

Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
Pharmacotherapy									
Mathus-Vliegen 390	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: Yes Subgroup of INDEX trial Mean age: 35.9 Mean weight: 110.7 Female/Total: 64/75	>135% IBW	Diet: low-calorie (1000 kcal less) Exercise: none Behavioral: none	1. Placebo 2. Dexfenfluramine 15 mg BID	3 (8%) 7 (19%)	(36) - 8 (36) - 10.7 p = ns	<u>FBS</u> 1. (39) 4.81 (4.6, 5.0) 2. (36) 5.56 (4.8, 6.4)	<u>FBS</u> 1.(36) 4.67 (4.5, 4.9) 2.(29) 4.81 (4.3, 5.3) <u>2vs1</u> -0.61 (-1.12, -0.10)	
Herwig 70037	Randomized: Yes Blinded Patients: Yes Providers: Yes Outcome: Yes Mean age: 42 Mean weight: Female/Total: 52/60	>120% IBW	Diet: LCD 1500 Exercise: No Behavioral: No	1. Placebo 2. Dexfenfluramine 15 mg BID	18/60	<u>Weight loss</u> (upper body obesity) 1. (8) -4.7 (-7.1, -2.3) 2. (12) -14.2 (-15.6, 12.8) <u>2vs1</u> -9.5 (-11.19, -7.81) <u>Weight loss</u> (lower body obesity) 1. (6) -2.6 (-5, -0.16) 2. (16) -11.1 (-12.7, -9.6) <u>2vs1</u> -8.5 (-10.14, -6.86)	<u>Blood glucose</u> (UBO) 1. (8) 5.12 (4.9, 5.3) 2. (12) 5.18 (5, 5.4) <u>Blood glucose</u> (LBO) 1. (6) 4.83 (4.6, 5.0) 2. (16) 4.8 (4.6, 4.9) <u>Insulin uu/ml</u> (UBO) 1. (8) 21 (14.5, 27.5) 2. (12) 23.4 (17.7, 29) <u>Insulin uu/ml</u> (LBO) 1. (6) 12.1 (7.2, 17) 2. (16) 14.4 (11.2, 17.6)	<u>Blood glucose</u> (UBO) 1. (8) 5.05 (4.8, 5.2) 2. (12) 4.4 (4.2, 4.6) <u>2vs1</u> -0.71 (-0.9, -0.52) <u>Blood glucose</u> (LBO) 1. (6) 4.66 (4.4, 4.9) 2. (16) 4.56 (4.4, 4.2) <u>2vs1</u> -0.07 (-0.26, 0.12) <u>Insulin uu/ml</u> (UBO) 1. (8) 18.2 (14.1, 22.3) 2. (12) 13.2 (10.5, 15.9) <u>2vs1</u> -7.4 (-12.18, -2.62) <u>Insulin uu/ml</u> (LBO) 1. (6) 11.8 (9.4, 14.2) 2. (16) 12.4 (10.7, 14.0) <u>2vs1</u> -1.7 (-4.58, 1.18)	
Bremer 386	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 49.4 Mean weight: 83.3 Female/Total: 15/26 *dyslipidemic patients	poor outcome to weight loss programs	Diet: low-fat diet Exercise: none Behavioral: none	1. Placebo 2. Dexfenfluramine 15 mg BID	0 3 (25%)	(14) -2.5 (-9.5, 4.5) (12) -4.2 (-11.9, 3.5) <u>2vs1</u> -1.7 (-8.6, 5.25)	<u>FBS, mmol/l</u> 1. (14) 5.6 (5.2, 6.0) 2. (12) 5.7 (5.5, 5.9) <u>Insulin levels, pmol/l</u> 1. (14) 99 (66.6, 131.4) 2. (12) 102 (80.0, 124.0)	<u>FBS, mmol/l</u> 1. (14) 5.3 (4.9, 5.7) 2. (12) 5.4 (5.2, 5.6) <u>2vs1</u> 0.00 (-0.32, 0.32) <u>Insulin levels, pmol/l</u> 1. (14) 85 (67.7, 102.3) 2. (12) 87 (43.0, 131.0) <u>2vs1</u>	40% in dF compared to 0% in placebo. Drowsiness, fatigue, sleepiness, memory loss, faintness, loss of sensation in arms and legs were reasons for withdrawal.

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								-1.00 (-32.49, 30.49)	
Mathus-Vliegen 391	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 36.5 Mean weight: 109 Female/Total: 35/42	>120% IBW	Diet: 1000 kcal less Exercise: none Behavioral: none	1. Placebo 2. Dexfenfluramine 15 mg BID	3 (17%) 4 (24%)	(18) -8.63 (17) -12.84 <u>2vs1</u> -4.2 (-13,4.8)	<u>FBS</u> 1. (18) 4.8 (4.6, 5.0) 2. (17) 5.9 (4.4, 7.4)	<u>FBS</u> 1. (18) 4.8 (4.5, 5.1) 2. (17) 4.9 (4.6, 5.2) <u>2vs1</u> -1.0 (-2.2, 0.21)	
Pfohl 393	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 38.5 Mean weight: 96.5 Female/Total: 38/48	>120% IBW	Diet: yes 1200-1500 kcal Exercise: no Behavioral: no	1. Placebo 2. Dexfenfluramine 15 mg BID	1. 9 (37%) 2. 5 (21%)	<u>Weight in kg</u> 1. (15) -9.6 (-13.2, -6.0) 2. (19) -10.9 (-14.7, -7.1) <u>2vs1</u> -1.30 (-4.87, 2.27) <u>Weight in kg 48 mo</u> 1. (11) -2.1 (-4.8, 0.6) 2. (11) 1.5 (-1.4, 4.4) <u>2vs1</u> 3.60 (0.98, 6.22)	<u>FBS</u> 1. (11) 4.06 (2.7, 5.5) 2. (11) 4.3 (2.5, 6.1)	<u>FBS 11 months</u> 1. (11) 3.89 (2.8, 5.0) 2. (11) 4.17 (2.8, 5.6) <u>2vs1</u> 0.04 (-1.36, 1.44) <u>FBS 48 mo</u> 1. (11) 4.87 (3.0, 6.7) 2. (11) 4.86 (3.3, 6.5) <u>2vs1</u> -0.25 (-.78, 1.28)	
Swinburn 70050	Randomized: Unclear Blinded Patient: Yes Providers: Yes Outcome: Yes Mean age: 45.7 Mean weight: 97 Female/Total: 57/84	BMI 30-40	Diet: Low fat Exercise: none Behavioral: none	1. Placebo 2. Dexfenfluramine 15 mg BID	13/97	<u>Weight (kg)</u> 1. (42) -0.3 (-0.4, -0.2) 2. (42) -42.2 (-4.3, 4.0) <u>2vs1</u> -3.9 (-6.79, -1.01)	<u>Blood glucose</u> 1. (42) 5.1 (4.9, 5.3) 2. (42) 5.08 (4.9, 5.2)	<u>Blood Glucose</u> 1. (42) 0.01 (-0.01, 0.02) 2. (42) -0.05 (-0.07, -0.03) <u>2vs1</u> -0.06 (-0.08, -0.04)	
O'Connor 392	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 40.2 Mean weight: 96.4 Female/Total: 31/58	BMI: 30-40 (kg/m ²)	Diet:1200 to 1500 kcal/d Exercise: none Behavioral: none	1. Placebo 2. Dexfenfluramine 15 mg BID	4 (14%) 3 (10%)	(24) -4.9 (27) - 9.7 <u>2vs1</u> -5.8 (-7.14, -4.46)	<u>FBS</u> 1. (24) 5.43 (5.2, 5.7) 2. (27) 5.15 (4.9, 5.4) <u>Insulin levels</u> 1. (24) 96.4 (70.4, 122.4) 2. (27) 105.1 (76.4, 134)	<u>FBS</u> 1. (24) 5.75 (5.4, 6.1) 2. (27) 5.26 (5.0, 5.5) <u>2vs1</u> -0.21 (-50, 0.08) <u>Insulin levels</u> 1. (24) 128 (96, 161) 2. (27) 89.4 (55, 124)	Diarrhea, ↓appetite, fatigue, headache more common in dF (ns), significantly more nausea, dry mouth, dizziness with dF.

