (kg) BM/ at start (intervention group) Mean10 weeksIntervention group: High intensity interval training (Intervention group)188Primary outcome: Pregnancy rates33.1 (±5.9)85.7 (±3.5)6Mitoria t85-96 weak week, 2 session simolutes to f at start moving at 85-96 weak HR for 4 minutes repeated 10 times. All session were supervised until the participant was functional advice weak and there to Norwegian diet repoated to admete to Nor	Intervention Length       Intervention (see )       Intervention (see )       Intervention (see )       Sample (see (see )       n (see (see )       Outcomes (see )       Age (intervention group) Mean (sc)       Weight (kg) (bill (kt) at start (sc)       Weight (kg) (ht) at start (sc)         10 weeks       Intervention group: High intensity interval training (HIT) performed 3 times a week. 2 seesions involved working at 85-9% (kt) of involved working at 100% mean tables but no doubles the participant was familiar with the protocol. Exercise regime continued until ovulation induction. Encourage to adhere to Norwegian diet recommendations but no other nutritional advice was provided.       18 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8

Study	Country/	Intervention Length	Intervention details	Sample Size/	<b>n</b> (interv ention)	Outcomes	Age (intervention group)	Weight (kg) BMI	Weight change (kg):	Weight change (kg):
	Setting			Sex	·		Mean yrs (SD)	at start (intervention group) Mean (ס)	<b>intervention</b> group Mean (SD)	<b>group</b> Mean (SD)
			from being active. Encouraged to adhere to Norwegian diet recommendations but no other nutritional advice was provided.							
Nasrekani et al., 2016 <sup>45</sup>	Iran Fertility Clinic,	12 weeks	Participants were followed up until they received results from their first round of IVF. <b>Intervention group:</b> 12- week aerobic exercise programme. Intensity gradually increased over 12 works, attaina off with	20 F	10	Primary outcome: Hormone levels; LH Secondary outcome:	30.9 ( <u>+</u> 7.14)	71.11 ( <u>+</u> 15.05)	-0.95 ( <u>+</u> 6.18)	0.05 ( <u>+</u> 5.93)
	Bojnurd		12 weeks, starting off with 10-minute warm up and 10 minutes of non-stop aerobic exercises, increasing this by 1 minute each session building up to three 60-minute sessions per week.			Weight in Kg		28.43 ( <u>+</u> 6.78)		
			<b>Control group:</b> no intervention; could maintain sedentary lifestyle.							
Pedometer exercise co	r plus diet & ounselling									
Nagelberg et al.,	USA	4 weeks	Intervention group: Referred to Wellness Clinic for dietary and	21	10	Primary outcome: Change in weight	Details unavailable	Details unavailable	Details unavailable	Details unavailable
2016 <sup>51</sup>	Reproductive Endocrinology Clinic, Los Angeles County		exercise counselling Provided with a pedometer.	F		Secondary outcomes: Ovulation improvement, pregnancy rates				

Study	Country/	Intervention Length	Intervention details	Sample Size/	<b>n</b> (interv ention)	Outcomes	<b>Age</b> (intervention group)	Weight (kg) BMI at start	Weight change (kg): intervention	Weight change (kg): control
	Setting			Sex			Mean yrs (SD)	(intervention group) Mean (SD)	<b>group</b> Mean (SD)	<b>group</b> Mean (SD)
	+ University of Southern California Medical Center		Received weekly phone calls to discuss exercise and nutrition goals, reviewed weekly step count and given specific goals to increase step count by 50% to achieve 10,000 steps per day. <b>Control group:</b> Referred to Wellness Clinic for dietary and exercise counselling Weekly phone call to discuss exercise and nutrition goals. No pedometer.							

Abbreviations: BMI: body mass index; FSH: follicle-stimulating hormone; GI: Glycaemic index; HR: heart rate; IVF: in vitro fertilisation; LH: luteinizing hormone; VLCD: very low-calorie diet; OCP: oral contraceptive pill; Clomiphene citrate: CC

\* Mean <u>+</u> SE

\*\* % weight change not actual weight reductio

#### Supplementary data S2: Search Strategy MEDLINE (Ovid)

- 1. exp infertility/
- 2. exp fertility/
- 3. exp Reproductive Techniques Assisted/
- 4. Polycystic Ovary Syndrome/
- 5. infertil\$.tw.
- 6. fertil\$.tw.
- 7. subfertil\$.tw.
- 8. fecund\$.tw.
- 9. infecund\$.tw.
- 10. subfecund\$.tw.
- 11. (concept\$ adj3 delay\$).tw.
- 12. (time adj3 pregnan\$).tw.
- 13. (pregnan\$ adj3 difficult\$).tw.
- 14. PCOS.tw.
- 15. (polycyst\$ adj3 ovar\$).tw.
- 16. ivf.tw.
- 17. (assist\$ adj3 concep\$).tw.
- 18. (assist\$ adj3 reproduc\$).tw.
- 19. (ovulat\$ adj3 induc\$).tw.
- 20. clomifene.tw.
- 21. clomiphene.tw.
- 22. icsi.tw.
- 23. (intracytoplas\$ adj3 sperm).tw.
- 24. or/1-23
- 25. weight loss/
- 26. Body Mass Index/
- 27. exp overweight/
- 28. Waist-Hip Ratio/
- 29. Waist-Height Ratio/
- 30. exp body fat distribution/
- 31. Waist Circumference/