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								<u>2vs1</u> -48.15 (-80.43, -15.87)	
Connacher 696	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 42.8 Mean weight: 100.5 Female/Total: 32/40	>120% IBW	Diet: 3.35 MJ/d Exercise: no Behavioral: no	1. Placebo 2. BRL 26830A (beta-adrenoreceptor agonist) start at 200 mg than 400 mg	none	<u>Weight in kg</u> 1. (16) -10 (95%CI -13.1, -6.9) 2. (16) -15.4 (95%CI -18.9, -11.9)	<u>FBS, mmol/l</u> 1. (20) 5 (95%CI 4.7, 5.3) 2. (20) 4.9 (95%CI 4.7, 5.1) <u>Insulin levels mU/l</u> 1. (20) 18.2 (95%CI 15.1, 21.3) 2. (20) 19.3 (95%CI 16.3, 22.3)	<u>FBS, mmol/l</u> 1. (16) 5 (95%CI 4.8, 5.2) 2. (16) 4.8 (95%CI 4.6, 5.0) <u>Insulin levels mU/l</u> 1. (16) 15.4 (95%CI 14.2, 16.6) 2. (16) 14.8 (95%CI 13.6, 16.0)	
Manning 414	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 55.6 Mean weight: ng Female/Total:101/104	BMI 28-45	Diet: groups 2, 3 Exercise: no Behavioral: group 4	1. Control (no routine advice) 2. Dietetic consultation at the clinic 3. Dietetic consultation at home and clinic 4. Behavioral therapy 5. Dexfenfluramine 15 mg BID x12 weeks	1. 0/58 2. 13/37 (35%) 3. 7/35 (20%) 4. 17/38 (45%) 5. 7/37 (19%)	<u>Weight in kg 12 weeks</u> 2. (37) -1.59 (95%CI -0.94, -2.24) 3. (35) -1.69 (95%CI -0.93, -2.45) 4. (38) -1.2 (95%CI -0.22, -2.18) 5. (37) -3.4 (95%CI -2.36, -4.44) <u>Weight in kg 6 months</u> 2. (37) -2.3 (95%CI -1.32, -3.28) 3. (35) -1.3 (95%CI -0.75, -3.19) 4. (38) -1.21 (95%CI -0.22, -4.61) 5. (37) -3.13 (95%CI -1.99, -5.09) <u>Weight in kg 12 months</u> 1. (58) 1.2 (95%CI n/a, n/a) 2. (37) -1.21 (95%CI -0.28, -3.73) 3. (35) -1.14 (95%CI 0.43, -2.43) 4. (38) -1.82 (95%CI -0.26, -2.84) 5. (37) -2.75 (95%CI -1.42, -4.68)	<u>HgbA_{1c} 12 weeks</u> 1. (58) 0.54 (95%CI n/a, n/a) 2. (37) -0.36 (95%CI -0.15, -0.77) 3. (35) -0.34 (95%CI 0.05, -0.81) 4. (38) -0.05 (95%CI 0.26, -0.36) 5. (37) -0.57 (95%CI -0.31, -1.17) <u>HgbA_{1c} 6 months</u> 1. (58) 0.18 (95%CI n/a, n/a) 2. (37) -0.39 (95%CI -0.15, -0.89) 3. (35) 0.02 (95%CI 0.75, -0.43) 4. (38) 0.11 (95%CI 0.44, -0.22) 5. (37) 0.02 (95%CI 0.40, -0.62) <u>HgbA_{1c} 12 months</u> 1. (58) 0.96 (95%CI n/a, n/a) 2. (37) -0.01 (95%CI 0.47, -0.75) 3. (35) 0.34 (95%CI 1.18, -0.38) 4. (38) 0.32 (95%CI 0.62, -0.20)		