- 32. (weight adj1 (los\$ or reduc\$ or maint\$ or control)).tw.
- 33. (obese or obesity).tw.
- 34. slim\$.tw.
- 35. overweight.tw.
- 36. bmi.tw.
- 37. body mas index.tw.
- 38. whr.tw.
- 39. (waist adj3 (hip or circumference)).tw.
- 40. or/25-39
- 41. randomized controlled trial.pt.
- 42. controlled clinical trial.pt.
- 43. randomi?ed.ab.
- 44. placebo.ab.
- 45. drug therapy.fs.
- 46. randomly.ab.
- 47. trial.ab.
- 48. groups.ab.
- 49. or/41-48
- 50. exp animals/ not humans/
- 51. 24 and 40 and 49
- 52. 51 not 50
- 53. exp "patient acceptance of health care"/
- 54. Health, Knowledge, Attitudes, Practice/
- 55. Patient Dropouts/
- 56. Physician-Patient Relations/
- 57. Nurse-Patient Relations/
- 58. exp motivation/
- 59. exp "attitude to health"/
- 60. barrier\$.tw.
- 61. obstacle\$.tw.
- 62. facilitat\$.tw.
- 63. discourag\$.tw.
- 64. encourag\$.tw.

- 65. motivat\$.tw.
- 66. (inhibit\$ or prohibit\$).tw.
- 67. burden\$.tw.
- 68. dropout?.tw.
- 69. (drop\$ adj1 out\$).tw.
- 70. (internal adj1 conflict\$).tw.
- 71. willpower\$.tw.
- 72. (self adj1 (efficac\$ or sabotag\$ or percep\$)).tw.
- 73. or/53-72
- 74. 24 and 40 and 73
- 75. Qualitative Research/
- 76. questionnaires/
- 77. exp interviews as topic/
- 78. (qualitative or interview\$ or focus group? or questionnaire\$ or survey\$).tw.
- 79. (ethnos\$ or grounded or thematic or interpretive or narrative).tw.
- 80. or/75-79
- 81. 24 and 40 and 80
- 82. 74 or 81
- 83. 52 or 82
- 84. 83 not abstract.pt.
- 85. limit 84 to ed=20160319-20200331



#### Supplementary data S3: Flow diagram process of study selection

# Supplementary data S4: Quality Assessment of all RCTs

Study	Random sequence generation	Allocation concealment	Blinding; participants and personnel	Blinding; outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Becker et al (2015) <sup>54</sup>	Unclear	Unclear	High	Unclear	High	Unclear	Low
Duval et al (2015) <sup>55</sup>	Low	Low	High	Unclear	High	Low	Low
Einarsson et al (2017) <sup>48</sup>	Low	Unclear	High	Low	Low	Unclear	High
Espinos et al (2017) <sup>44</sup>	Low	Unclear	High	Unclear	Unclear	Low	Low
Guzick et al (1994) <sup>53</sup>	Unclear	Unclear	High	Unclear	Unclear	Low	Low
Hoeger et al (2004) <sup>49</sup>	Low	Low	High	Unclear	Low	Low	Low
Kiel et al (2018) <sup>50</sup>	Low	Low	High	Unclear	Low	Low	Low
Legro et al (2015) <sup>56</sup>	Low	Low	High	Unclear	Low	Unclear	High
Moran et al (2011) <sup>57</sup>	Low	Unclear	High	Unclear	High	Unclear	Low
Mutsaerts (2106) <sup>41</sup>	Low	Low	High	Unclear	Low	Low	Low