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							5. (37) 0.51 (95%CI 0.77, -0.21)		
Connolly 712	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 66 Mean weight: 88.3 Female/Total: 9/15 of completers	BMI >29	Diet: 1200-1600 Exercise: no Behavioral: no	1. Placebo 2. Fluoxetine start at 60 mg	1. 2/13 2. 4/17	<u>Weight in kg</u> 1. (11) 0 (95%CI -0.3, 0.3) 2. (7) -3.9 (95%CI -5.3, -2.5)	<u>HgbAc</u> 1. (13) 8.7 (95%CI 7.6, 9.8) 2. (11) 8 (95%CI 6.7, 9.3) <u>FBS</u> 1. (13) 10.2 (95%CI 6.5, 13.9) 2. (11) 7.3 (95%CI 6.2, 8.4)	<u>HgbAc</u> 1. (11) 0.1 (95%CI -0.1, 0.3) 2. (7) -0.9 (95%CI -1.0, -0.8) <u>FBS</u> 1. (11) 1.2 (95%CI 0.8, 1.6) 2. (7) -0.8 (95%CI -1.9, 0.3)	
O'Kane 408	Randomized: unclear Blinded Patients: yes Providers: yes Outcome: yes Mean age: 57.1 Mean weight: 98.7 Female/Total: 13/19 * Type II diabetes	BMI: >30	Diet: ns Exercise: none Behavioral: none	1. Placebo 2. Fluoxetine 60 mg qd	1. (11%) 2. (29%)	(9) 1.5 (0.2, 2.8) (7) -4.3 (-6.0, -2.6) <u>2vs1</u> -5.8 (-7.4,-4.2)	<u>FBS</u> 1. (9) 7.2 (6.3, 8.1) 2. (7) 7.9 (6.9, 8.9) <u>HbA1C</u> 1. (9) 8.8 (8.4, 9.2) 2. (7) 9.4 (8.8, 10)	<u>FBS</u> 1.(9) 0.5 (0.0, 1.0) 2.(7) -0.3 (-0.9, 0.3) <u>2vs1</u> -0.8 (-1.29, -0.31) <u>HbA1C</u> 1. (9) 1 (0.4, 1.6) 2. (7) -0.8 (-1.4, -0.2) 2. vs. 1. -1.8 (-2.4, -1.2) <u>FBS at 24 weeks</u> 1. (9) -0.1 (-1.3,1.1) 2. (7) -1.9 (-2.6,-1.2) <u>2vs1</u> -1.8 (-2.73, -0.87) <u>HbA1c at 24 weeks</u> 1. (9) 0.8 (0.7, 0.9) 2. (7) -0.9 (-1.6, -0.2)	Diabetic symptoms, infection more common in placebo. GI symptoms, falls, migraines were common with fluoxetine.
Marin 698	Randomized: unclear Blinded Patients: no Providers: no Outcome: no Mean age: 50.8 Mean weight: 95.6 Female/Total: 0/25	BMI >25	Diet: no Exercise: none Behavioral: none	1. Placebo 2. Testosterone Decanoate 80 mg BID	1 (8%) 1 (9%)	(12) -0.2 (11) -1.4 <u>2vs1</u> -1.2 (-8,5.7)	<u>FBS, mmol/l</u> 1. (12) 5.3 (4.6, 6.0) 2. (11) 5.2 (5.0, 5.4) <u>Insulin levels, mu/l</u> 1. (12) 11.9 (9.0, 14.8) 2. (11) 13.3 (9.3, 17.3)	<u>FBS, mmol/l</u> 1. (12) 5.4 (4.3, 6.5) 2. (11) 5 (4.8, 5.2) <u>2vs1</u> -0.3 (-0.98, 0.38) <u>Insulin levels, mu/l</u> 1. (12) 11.8 (8.5, 15.1)	Side effects: a statistically significant enlargement of the prostate was found in the testosterone group. PSA unchanged.

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								2. (11) 12.5 (8.3, 16.7) <u>2vs1</u> -0.70 (-4.19, 2.79)	
	Exercise								
Gillett 678	Randomized: yes Self-selected: unclear Included: not specified Mean age: 41.9 Mean weight: 165.8 Female/Total 38/38	not given	Diet: no Behavioral: no	1. Aerobic dance not individualized 2. Intensity-controlled individualized aerobic	1. 3/20 (15%) 2. 1/18 (6%)	1. -5.9 2. -5.5 <u>2vs1</u> 0.4 (-8.5,9.3)	<u>FBS</u> 1. (17) 88.5 (85.3, 91.7) 2. (17) 94.3 (89.2, 99.4)	<u>FBS</u> 1. (17) 86.2 (83.3, 89.1) 2. (17) 91.3 (87.4, 95.2) <u>2vs1</u> -0.7 (-4.4, 2.9)	
Coon 700	Randomized: unclear Self-selected: yes Included: not specified Mean age: 59 Mean weight: 94 Female/Total: none/20	not given	Diet: group 1 only AHA Step I Behavioral: yes group weekly	1. Weight-loss diet 2. Exercise training	none	1. -11.4 2. -0.3 <u>2vs1</u> 11.1 (5.31,16.8)	<u>FBS, mg/dl</u> 1. (10) 98 (92.3, 103.7) 2. (10) 97 (89.8, 104.2) <u>Insulin levels, uU/ml</u> 1. (10) 18 (13.7, 22.3) 2. (10) 13 (9.4, 16.6)	<u>FBS, mg/dl</u> 1. (10) 96 (90.3, 101.7) 2. (10) 97 (89.1, 104.9) <u>2vs1</u> 2 (-4.3, 8.3) <u>Insulin levels,uU/ml</u> 1. (10) 14 (10.4, 17.6) 2. (10) 16 (12.4, 19.6) <u>2vs1</u> 7 (3.4, 10.6)	
Kaplan 474	Randomized: unclear Self-selected: yes Included: diabetes Mean age: ng Mean weight: ng Female/Total: 44/76	includes non-overweight	Diet: yes approx 1200 Exercise: yes group 4 60 min x3 Behavioral: yes group, weekly	1. No intervention 2. Diet alone 3. Exercise alone 4. Diet and exercise	not stated	<u>Weight in kg 6 months</u> 1. (ns) 1 (n/a, n/a) 2. (ns) -3.49 (n/a, n/a) 3. (ns) -1.42 (n/a, n/a) 4. (ns) -0.24 (n/a, n/a) <u>Weight in kg 12 weeks</u> 1. (ns) 1.37 (n/a, n/a) 2. (ns) -2.52 (n/a, n/a)		<u>HgbA1c 72 weeks</u> 1. (ns) 0.36 2. (ns) -0.46 3. (ns) 1.3 4. (ns) -1.48	
Singh 690	Randomized: yes Self-selected: no Included: AMI within 24 hrs Mean age: 50.5 Mean weight: 66 Female/Total: ng/406	includes non-overweight	Diet: yes 1. usual diet 2. low-fat Exercise: no Behavioral: no	1. Usual diet 2. Low-energy, high fruit and vegetable diet	1.5/202 (2%) 2.6/204 (2%)	<u>Weight in kg</u> 1.(179) -2.2 (n/a, n/a) 2.(182) -5.3 (n/a, n/a) net change: 3.1(1.28, 4.92)	<u>FBS, mmol/l</u> 1. (202) 6.42 (6.4, 6.5) 2. (204) 6.12 (6.1, 6.2)	<u>FBS, mmol/l</u> 1. (179) -0.19 (n/a, n/a) 2. (182) -0.74 (n/a, n/a) net change: 0.55 (0.15, 1.15)	