#### WEIGHT-LOSS TO IMPROVE FERTILITY, SUPPLEMENTARY DATA



#### Supplementary data S5: Funnel Plots

Figure S5a. Funnel Plot: Change in weight



#### Figure S5b. Funnel Plot: Live Birth Rate



Figure S5c. Funnel Plot: Pregnancy Rate



#### Supplementary data: Forest Plots

#### Intervention Control Mean Difference Mean Difference Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 2.1.1 Diet and exercise vs Control/ Minimal intervention Guzick 1994 -16.2 10.5 6 0 5.92 -16.20 [-25.84, -6.56] 6 2.8% Hoeger 2004 11 -2.59 8.3% -5.16 [-8.27, -2.05] -7.753.4 4.2 12 Legro 2015 -6.1 3.2 50 -1.1 3.1 49 10.2% -5.00 [-6.24, -3.76] Moran 2003 -3.8 3 18 -0.5 1.2 20 10.0% -3.30 [-4.78, -1.82] Palomba 2008 -4.42 9.22 32 -0.69 9.47 32 6.6% -3.73 [-8.31, 0.85] Sim 2014 -6.6 4.6 26 17 9.1% -5.00 [-7.46, -2.54] -1.6 3.6 Subtotal (95% CI) 143 136 47.0% -4.66 [-6.03, -3.30] Heterogeneity: Tau<sup>2</sup> = 1.14; Chi<sup>2</sup> = 9.23, df = 5 (P = 0.10); l<sup>2</sup> = 46% Test for overall effect: Z = 6.69 (P < 0.00001) 2.1.2 Diet and exercise vs Assisted Reproductive Technology Espinos 2017 -6.4 7.72 21 7.0% 0 5.92 20 -6.40 [-10.60, -2.20] Mutsaerts 2016 -4.4 5.8 236 -1.1 4.3 128 10.3% -3.30 [-4.35, -2.25] Subtotal (95% CI) 257 -4.16 [-6.87, -1.44] 148 17.3% Heterogeneity: Tau<sup>2</sup> = 2.37; Chi<sup>2</sup> = 1.97, df = 1 (P = 0.16); l<sup>2</sup> = 49% Test for overall effect: Z = 3.00 (P = 0.003) 2.1.3 Very low calorie diet and exercise vs Standard diet and exercise -9.00 [-15.50, -2.50] Rothberg 2016 -14 6 6 -5 5 5 4.7% Subtotal (95% CI) -9.00 [-15.50, -2.50] 6 5 4.7% Heterogeneity: Not applicable Test for overall effect: Z = 2.71 (P = 0.007) 2.1.4 Diet only vs Control/ Minimal intervention Becker 2015 -4.51 3.11 14 0.72 2.6 12 9.3% -5.23 [-7.42, -3.04] Subtotal (95% CI) 14 12 9.3% -5.23 [-7.42, -3.04] Heterogeneity: Not applicable Test for overall effect: Z = 4.67 (P < 0.00001) 2.1.5 Diet only vs Assisted Reproductive Technology Einarsson 2017 -9.1 6.83 152 1.19 1.95 153 10.3% -10.29 [-11.42, -9.16] Subtotal (95% CI) 152 153 10.3% -10.29 [-11.42, -9.16] Heterogeneity: Not applicable Test for overall effect: Z = 17.87 (P < 0.00001) 2.1.6 Exercise only vs Control/ Minimal intervention Kiel 2018 -0.6 6.08 8 -0.7 6.11 0.10 [-5.56, 5.76] 10 5.5% Nasrekani 2016 5.8% -0.95 6.18 10 0.05 5.93 10 -1.00 [-6.31, 4.31] Subtotal (95% CI) -0.49 [-4.36, 3.39] 18 20 11.3% Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.08, df = 1 (P = 0.78); I<sup>2</sup> = 0% Test for overall effect: Z = 0.25 (P = 0.81) Total (95% CI) 590 474 100.0% -5.24 [-7.14, -3.35] Heterogeneity: Tau<sup>2</sup> = 8.79; Chi<sup>2</sup> = 108.47, df = 12 (P < 0.00001); l<sup>2</sup> = 89% -20 -10 10 20 Ó Test for overall effect: Z = 5.41 (P < 0.00001) Favours intervention Favours control Test for subgroup differences: Chi<sup>2</sup> = 61.77, df = 5 (P < 0.00001), l<sup>2</sup> = 91.9%

#### Supplementary data S6. Change in weight: effect of interventions versus control on weight change in kg

#### Supplementary data S7a. Forrest plots exploring differences in Change in Weight (subgroups).

	Inte	rventio	on	с	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.16.1 Randomised	studies -	Diet 8	Exerc	ise vs (	Control				
Espinos 2017	-6.4	7.72	21	0	5.915	20	7.9%	-6.40 [-10.60, -2.20]	<b>-</b>
Guzick 1994	-16.2	10.5	6	0	5.915	6	3.2%	-16.20 [-25.84, -6.56]	
Hoeger 2004	-7.75	3.4	11	-2.59	4.2	12	9.3%	-5.16 [-8.27, -2.05]	_ <b>—</b>
Legro 2015	-6.1	3.2	50	-1.1	3.1	49	11.5%	-5.00 [-6.24, -3.76]	+
Moran 2011	-3.8	3	18	-0.5	1.2	20	11.3%	-3.30 [-4.78, -1.82]	
Mutsaerts 2016	-4.4	5.8	236	-1.1	4.3	128	11.7%	-3.30 [-4.35, -2.25]	+
Palomba 2010	-4.42	9.22	32	-0.69	9.47	32	7.4%	-3.73 [-8.31, 0.85]	<b>-</b>
Rothberg 2016	-14	6	6	-5	5	5	5.3%	-9.00 [-15.50, -2.50]	
Sim 2014	-6.6	4.6	26	-1.6	3.6	17	10.2%	-5.00 [-7.46, -2.54]	
Subtotal (95% CI)			406			289	77.8%	-4.56 [-5.68, -3.44]	•
Heterogeneity: Tau² :	= 1.12; C	hi² = 1:	5.72, di	f= 8 (P =	= 0.05);	I <sup>z</sup> = 49°	%		
Test for overall effect	: Z = 7.98	8 (P < 0	0.00001	)					
1.16.2 Randomised	studies -	Diet a	lone vs	Contro	bl				
Becker 2015	-4.51	3.11	14	0.72	2.6	12	10.5%	-5.23 [-7.42, -3.04]	
Einarsson 2017	-9.1	6.83	152	1.19	1.95	153	11.6%	-10.29 [-11.42, -9.16]	+
Subtotal (95% CI)			166			165	22.2%	-7.85 [-12.81, -2.90]	◆
Heterogeneity: Tau <sup>2</sup> :	= 12.01; (	Chi <sup>z</sup> = 1	16.14,	df = 1 (P	< 0.00	01); I <b>r</b> =	94%		
Test for overall effect	: Z = 3.11	(P=0	).002)						
Total (95% CI)			572			454	100.0%	-5.85 [-7.84, -3.85]	•
Heterogeneity: Tau <sup>2</sup> :	= 8 59 <sup>.</sup> C	hi² = 11	01 76	f = 10.0	P < 0 0	00011	<sup>≈</sup> = 90%		
Test for overall effect	· 7 = 5 74	– ⊓ 1 /P < ſ	0,00001	u = 10 ( D					-20 -10 0 10 20
Test for subgroup dit	ferences	rvi ⊂ u trChi <del>?</del> :	- 1 61		P = 0.20	) F= 3	8.0%		Favours [intervention] Favours [control]
restion subgroup an	rerences	s. Onite	= 1.01,	$u_1 = 1 (r$	-= 0.20	n, r= 3	0.070		

#### Change in weight, diet and exercise versus diet only: effect of interventions versus control on weight change in kg

#### Supplementary data S7b. Forrest plots exploring differences in Change in Weight (subgroups).

#### Change in weight, diet and exercise versus exercise only: effect of interventions versus control on weight change in kg

	Inte	rventio	n	c	ontrol	•		Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI				
1.16.1 Randomised s	studies -	Diet &	Exerc	ise vs (	Control								
Espinos 2017	-6.4	7.72	21	0	5.915	20	5.6%	-6.40 [-10.60, -2.20]	<b>_</b>				
Guzick 1994	-16.2	10.5	6	0	5.915	6	1.3%	-16.20 [-25.84, -6.56]					
Hoeger 2004	-7.75	3.4	11	-2.59	4.2	12	8.6%	-5.16 [-8.27, -2.05]	_ <b></b>				
Legro 2015	-6.1	3.2	50	-1.1	3.1	49	19.6%	-5.00 [-6.24, -3.76]	+				
Moran 2011	-3.8	3	18	-0.5	1.2	20	17.8%	-3.30 [-4.78, -1.82]					
Mutsaerts 2016	-4.4	5.8	236	-1.1	4.3	128	21.0%	-3.30 [-4.35, -2.25]	-				
Palomba 2010	-4.42	9.22	32	-0.69	9.47	32	4.8%	-3.73 [-8.31, 0.85]					
Rothberg 2016	-14	6	6	-5	5	5	2.7%	-9.00 [-15.50, -2.50]					
Sim 2014	-6.6	4.6	26	-1.6	3.6	17	11.5%	-5.00 [-7.46, -2.54]					
Subtotal (95% CI)			406			289	92.8%	-4.56 [-5.68, -3.44]	•				
Heterogeneity: Tau <sup>2</sup> = 1.12; Chi <sup>2</sup> = 15.72, df = 8 (P = 0.05); i <sup>2</sup> = 49%													
Test for overall effect:	Z = 7.98	8 (P < 0	.00001	)									
1.16.5 Randomised s	studies-	Exerci	se aloi	ne vs Co	ontrol								
Kiel 2018	-0.6	6.08	8	-0.7	6.11	10	3.4%	0.10 [-5.56, 5.76]					
Nasrekani 2016	-0.95	6.18	10	0.05	5.93	10	3.8%	-1.00 [-6.31, 4.31]					
Subtotal (95% CI)			18			20	7.2%	-0.49 [-4.36, 3.39]	<b>•</b>				
Heterogeneity: Tau <sup>2</sup> =	= 0.00; C	hi <b>²</b> = 0.	08, df=	= 1 (P =	0.78); P	'= 0%							
Test for overall effect:	Z = 0.25	5 (P = 0	.81)										
Total (95% CI)			424			309	100.0%	-4.30 [-5.41, -3.18]	•				
Heterogeneity: Tau <sup>2</sup> =	= 1.26; C	hi² = 19	9.13, df	f = 10 (P	P = 0.04	; <b>I</b> ² = 48	3%						
Test for overall effect:	Z= 7.53	8 (P < 0	.00001	)					Eavours [intervention] Eavours [control]				
Test for subgroup dif	ferences	:: Chi <b>≃</b> ⊧	= 3.92,	df = 1 (F	P = 0.05	), l² = 7	4.5%		. create (interferment) - create [centrol]				

#### Supplementary data S7c. Forrest plots exploring differences in Change in Weight (subgroups).

Change in weight, diet only versus and exercise only: effect of interventions versus control on weight change in kg