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Collins 676	Randomized: unclear Self-selected: yes Included: BMI 30-40 diabetes Mean age: ng Mean weight: ng Female/Total: ng/40	BMI 30-40	Diet: yes 800 kcal Exercise: no Behavioral: yes group, weekly	1.HMR 800 (2 supplements per day) 2. HMR 800 (5 supplements per day)	1/32 (3%) * 7 not included (\$ medication)	<u>Weight in kg</u> 0. (32) -15.3 (87.6, 89.2)	<u>FBS, mmol/l</u> 0. (32) 12.6 (10.8, 14.4) <u>HgbAc</u> 0. (32) 8.4 (7.6, 9.2)	<u>FBS, mmol/l</u> 0. (32) 8.5 (7.3, 9.7) <u>HgbAc</u> 0. (32) 6.6 (6.2, 7.0) <u>FBS, mmol/l</u> 64 weeks 0. (30) 11 (9.4, 12.6) <u>HgbAc</u> 64 weeks 0. (30) 8.1 (7.3, 8.9)	
Katzel 369	Randomized: yes Self-selected: yes Included: 120-160% IBW, non-smokers Mean age: 61 Mean weight: 91.07 Female/Total: 0/170	120-160% IBW	Diet: yes 1260-2100 kcal Exercise: yes 45 min x3 Behavioral: no	<u>Group description</u> 1. Control 2. Weight loss 3. Aerobic exercise	1.8/26 (31%) 2.25/73 (34%) 3.19/71 (27%)	<u>Weight in kg</u> 2. (44) -9.5 (8.1, 10.9)	<u>FBS</u> 1. (26) 5.77 (5.4, 6.1) 2. (73) 5.66 (5.4, 5.9) 3. (3) 5.6 (5.1, 6.1)	<u>Insulin levels</u> 1. (18) 0, estimate (n/a) 2. (44) 18, p<0.01 (n/a) 3. (44) 0, estimate (n/a) <u>FBS</u> 1. (18) -2, estimate (n/a) 2. (44) 2, estimate (n/a) 3. (49) -1, estimate (n/a)	
Ronnemaa 404	Randomized: unclear Self-selected: unclear Included: non-overweight and diabetics Mean age: 52.5 Mean weight: 84 Female/Total:10/25	not given	Diet: No Exercise: yes 45 min 5-7x/wk Behavioral: no	1. No intervention 2. Aerobic exercise	none	1. +0.5 2. -2.0 <u>2vs1</u> -2.5 (-12.8, 7.8)	<u>FBS</u> 1. (12) 11.4 (10.3, 12.5) 2. (13) 11.8 (9.7, 13.9) <u>HgbA1c</u> 1. (12) 10 (9.0, 11.0) 2. (13) 9.6 (8.6, 10.6) <u>Insulin levels, mU/l</u> 1. (12) 16.3 (13.4, 19.2) 2. (13) 17.3 (8.7, 25.9)	<u>FBS</u> 1. (12) 11.2 (9.8,12.6) 2. (13) 10.5 (7.8,13.2) <u>2vs1</u> -1.1 (-3.0, 0.8) <u>HgbA1c</u> 1. (12) 9.9 (8.8, 11.0) 2. (13) 8.6 (7.5, 9.7) <u>2vs1</u> -0.9 (-1.9, 0.1) <u>Insulin levels, mU/l</u> 1. (12) 15.5 (10.3, 20.7) 2. (13) 15.4 (8.9, 21.9) <u>2vs1</u> -1.1 (-7.3, 5.1)	The decrease in FBS, HgbA1c, and fasting plasma insulin were positively correlated to decreases in serum cholesterol and TG but not to increases in HDL.
	Diet and Exercise								
Page	Randomized: unclear	includes non-	Diet: yes	1. No intervention	1. 1/8 (12%)	1. (7) -1.0 mg/kg ²	<u>FBS</u>	<u>FBS</u>	<u>Insulin sensitivity</u>

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684	Self-selected: unclear Included: non-overweight, subjects with impaired glucose tolerance Mean age: 39 Mean weight: not given Female/Total: ng/31	overweight	ADA with increased fiber Kcal to lose 0.5-1.0 kg/w Behavioral: No	2. Low-fat diet and exercise	2. 5/23 (22%)	2. (18) -1.0 mg/kg ² <u>2vs1</u> 0 (-2.38,2.38)	1. (7) 5.8 (5.3, 6.3) 2. (18) 5.6 (5.3, 5.9)	1. (6) 5.6 (5.3, 6.3) 2. (17) 5.3 (5.3, 5.9) <u>2vs1</u> -0.10 (-.43, 0.23) At 2 years <u>FBS</u> 1. (6) 6 (5.4, 6.6) 2. (17) 6 (5.4, 6.6) <u>2vs1</u> 0.2 (-0.3, 0.7)	Placebo (N=7): before 56 (35-90) after 56 (41-75) Group 2 (N=18) before 56 (33-97) after 6 months 68 (41-114).
Kanaley 681	Randomized: unclear Self-selected: unclear Included: BMI >29 Mean age: 36 Mean weight: 88.3 Female/Total: 24/24	BMI >29	Diet: 2.1 MJ less than BMR Exercise: 1. encouraged 2. 30 min x3/wk at Max HR 60-80% Behavioral: no	1. Diet with informal exercise 2. Diet with formal exercise	overall 5/24 (21%)	<u>Weight in kg, lower obesity</u> 1,2 (9) -7.7 (-13.39, -2.01) <u>Weight in kg, upper obesity</u> 1,2 (10) -9.2 (-15.3, -3.1)	<u>FBS, lower body obesity</u> 1,2. (9) 5.41 (5.3, 5.5) <u>Insulin levels, lower body obesity</u> 1,2. (9) 76 (41.4, 110.6) <u>FBS, upper body obesity</u> 1,2. (10) 5.77 (5.3, 6.2) <u>Insulin levels, upper body obesity</u> 1,2. (10) 113 (76.8, 149)	<u>FBS, lower body obesity</u> 1,2. (9) 5.25 (5.1, 5.4) <u>Insulin levels, lower body obesity</u> 1,2. (9) 62 no statistics available <u>FBS, upper body obesity</u> 1,2. (10) 5.45 (5.3, 5.6) <u>Insulin levels, upper body obesity</u> 1,2. (10) 99 (62.8, 135)	
Blonk 470	Randomized: unclear Self-selected: no Included: BMI>27 diabetes Mean age: ng Mean weight: ng Female/Total: ng/53	BMI >27	Diet: yes 500 kcal less than usual intake Exercise: yes 60 min daily Max HR 60-80% Behavioral: yes q4mo	1. Conventional diet program (diet counseling alone) 2. Comprehensive diet, behavioral and exercise program	1. 4/26 (15%) 2. 3/27 (11%)	*Median difference between groups (comprehensive vs conventional) <u>Weight in kg</u> <u>2vs1</u> -1.3 (-3.3, 0.7)	<u>HgbA_{1c}</u> 1. (27) 7.5 (5.6, 11.4) 2. (26) 8 (6.3, 11.7) <u>Insulin levels</u> 1. (27) 22 (8.0, 46.0) 2. (26) 20 (10.0, 38.0)	<u>Insulin levels</u> 1. (22) -4 (-24.0, 7.0) 2. (24) -5 (-18.0, 1.0) <u>HgbA_{1c}</u> <u>2vs1</u> -0.3 (-1.0, 0.6) <u>Insulin levels uU/ml</u> <u>2vs1</u> -1.0 (-5.0, 3.0)	Three variables were independently associated with 2-year body percent weight loss: HbA1c (beta=1.5; p<0.001) the energy % CHO intake (beta= -15.2; p=.04) and the % of obese subjects within the family (beta= -3.9, p= 0.03) . These three variates together explained 43.7% of the observed variance of body weight changes. A reduction in HgbA1c of more than 1% after 2 years

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									of treatment was observed in only 6 patients in the comprehensive program (22.2%) and 4 in the conventional program (15.3%).
Pan XR 80225	Randomized: unclear Self-selected: unclear Included: glucose intolerant, nonoverweight Mean age: 45 Mean weight: 25.8 kg/m ² Female/Total: 283/577	BMI >25	Diet: yes if >25 kg/m ² encouraged to reduce calorie intake to lose 0.5-1.0 kg/mo until BMI of 23 kg/m ² Exercise: yes 10-30 min daily Behavioral: no	1. Control 2. Diet 3. Exercise 4. Diet and exercise	47/577	BMI (overweight subgroup) 1. -1 (-1.63, -0.37) 2. -1.2 (-1.8, -0.6) 3. -0.9 (-1.44, -0.36) 4. -1.60 (-2.28, -0.92)		Incidence of diabetes (per 100 person years) 1. 17.2 (13.3, 21.3) 2. 11.5 (8.0, 15.0) 3. 10.8 (7.8, 13.8) 4. 11.4 (8.1, 14.6)	
Wing 473	Randomized: unclear Self-selected: unclear Included:>120% IBW Diabetes Mean age: 55 Mean weight:103 Female/Total: 42/55	>120% IBW	Diet: ADA to lose 1 kg/wk Exercise: yes group 2: 2x/wk group 4: 3-5x/wk 60 min/3 x10w then monthly Max HR: ng Behavioral: yes q2w x10, q mo	1. Diet plus placebo exercise 2. Diet plus moderate exercise Duration: 10 week intensive than up to 24 weeks of maintenance Study 2 3. Diet alone (study 2) 4. Diet and more intensive exercise (study 2)	1. 1/13 (7%) 2. 2/12 (17%) 3. 0/15 (0%) 4. 2/15 (13%)	Weight in kg (week 10) 1. (12) -7.3 2. (10) -8.5 3. (15) -5.6 4. (13) -9.3 Weight in kg 12 months 1. (11) -4 (-8.2, 0.2) 2. (8) -7.8 (-16.5, 0.9) Study 2 Weight in kg 12 months 3. (15) -3.8 (-14.9, 7.3) 4. (13) -7.9 (-22, 6.3)	HgbA1c 1. (12) 9.4 (8.3, 10.5) 2. (10) 9.7 (8.6, 10.8) FBS, mmol/l 1. (12) 9.9 (8.1, 11.7) 2. (10) 10.2 (8.4, 12.0) Study 2 HgbA1c 3. (15) 10.9 (9.8, 12.0) 4. (13) 10.6 (9.5, 11.7) FBS 3. (15) 12.6 (11.1, 14.1) 4. (13) 11.6 (10.3, 12.9) Insulin levels 3. (15) 175 (110.7, 239.3) 4. (13) 240 (168.1, 311.9)	HgbA1c 10 weeks 1. (12) 7.9 (6.8, 9.0) 2. (10) 8 (7.1, 8.9) 2vs1 -2.0 (-1.22, 0.82) FBS, mmol/l 10 weeks 1. (12) 7.8 (5.8, 9.8) 2. (10) 7.6 (5.8, 9.4) 2vs1 -0.5 (-2.3, 1.3) HgbA1c 10 weeks 3. (15) 9 (8.4, 9.6) 4. (13) 8.2 (7.5, 8.9) 4vs3 -0.5 (-1.4, 0.4) FBS 10 weeks 3. (15) 9.2 (7.7, 10.7) 4. (13) 8.4 (7.3, 9.5) 4. vs. 3. 0.2 (-1.2, 1.6) Insulin levels 10 weeks 3. (15) 176 (85.9, 266.1) 4. (13) 183 (115.5, 250.5) 3vs4 -56 (-129.3, 15.3)	

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								HgbA1c 12 months 3. (15) 10.1 (9.2, 11.0) 4. (13) 9.2 (8.1, 10.3) 3vs4 -0.6 (-1.6, 0.4) FBS 12 months 3. (15) 11.8 (9.7, 13.9) 4. (13) 9.9 (8.2, 11.6) 4vs3 -0.9 (-2.6, 0.8)	
Verity 446	Randomized: unclear Self-selected: unclear Included: >120% IBW postmenopausal women with NIDDM Mean age: 59.2 Mean weight: 79.2 Female/Total: 10/10	>120% IBW	Diet: yes Encouraged Exercise: yes group 2: 60-90/3 Max HR: 65-80% Behavioral: no	1. Control (diet) 2. Exercise	not reported	Weight in kg 1. (5) -2.9 2. (5) -2.1 2vs1 -2.1 (-20,15.7)	Insulin levels, uu/ml 1. (5) 14.7 (5.8, 23.6) 2. (5) 12.7 (4.6, 20.8)	Insulin levels, uu/ml 1. (5) 14.5 (3.7, 25.3) 2. (5) 10 (-0.6, 20.6) 2vs1 -2.50 (-9.87, 4.87)	
	Diet Interventions								
Mellies 683	Randomized: unclear Self-selected: unclear Included: >115% IBW Dyslipidemic subjects Mean age: 52.9 Mean weight: ng Female/Total: ng/45	>115% IBW	Diet: yes group 2: 17g fiber Exercise: no Behavioral: no	1. Control (no diet) 2. Low-fat diet plus placebo 3. Low-fat diet plus sucrose polyester (17g)	1. 4/15 (27%) 2. 0/12 3. 5/18 (28%)	Weight in kg 1. (11) -2.6 (-4.2, -1.0) 2. (12) -3.9 (-5.4, -2.4) 3. (13) -3.4 (-4.9, -1.9) 2vs1 -1.3 (-2.8, 0.20) 3vs2 0.5 (-0.9, 1.9) 3vs1 -0.8 (-2.26, 0.66)	not given	FBS 1. (11) -3 (-7.5, 1.5) 2. (12) -1 (-5.4, 3.4) 3. (13) -9 (-15.5, -2.5) 2vs1 2.0 (-2.18, 6.18) 3vs2 -8.0 (-13, -2.7)	
Simkin-Silverman 373	Randomized: unclear Self selected: no Included: BMI 20-34 includes non-overweight Mean age: 47 Mean weight: ng Female/Total: 535/535	BMI 20-34	Diet: yes 1300-1500 kcal/d Exercise: yes 1500 cal/week Behavioral: yes group, qw x10,q 2w	1. Control (no intervention) 2. Intervention group (low-fat, exercise and behavioral therapy)	3%	Weight in kg 6 months 1. (267) -0.22 (-0.59, -.15) 2. (253) -4.8 (-5.4, -4.3) 2vs1 -4.58 (-5.1, -4.1)	FBS, mmol/l 1. (267) 5.4 (5.4, 5.5) 2. (253) 5.5 (5.4, 5.5)	FBS, mmol/l 6 months 1. (267) .05 (-0.01, 0.11) 2. (253) 0.02 (-0.5, 0.54) 2vs1 -0.03 (-0.53, 0.47)	Compliance: The number of treatment sessions attended was significantly correlated with change in risk factors such as weight (r = -0.48, p<0.001), WHR (r = -0.13, p<0.001), LDL (r = -0.19, p<0.001), TG (r = -0.1, p<0.05) and glucose (r = 0.18, p<0.005).