#### Supplementary data S8. Live birth rates: effect of interventions versus control

	Interventio	on Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events T	Total Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.2.1 Diet and exerci	se vs Contro	ol/ Minimal inte	erventi	on		
Legro 2015	12	50 5	49	8.4%	2.35 [0.90, 6.18]	+ <b>-</b>
Moran 2011	7	18 5	20	8.5%	1.56 [0.60, 4.04]	- <b>+-</b>
Sim 2014	12	27 3	22	6.7%	3.26 [1.05, 10.12]	
Subtotal (95% CI)		95	91	23.6%	2.20 [1.23, 3.94]	•
Total events	31	13				
Heterogeneity: Tau² =	= 0.00; Chi <b>=</b> =	: 1.01, df = 2 (F	P = 0.60	)); I² = 0%		
Test for overall effect:	Z = 2.65 (P =	= 0.008)				
2.2.2 Diet and exerci	se vs Assist	ted Reproduct	ive Te	chnology		
Duval 2015	15	24 12	31	16.0%	1 61 [0 94 2 77]	+ <b>-</b> -
Espinos 2017	12	21 6	20	11.3%	1 90 [0.89 4 09]	+ <b>-</b> -
Mutsaerts 2016	149	280 165	284	25.7%	0.92 [0.79, 1.06]	-
Subtotal (95% CI)		325	335	53.0%	1.29 [0.78, 2.14]	◆
Total events	176	183				-
Heterogeneity: Tau <sup>2</sup> =	= 0.14; Chi <sup>2</sup> =	7.02, df = 2 (F	? = 0.03	3); <b>I</b> ² = 729	6	
Test for overall effect:	Z = 0.99 (P =	= 0.32)				
2.2.3 Very low calori	e diet and ex	kercise vs Sta	ndard	diet and e	exercise	
Rothberg 2016	3	7 0	7	1.4%	7.00 [0.43, 114.70]	
Subtotal (95% CI)		1	(	1.4%	7.00 [0.43, 114.70]	
Total events	3	U				
Heterogeneity: Not ap	opiicable	0.47)				
lest for overall effect	Z = 1.36 (P =	= 0.17)				
2.2.4 Diet alone vs C	ontrol/ Minim	n <mark>al intervent</mark> io	n			
Becker 2015	3	14 0	12	1.3%	6.07 [0.34, 106.85]	
Subtotal (95% CI)		14	12	1.3%	6.07 [0.34, 106.85]	
Total events	3	0				
Heterogeneity: Not ap	oplicable					
Test for overall effect:	Z = 1.23 (P =	= 0.22)				
2.2.5 Diet alone vs A	ssisted repr	oductive Tech	nology	,		
Finarsson 2017	45	160 42	157	20.7%	1 05 0 73 1 50	<b>↓</b>
Subtotal (95% CI)	40	160 42	157	20.7%	1.05 [0.73, 1.50]	•
Total events	45	42				ſ
Heterogeneity: Not at	oplicable					
Test for overall effect:	Z=0.27 (P=	= 0.78)				
	,					
Total (95% CI)		601	602	100.0%	1.46 [1.04, 2.04]	•
Total events	258	238				
Heterogeneity: Tau <sup>2</sup> =	= 0.11; Chi <sup>2</sup> =	= 19.26, df = 8 (	(P = 0.0	01); I <sup>2</sup> = 58	%	0.001 0.1 1 10 1000
Test for overall effect:	∠ = 2.19 (P =	= 0.03)				Favours control Favours intervention
lest for subgroup dif	terences: Ch	u* = 6.96, df = 4	4 (P = 0	J.14), I* = 4	12.5%	

## Supplementary data S9. Clinical pregnancy rates: effect of interventions versus control

	Intervent	tion	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.3.1 Diet and exercise	se vs Conti	rol/ Min	imal inte	rventi	on		
Legro 2015	14	50	8	49	8.3%	1.72 [0.79, 3.72]	
Moran 2011	12	21	9	25	10.4%	1.59 [0.84, 3.01]	+ <b>-</b> -
Palomba 2010	1	32	0	32	0.7%	3.00 [0.13, 71.00]	
Sim 2014	13	27	3	22	4.8%	3.53 [1.15, 10.84]	
Subtotal (95% CI)		130		128	24.3%	1.87 [1.20, 2.93]	◆
Total events	40		20				
Heterogeneity: Tau² =	0.00; Chi <sup>z</sup> :	= 1.69,	df = 3 (P	= 0.64	·); I² = 0%		
Test for overall effect:	Z = 2.75 (P	= 0.00	6)				
2.2.2 Distand sussei		ted De					
Z.J.Z Diet and exercis	se vs Assis	sted Re	producu	vere	mology		
Duvai 2015 Faminaa 2017	19	24	13	31	14.1%	1.89[1.19, 3.00]	
Espinos 2017 Mutacarta 2016	14	21	100	20	9.9%	1.90 [0.98, 3.72]	
Subtotal (05% CI)	179	280	188	284	ZZ.3%	0.97 [0.86, 1.09]	
Total overta	24.2	JZJ	200	333	40.3%	1.45 [0.05, 2.40]	•
Hotorogonoity: Tou <sup>2</sup> -	212 ∩ 10: ∩hi≇-	- 11 00	200 2015 - 27	- n n	04V-18 - 0	0.000	
Tect for overall effect:	7 = 1 20 /P	- 11.00	), ui – 2 (i \	r = 0.0	104), I' – c	02.70	
restion overall ellect.	Z = 1.29 (F	- 0.20	,				
2.3.3 Very low calorie	e diet and e	exercis	e vs Sta	ndard	diet and e	exercise	
Rothhera 2016	3	7	0	7	0.9%	7 00 0 43 114 701	
Subtotal (95% CI)		7	Ŭ	7	0.9%	7.00 [0.43, 114.70]	
Total events	3		0				
Heterogeneity: Not ap	plicable		-				
Test for overall effect:	Z = 1.36 (P	= 0.17	)				
	<b>,</b>		, 				
2.3.4 Diet alone vs Co	ontrol/ Minii	mal int	erventio	1			
Becker 2015	3	14	0	12	0.9%	6.07 [0.34, 106.85]	
Subtotal (95% CI)		14		12	0.9%	6.07 [0.34, 106.85]	
Total events	3		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.23 (P	= 0.22	)				
2.2.5 Dist slave ve As	ninted Dee		tive Teek	-			
2.3.5 Diet alone vs As	sisted kep	produc	tive recr	nolog	y 17.00		
Einarsson 2017	53	160	47	157	17.6%	1.11 [0.80, 1.53]	T
Sublotal (95% CI)	<b>50</b>	100	47	157	17.0%	1.11 [0.80, 1.55]	Ť
i otal events	53 nlianhla		47				
Test for everall offect:	piicapie 7 - 0 64 /0	- 0.54	、 、				
restior overall ellect.	Z = 0.01 (F	= 0.04	)				
2.3.6 Exercise alone	vs Control/	Minim	al Interv	ention			
kiel 2018	4	8	4	q	57%	1 1 3 (0 41 3 08)	_ <b>_</b>
Subtotal (95% CI)	-	8	-	9	5.7%	1.13 [0.41, 3.08]	•
Total events	4		4				Ť
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.23 (P	= 0.82	)				
			·				
2.3.7 Pedometer, die	t and exerc	cise co	unselling	j vs di	et and ex	ercise counselling	
Nagelberg 2016	4	10	3	11	4.2%	1.47 [0.43, 5.01]	
Subtotal (95% CI)		10		11	4.2%	1.47 [0.43, 5.01]	-
Total events	4		3				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=0.61 (P	= 0.54	)				
T-4-1/05/ 00				000	400.04	4 47 14 44 4 6 12	
Total (95% CI)		054	<b>.</b>	659	100.0%	1.47 [1.11, 1.94]	▼
Total events	319	00.00	282	<i>(</i> <b>D</b> ) -	o		
Heterogeneity: Tau <sup>2</sup> =	0.09; Chi <sup>2</sup> :	= 23.98	s, dt = 11	(P = 0	.01); I² = 5	)4%	0.002 0.1 1 10 500
i est for overall effect:	∠ = 2.71 (P	' = U.OO	() 00 -:::	(D) -			Favours control Favours intervention
lest for subaroup diff	erences: C	ni≝ = 6.	υю.df=6	-(P=0	t.42). I≚ = 1	1.0%	