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Project									
Colman 415	Randomized: unclear Self selected: unclear Included: includes non overweight Mean age: 60.5 Mean weight: 90.4 Female/Total: 0/99	includes non overweight	Diet: yes AHA step I goal to lose 0.25-0.5 kg/wk Exercise: no Behavioral: yes format: group, weekly	1. Control 2. Low-fat diet	1. 11/26 (42%) 2. 38/73 (52%)	<u>Weight in kg</u> 1. (15) 1.0 2. (35) -9.0 <u>2vs1</u> -10 (-14.72, -5.28)	<u>Insulin levels, pmol/l</u> 1. (15) 78 (n/a, n/a) 2. (35) 90 (n/a, n/a)	<u>Insulin levels, pmol/l</u> 1. (15) 72 (n/a, n/a) 2. (35) 72 (n/a, n/a) p<0.01 from baseline for group 2	FBS levels did not significantly change in either group, but the glucose area decreased by 25% in the weight loss group and increased by 32% in control group. There were significant correlations between the weight loss-induced change in glucose area during the OGTT and the change in waist circumference (r=0.49, p=0.005), the change in fat mass (r=0.40, p=0.02), the baseline glucose area (r= -0.37, p=0.02) and the change in % body fat (r=0.36, p=0.03).
Golay 70167	Randomized: unclear Self-selected: no Included: BMI >30 kg/m ² History of failure to lose weight Mean age: 43 Mean weight: 104.5 Female/Total: 34/43	BMI >30	Exercise: yes aerobic 120 min daily Behavioral: yes behavioral modification weekly meeting	1. Low calorie diet with low carbohydrate 2. Low calorie diet with high carbohydrate	none	<u>Weight in kg</u> 1. (22) -8 (-18.05, 2.05) 2. (21) -7 (-14.93, 0.93) <u>2vs1</u> 1.0 (-7.8, 9.8)	<u>Blood glucose (mmol/L)</u> 1. (22) 5.3 (4.9, 5.7) 2. (21) 5.4 (4.8, 6.0) <u>Plasma insulin (pmol/L)</u> 1. (22) 106.8 (74, 139) 2. (21) 96 (68, 123)	<u>Blood glucose</u> 1. (22) 4.4 (4.2, 4.6) 2. (21) 5.0 (4.6, 5.4) <u>Plasma Insulin</u> 1. (22) 57.6 (44, 71) 2. (21) 88.2 (68, 108)	
Wing 576	Randomized: unclear Self-selected: unclear Included: >130% IBW Diabetes Mean age: ng Mean weight: 103.2 Female/Total: ng/36	>130% IBW	Diet: yes 1. ADA 2. VLCD Exercise: no Behavioral: yes group, weekly	1. Low-calorie diet 2. VLCD	overall 3/36 (8%)	<u>Weight in kg</u> 1. (ns) -10.1 2. (ns) -18.6 p<0.003	<u>FBS, mmol/l</u> 1. (ns) 12.68 (n/a, n/a) 2. (ns) 14.12 (n/a, n/a)	<u>FBS, mmol/l</u> 1. (ns) 9.28 (n/a, n/a) 2. (ns) 7.67 (n/a, n/a) p<0.03	
Wing 439	Randomized: unclear Self-selected: unclear	>130% IBW	Diet: yes 1. LCD	1. Low-calorie diet 2. VLCD	Not reported	<u>Weight in kg, 12 weeks</u> 1. (17) -11 (-11.8, -10.2)	<u>FBS</u> 1. (17) 13.4 (11.5, 15.3)	<u>FBS 12 weeks</u> 1. (17) 10.13 (7.8, 12.5)	Observed that weight loss markedly improves insulin

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	Included: >130% or 18 kg above IBW Mean age: 51 Mean weight: ng Female/Total: 60/93		2. VLCD Exercise: no Behavioral: no			2. (36) -11 (-11.6, -10.4) <u>2vs1</u> 0 (-0.7, 0.7)	2. (36) 13.5 (11.7, 15.3) <u>Insulin sensitivity</u> 1. (17) 0.5 (0.3, 0.7) 2. (36) 0.62 (0.4, 0.8) <u>Insulin levels</u> 1. (17)169 (20.2, 217.8) 2. (36)186 (41.3, 230.7)	2. (36) 7.61 (6.5, 8.7) <u>2vs1</u> -2.6 (-4.4, -0.8) <u>Insulin sensitivity</u> 12 weeks 1. (17) 1.13 (0.9, 1.4) 2. (36) 1.79 (1.3, 2.3) <u>2vs1</u> 0.5 (0.2,0.9) <u>Insulin levels</u> 12 weeks 1. (17) 91 (67.7, 114.3) 2. (36) 89 (70.7, 107.3) <u>2vs1</u> -19 (-59, 21) <u>FBS</u> 27 weeks 1. (17) 8.43 (6.3, 10.5) 2. (36) 8.48 (7.2, 9.8) <u>Insulin sensitivity</u> 27 weeks 1. (17) 1.7 (1.3, 2.1) 2. (36) 1.9 (1.3, 2.5) <u>2vs1</u> 0.1 (-0.4, 0.6) <u>Insulin levels, pmol</u> 27 weeks 1. (17) 120 (52.2, 187.8) 2. (36) 84 (57.6, 110.4) <u>2vs1</u> -53 (-100.5, -5.5)	sensitivity from a baseline value of 0.58 to 1.6 after an 11 kg weight loss
Wing 708	Randomized: unclear Self-selected: unclear Included: diabetes, >130% IBW Mean age: 51 Mean weight: 103.3 Female/Total: 26/36	>130% IBW	Diet: yes 1. LCD: 4200 J/d 2.Optifast-70 Exercise: yes 4200 J/wk Behavioral: yes group	1. Behavioral therapy 2. Behavioral therapy plus VLCD	1. 3/19 (16%) 2. 0/17	<u>Weight in kg</u> 1. (16)-10.1 (-21.7, 1.52) 2. (17)-18.6 (-24, -12.8) <u>2vs1</u> -8.5 (-17.21, 0.21) <u>Weight in kg</u> 12 months 1. (16) -6.8 (-17.9, 4.3) 2. (17) -8.6 (-14.6, -2.6) <u>2vs1</u> -1.8 (-10.24, 6.64)	<u>FBS</u> 1. (16) 12.8 (10.7, 14.9) 2. (17) 14.2 (11.9, 16.5) <u>HgbAc</u> 1. (16) 10.4 (9.3, 11.5) 2. (17) 10.4 (9.3, 11.5) <u>Insulin levels, pmol/l</u> 1. (16) 141 (101.6, 180.4) 2. (17) 163 (120.8, 205.2)	<u>FBS</u> 1. (16) 9.3 (8.4, 10.2) 2. (17) 7.7 (6.6, 8.8) <u>2vs1</u> -3.0 (-4.87, -1.13) <u>HgbAc</u> 1. (16) 8.6 (8.1, 9.1) 2. (17) 7.3 (6.8, 7.8) <u>2vs1</u> -1.3 (-2.23, -0.37) <u>Insulin levels, pmol/l</u> 1. (16) 120 (86.9, 153) 2. (17) 104 (58.8, 149.2) <u>2vs1</u> -38 (-78.8, 2.81) <u>FBS</u> 12 months	