#### Supplementary data S10. Improvement in ovulation: effect of interventions versus control

	Interver	ntion	Contr	rol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.4.1 Diet and exerci	se vs Con	trol/ Mi	nimal inte	erventi	on		
Guzick 1994	3	5	0	4	10.9%	5.83 [0.39, 88.12]	
Palomba 2010	12	32	3	32	59.1%	4.00 [1.25, 12.84]	
Subtotal (95% CI)		37		36	70.0%	4.24 [1.45, 12.39]	
Total events	15		3				
Heterogeneity: Tau <sup>2</sup> =	: 0.00; Chi	<b>²</b> = 0.06	, df = 1 (F	P = 0.80	l); l² = 0%		
Test for overall effect:	Z=2.64 (	P = 0.00	)8)				
2.4.2 Very low calori	e diet and	exerci	se vs Sta	indard	diet and (	exercise	
Rothberg 2016	3	7	0	7	10.3%	7.00 [0.43, 114.70]	
Subtotal (95% CI)		1		1	10.3%	7.00 [0.43, 114.70]	
Total events	3		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.36 (	P = 0.17	7)				
2.4.3 Pedometer, die	t and exe	rcise co	ounsellin	g vs Di	et and ex	ercise counselling	
Nagelberg 2016	4	10	1	11	19.8%	4.40 (0.59, 33.07)	
Subtotal (95% CI)		10		11	19.8%	4.40 [0.59, 33.07]	
Total events	4		1				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.44 (	P = 0.16	5)				
Total (95% CI)		54		54	100.0%	4.50 [1.84, 11.03]	-
Total events	22		4				
Heterogeneity: Tau² =	: 0.00; Chi	<sup>2</sup> = 0.17	, df = 3 (F	P = 0.98	3); I² = 0%		
Test for overall effect:	Z=3.29 (	P = 0.00	01)				Eavours control Eavours intervention
Test for subaroup diff	erences: (	Chi² = O	.11. df = 3	2 (P = 0	).95), I <sup>z</sup> = 1	0%	

#### Supplementary data S11. Menstrual cycle irregularity: effect of interventions versus control

	Interven	tion	Contr	ol		Risk Ratio	Risk Ratio	
 Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	
2.5.1 Diet and exercise	se vs Cont	trol/ Mii	nimal inte	erventi	on			
Palomba 2010	11	32	3	32	100.0%	3.67 [1.13, 11.92]		
Subtotal (95% CI)		32		32	100.0%	3.67 [1.13, 11.92]		
Total events	11		3					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 2.16 (F	P = 0.03	3)					
Total (95% CI)		32		32	100.0%	3.67 [1.13, 11.92]		
Total events	11		3					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 2.16 (F	P = 0.03	3)				U.U1 U.1 1 1U 1UU Eavoure control. Eavoure intervention	
Test for subaroup diffe	erences: N	Vot app	licable				ravours control Favours intervention	

## Supplementary data S12. Natural conceptions: effect of interventions versus control

	Interven	tion	Contr	ol		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl
2.6.1 Diet and exerci	se vs Cont	rol/ Min	nimal inte	erventi	on			
Hoeger 2004 Subtotal (95% CI)	2	20 <b>20</b>	0	18 <b>18</b>	2.4% <b>2.4%</b>	4.52 [0.23, 88.38] 4.52 [0.23, 88.38]		
Total events	2		0					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z=1.00 (F	P = 0.32	!)					
2.6.2 Diet and exerci	se vs Assi	sted Re	eproduct	ive Teo	chnology			
Duval 2015	12	24	4	31	17.3%	3.88 [1.43, 10.51]		
Mutsaerts 2016	74	280	46	284	60.6%	1.63 [1.17, 2.27]		
Subtotal (95% CI)		304		315	78.0%	2.20 [0.98, 4.93]		$\bullet$
Total events	86		50					
Heterogeneity: Tau² =	= 0.23; Chi <b>=</b>	= 2.60,	df = 1 (P	= 0.11	); <b>I<sup>z</sup> =</b> 629	6		
Test for overall effect:	Z = 1.92 (F	° = 0.06	i)					
2.6.3 Diet alone vs A	ssisted Re	produc	tive Tech	nolog	у			
Einarsson 2017	16	160	4	157	15.4%	3.92 [1.34, 11.48]		
Subtotal (95% CI)		160		157	15.4%	3.92 [1.34, 11.48]		
Total events	16		4					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z = 2.50 (F	° = 0.01	)					
2.6.4 Exercise alone	vs Control	/ Minim	al interv	ention				
Kiel 2018	2	8	1	9	4.2%	2.25 [0.25, 20.38]		
Subtotal (95% CI)		8		9	4.2%	2.25 [0.25, 20.38]		
Total events	2		1					
Heterogeneity: Not ap	oplicable							
Test for overall effect:	Z = 0.72 (F	° = 0.47	")					
Total (95% CI)		492		499	100.0%	2.25 [1.42, 3.59]		◆
Total events	106		55					
Heterogeneity: Tau² =	= 0.06; Chi <sup>2</sup>	= 4.94	df = 4 (P	= 0.29	9); I <sup>2</sup> = 199	6		
Test for overall effect:	Z = 3.43 (F	P = 0.00	106)				0.01	Favours control Eavours intervention
Test for subgroup dif	ferences: C	;hi² = 0.	85, df = 3	) (P = 0	).84), I <sup>z</sup> = (	D%		

	Interven	tion	Contro	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
2.7.1 Diet and exerci	se vs Cont	trol/ Min	imal inte	rventi	on		
Sim 2014	10	27	3	22	9.5%	2.72 [0.85, 8.67]	
Subtotal (95% CI)		27		22	9.5%	2.72 [0.85, 8.67]	
Total events	10		3				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=1.69 (F	P = 0.09	)				
2.7.2 Diet and exerci	se vs Assi	sted Re	producti	ve Teo	hnology		
Duval 2015	7	24	g	31	14.9%	1 00 0 44 2 311	
Espinos 2017	14	21	7	20	18.9%		<b>_</b> _
Mutsaerts 2016	22	280	32	284	23.5%	0.70 [0.42, 1.17]	
Subtotal (95% CI)		325		335	57.2%	1.08 [0.57, 2.05]	<b>•</b>
Total events	43		48				
Heterogeneity: Tau <sup>2</sup> =	= 0.21; Chi <sup>z</sup>	= 5.61,	df = 2 (P	= 0.06	i); <b>i</b> ² = 649	6	
Test for overall effect:	Z=0.23 (F	° = 0.82	)				
2.7.3 Diot alono ve A	ecictod Do	nroduc	tivo Toch	nolog			
Zirij Diet diolle vs A	33131EU RE	400	uve reci	457	) 	0.75 (0.40.4.45)	
Subtotal (95% CI)	29	160	38	157	20.4%	0.75 [0.49, 1.15]	-
Total events	20	100	38	151	20.4/0	0.10 [0.40, 1.10]	•
Heterogeneity: Not ar	nlicable		50				
Test for overall effect:	Z = 1.32 (F	<sup>o</sup> = 0.19	0				
	(		,				
2.7.4 Exercise alone	vs Control	/ Minim	al interve	ention			
Kiel 2018	2	6	3	8	6.8%	0.89 [0.21, 3.76]	
Subtotal (95% CI)		6		8	6.8%	0.89 [0.21, 3.76]	
Total events	2		3				
Heterogeneity: Not a	oplicable						
Test for overall effect:	Z = 0.16 (F	<sup>o</sup> = 0.87	)				
Total (95% CI)		518		522	100.0%	1.05 [0.69, 1.59]	
Total events	84		92			-	
Heterogeneity: Tau <sup>2</sup> =	= 0.12; Chi <sup>2</sup>	= 9.91,	df = 5 (P	= 0.08	i); l² = 509	%	
Test for overall effect:	Z = 0.23 (F	° = 0.82	)				Eavours control Eavours intervention
Test for subgroup dif	ferences: C	⊳hi <b>²</b> = 4.	46, df = 3	(P = 0	.22), I <b>²</b> = 3	32.7%	

## Supplementary data S13. Conceptions following Assisted Reproductive Technology: effect of interventions versus control