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								1. (16)13.5 (11.8, 15.2) 2. (17)10.4 (8.3, 12.5) <u>2vs1</u> -4.5 (-6.59, -2.41) <u>HgbAc</u> 12 months 1. (16) 11.8 (10.4, 13.2) 2. (17) 9.2 (8.1, 10.3) <u>2vs1</u> -2.6 (-3.8, -1.4) <u>Insulin levels, pmol/l</u> 12 months 1. (16) 133 (105.8, 160.2) 2. (17) 205 (132.5, 277.5) <u>2vs1</u> 50 (-1.07, 101.07)	
Wing 709	Randomized: unclear Self-selected: yes Included: >130% or more than 18 kg >IBW diabetes Mean age: 52 Mean weight: 107 Female/Total: 60/93	>130% IBW or >18 kg >IBW	Diet: yes 1. LCD 2. Intermittent VLCD Exercise: no Behavioral: yes group, weekly	1. LCD 2. Intermittent VLCD for 12 weeks x 2	1. 7/48 (15%) 2. 7/38 (18%)	<u>Weight in kg</u> 1. (41) -10.5 (-14.2, -6.8) 2. (38) -14.2 (-17.6, -0.8)	<u>HgbAc</u> 1. (41) 10.5 (9.9, 11.1) 2. (38) 10.4 (9.7, 11.1) <u>FBS</u> 1. (41) 12.18 (11.2, 13.2) 2. (38) 12.29 (10.8, 13.7) <u>Insulin levels, pmol/l</u> 1. (41) 208 (158.1, 257.9) 2. (38) 201 (154.0, 248.0)	<u>HgbAc</u> 1. (41) 9.2 (8.6, 9.8) 2. (38) 8.9 (8.1, 9.7) <u>FBS</u> 1. (41) 9.78 (8.7, 10.8) 2. (38) 9.28 (8.1, 10.5) <u>Insulin levels, pmol/l</u> 1. (41) 122 (92.6, 151.4) 2. (38) 129 (88.9, 169.1) <u>HgbAc</u> 104 weeks 1. (37) 0.24 (-0.6, 1.0) 2. (36) 0.07 (-0.7, 0.8) <u>FBS</u> 104 weeks 1. (37) 0.39 (-1.2, 1.9) 2. (36) -1.22 (-2.8, 0.3) <u>Insulin levels, pmol/l</u> 104 weeks 1. (37) -74 (-134.7, -13.3) 2. (36) -9 (-69.6, 51.6)	
Walker 693	Randomized: unclear Self-selected: unclear Included: diabetes,	not given	Diet: yes 1. HCLF 2. Modified fat	1. High-CHO low-fat diet 2. Modified-fat diet	none	<u>Weight in kg</u> 1. (24) -0.7 2. (24) -1.3	<u>FBS</u> 1. (24) 8.5 (7.3, 9.7) 2. (24) 9.6 (7.9, 11.3)	<u>FBS</u> 1. (24) 8.8 (7.6, 10.0) 2. (24) 8.7 (7.5, 9.9)	

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	includes non-overweight Mean age: 58.3 Mean weight: 79.8 Female/Total: 15/48		Exercise: no Behavioral: no	*Cross-over 1 month wash-out period Duration: 12 weeks		<u>2vs1</u> -0.6 (-0.77, -1.43)	<u>Insulin levels</u> 1. (24) 14.4 (10.5, 18.3) 2. (24) 12.9 (9.8, 16.0) <u>HgbAc</u> 1. (24) 6.4 (5.8, 7.0) 2. (24) 6.8 (6.0, 7.6)	2vs1 -1.2 (-2.6, 0.2) <u>Insulin levels</u> 1. (24) 12.8 (9.5, 16.1) 2. (24) 13.2 (9.3, 17.1) <u>2vs1</u> 1.9 (-1.8, 5.6) <u>HgbAc</u> 1. (24) 6.5 (5.9, 7.1) 2. (24) 6.6 (5.8, 7.4) <u>2vs1</u> -0.3 (-1.0, 0.4)	
Franz 701	Randomized: unclear Self selected: yes Mean age: 55.9 Mean weight: 93.7 Included: diabetes non-overweight Female/Total: ng/247	not given	Diet: yes to control glycemia Exercise: no Behavioral: no	1. Basic nutrition care 2. Practice guidelines nutrition care	68/247 (28%)	<u>Weight in kg</u> 6 months 1. (85) -1.70 (-6.81, 3.41) 2. (94) -1.40 (-5.81, 3.01)	<u>FBS</u> 1. (85) 9.8 (9.2, 10.4) 2. (94) 10.2 (9.6, 10.8) <u>HgbAc</u> 1. (85) 8.3 (7.9, 8.7) 2. (94) 8.3 (7.9, 8.7)	<u>FBS</u> 3 months 1. (85) 8.7 (8.2, 9.2) 2. (94) 8.5 (8.03, 8.97) <u>HgbAc</u> 3 months 1. (85) 7.5 (7.2, 7.8) 2. (94) 7.2 (7.0, 7.4) <u>FBS</u> 6 months 1. (85) 9.2 (8.6, 9.8) 2. (94) 9.1 (8.5, 9.7) <u>HgbAc</u> 6 months 1. (85) 7.6 (7.2, 8.0) 2. (94) 7.4 (7.1, 7.7)	
Milne 702	Randomized: unclear Self-selected: no Included: diabetes, includes non-overweight Mean age: 59 Mean weight: 80.7 Female/Total: 35/70	not given	Diet: yes 1. 500 kcal below EER 2. Modified fat 3. High CHO, High fiber Exercise: no Behavioral: no	1. Weight-management diet 2. Modified lipid diet 3. High carbohydrate/high fiber diet	over all 6/70 (8.6%)	<u>Weight in kg</u> 1. (21) 1.5 2. (22) -1.0 3. (21) -0.1 <u>2vs1</u> -2.5 (-9, 4.08) <u>3vs1</u> -1.6 (-7.18, 3.98)	<u>HgbAc</u> 1. (21) 9 (8.1, 9.9) 2. (22) 9.8 (8.4, 11.2) 3. (21) 8.7 (7.7, 9.7)	<u>HgbAc</u> 1. (21) 8.9 (7.8, 10.0) 2. (22) 9.7 (8.5, 10.9) 3. (21) 8.5 (7.6, 9.4) <u>2vs1</u> 0 (-1.21, 1.21) <u>3vs1</u> -0.1 (-1.11, 0.91)	
de Bont 440	Randomized: unclear Self-selected: no Included: diabetes, includes non-overweight	includes non-overweight	Diet: yes 1. 40% CHO 2. 30% fat	1. Low-CHO diet 2. Low-fat diet	overall 12/148 (8%)	<u>Weight in kg. obese</u> 1. (35) -0.9 (-2.1, 0.3) 2. (34) -2.7 (-4.0, -1.4) <u>2vs1</u> -1.8 (-3, -0.6)	<u>FBS</u> 1. (65) 9.7 (n/a, n/a) 2. (70) 9.1 (n/a, n/a)	<u>FBS</u> 1. (65) -0.5 (n/a, n/a) 2. (70) -0.3 (n/a, n/a)	Diabetic management: Diet alone group 2 37%, group 1 34%. Diet plus oral