#### Supplementary data S14. Number of oocytes retrieved: effect of interventions versus control

	Inte	rventio	on	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.8.1 Diet alone vs Co	ontrol/ N	linima	l interv	ention					
Becker 2015 Subtotal (95% CI)	4.18	3.01	12	7.75	5.39	14	37.6%	-3.57 [-6.87, -0.27]	
Heterogeneity: Not an	nlicable		12			14	51.0%	-5.57 [-0.07, -0.27]	
Test for overall effect:	Z = 2.12	, 2 (P = 0	).03)						
2.8.2 Diet alone vs As	sisted	Repro	ductive	Techn	ology				
Einarsson 2017 Subtotal (95% CI)	8.56	5.28	152 <b>152</b>	9	5.85	153 <b>153</b>	62.4% <b>62.4%</b>	-0.44 [-1.69, 0.81] - <b>0.44 [-1.69, 0.81]</b>	
Heterogeneity: Not ap	plicable	;							
Test for overall effect:	Z = 0.69	9 (P = 0	).49)						
Total (95% CI)			164			167	100.0%	-1.62 [-4.59, 1.35]	
Heterogeneity: Tau <sup>2</sup> =	3.28; C	hi² = 3.	-10 -5 0 5 10						
lest for overall effect:	Z=1.07	(P=U	1.29)			~			Favours intervention Favours control
lest for subgroup diff	erences	: Chifi:	= 3.03,	at = 1 (i	- = U.U	8), 1* =	67.0%		

#### Supplementary data S15. Miscarriage per participant: effect of interventions versus control Risk Ratio (Non-event) Intervention Control Risk Ratio (Non-event) Events Total Events Total Weight M-H, Random, 95% CI Study or Subgroup M-H, Random, 95% CI 2.9.1 Diet and exercise vs Control/ Minimal intervention Legro 2015 1.02 [0.93, 1.12] 2 50 3 49 15.2% Sim 2014 5 27 22 3.4% 0.85 [0.70, 1.04] 1 Subtotal (95% CI) 77 71 18.6% 0.95 [0.79, 1.15] Total events 7 4 Heterogeneity: Tau<sup>2</sup> = 0.01; Chi<sup>2</sup> = 2.93, df = 1 (P = 0.09); l<sup>2</sup> = 66% Test for overall effect: Z = 0.51 (P = 0.61) 2.9.2 Diet and exercise vs Assisted Reproductive Technology Espinos 2017 1 21 1 20 7.0% 1.00 [0.87, 1.15] Mutsaerts 2016 0.94 [0.89, 1.00] 41 280 27 284 29.3% Subtotal (95% CI) 301 304 36.4% 0.95 [0.90, 1.01] Total events 42 28 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.66, df = 1 (P = 0.42); $I^2 = 0\%$ Test for overall effect: Z = 1.69 (P = 0.09) 2.9.3 Diet alone vs Assisted Reproductive Technology Einarsson 2017 160 157 45.0% 0.98 [0.94, 1.03] 8 5 157 Subtotal (95% CI) 160 45.0% 0.98 [0.94, 1.03] Total events 8 5 Heterogeneity: Not applicable Test for overall effect: Z = 0.82 (P = 0.41) Total (95% CI) 538 532 100.0% 0.97 [0.94, 1.01] Total events 57



Test for subgroup differences:  $Chi^2 = 0.67$ , df = 2 (P = 0.71),  $I^2 = 0\%$ 

#### 0.7 0.85 1.2 1.5 Favours control Favours intervention

#### Supplementary data S16. Miscarriage per pregnancy: effect of interventions versus control

,	Interven	tion	Contr	ol	ŕ	Risk Ratio (Non-event)	Risk Ratio (Non-event)
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% CI
2.10.1 Diet and exerc	ise vs Co	ntrol/ N	linimal in	terven	tion		
Legro 2015	2	14	3	8	1.6%	1.37 [0.77, 2.44]	
Sim 2014	5	13	1	3	0.7%	0.92 [0.37, 2.29]	
Subtotal (95% CI)		27		11	2.3%	1.22 [0.75, 1.99]	
Total events	7		4				
Heterogeneity: Tau² =	0.00; Chi	²= 0.52	, df = 1 (F	P = 0.47	'); I² = 0%		
Test for overall effect:	Z = 0.81 (I	P = 0.42	2)				
2.10.2 Diet and exerc	ise vs As	sisted	Reprodu	ctive Te	echnology		
Espinos 2017	1	14	1	7	4.9%	1.08 [0.77, 1.52]	
Mutsaerts 2016	41	179	27	188	55.8%	0.90 [0.82, 0.99]	
Subtotal (95% CI)		193		195	60.6%	0.92 [0.82, 1.03]	◆
Total events	42		28				
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>a</sup>	²= 1.09	, df = 1 (F	P = 0.30	l); I <sup>z</sup> = 8%		
Test for overall effect:	Z = 1.42 (I	P = 0.16	5)				
2.10.3 Diet alone vs A	ssisted R	eprodu	ictive Te	chnolo	gy		
Einarsson 2017	8	66	5	56	37.1%	0.96 [0.85, 1.09]	
Subtotal (95% CI)		66		56	37.1%	0.96 [0.85, 1.09]	<b>•</b>
Total events	8		5				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.58 (I	P = 0.56	6)				
Total (95% CI)		286		262	100.0%	0.94 [0.87, 1.01]	◆
Total events	57		37				
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>a</sup>	°= 3.25	, df = 4 (F	<sup>2</sup> = 0.52	?); I² = 0%		
Test for overall effect:	Z = 1.68 (I	P = 0.09	3)				Eavours control Eavours intervention
Test for subgroup diffe	erences: (	Chi² = 1	.40, df = 0	2 (P = 0	).50), I <sup>z</sup> = 0	1%	. create control in avoir of intervention