Reference numbers refer to the Reference List in the Clinical Guidelines Report.

Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
	Mean age: 55 Mean weight: 72.5 Female/Total: 148/148		Exercise: no Behavioral: no			<u>Weight in kg, non-obese</u> 1. (29) 0.1 (-0.7, 0.9) 2. (36) -0.4 (-1.3, 0.5) <u>2vs1</u> -0.5 (-1.3, 0.34)	<u>HgbAc</u> 1. (65) 10.1 (n/a, n/a) 2. (70) 10 (n/a, n/a)	<u>HgbAc</u> 1. (65) -0.6 (n/a, n/a) 2. (70) -0.7 (n/a, n/a) p values not given	hypoglycemic agents group 1 65%, group 2 62%. Diet plus insulin group 1 2%, group 2 1%. During study Group 1: 10 patients had dosage increased and 3 started insulin. Group 2: 6 patients had dosage increased and 6 had dosage decreased.
Heller 413	Randomized: unclear Self-selected: no Included: BMI >27 kg/m ² diabetes Mean age: 56.4 Mean weight: 86.5 Female/Total: 39/75	BMI >27	Diet: yes group 2: instructed to avoid sugar Exercise: no Behavioral: no	1. Usual clinic care (control) 2. Group education	1. 8/47 (17%) 2. 4/40 (10%)	<u>Weight in kg</u> 1. (39) -3 (-2.76, -3.24) 2. (36) -5.5 (-5.61, -5.39) <u>2vs1</u> -2.50 (-2.69, -2.31) <u>Weight in kg 6 months</u> 1. (39) -2 (-2.5, -3.1) 2. (36) -7 (-6.39, -7.61) <u>2vs1</u> -5.0 (-5.47, -4.53) <u>Weight in kg 3 months</u> 1. (39) -3.5 (-3.24, -3.24) 2. (36) -6 (-5.49, -5.49) -2.5 (-2.89, -2.11)	<u>HgbA1c</u> 1. (39) 12.7 (95%CI 11.90, 13.50) 2. (36) 12.3 (95%CI 11.40, 13.20)	<u>HgbA1c</u> 1. (39) 9.9 (95%CI 8.9,10.9) 2. (36) 9 (95%CI 8.20, 9.8) <u>2vs1</u> -0.50 (-1.44, 0.44) <u>HgbA1c 6 months</u> 1. (39) 9.5 (95%CI 9.55, 10.40) 2. (36) 7.5 (95%CI 8.70, 8.10) <u>2vs1</u> -1.60 (-2.48, -0.72) <u>HgbA1c 3 mo</u> 1. (39) 9.7 (95%CI 9.00, 9.00) 2. (36) 8.6 (95%CI 7.90, 7.90) <u>2vs1</u> -0.70 (-1.53, 0.13)	A similar proportion of patients in both groups had a 1 year HbA1 below 7.5% (normal range 5.0-7.5%); group 1: 11/39 and group 2: 13/36. Fasting blood sugar <7 mmol/l; group 1: 9/39, group 2: 14/36.
Berglund 431	Randomized: no Self-selected: unclear Included: BMI ≥26 Hypertension Mean age: 54 Mean weight: 99	BMI ≥26	Diet: yes Low-fat Exercise: no Behavioral: no	1. Low-salt, weight-loss diet 2. Atenolol	overall 3/64 (5%)	<u>Weight in kg 12 months</u> 2 (30) 1.0 (95% CI 1. (31) -7.9 (95% CI <u>2vs1</u> 8.80 (41.79, -24.19)	not given	<u>FBS 12 months</u> 2. (30) 0.8 (0.5, 2 1) 1. (31) 1 (0.8, 2 2) <u>2vs1</u> 0.20 (-0.05, 0.45)	Correlations between changes after 1 year in sum of plasma [insulin] waist/hip 0.24 BMI 0.36 waist 0.52

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
	Female/Total: 0/64							Insulin levels 12 months 2 (26) 1.4 (-3.4, 8.2) 1. (27) -5.1 (-8.6, -2.6) <u>2vs1</u> -6.5 (-11.7, -1.28)	(p<0.0058)
Singh 689	Randomized: yes Self-selected: yes Included: hypertension Mean age: 47.0 Mean weight: 66.7 Female/Total: ng/217	BMI >25	Diet: yes 1. 2100 kcal 2. 1600 kcal Exercise: no Behavioral: no	1. Usual diet 2. Low-calorie, low-cholesterol, low-salt diet	none	Weight in kg 1. (109) -0.8 (n/a, n/a) 2. (108) -3.6 (n/a, n/a) net change: 2.8 (1.5, 4.1) Weight in kg, in overwgt patients 1. (83) -1.8 (n/a, n/a) 2. (82) -4.2 (n/a, n/a) net change: 2.4 (0.44, 4.36)	FBS 1. (108) 6.06 (5.9, 6.3) 2. (108) 6 (5.8, 6.2) FBS, in overwgt patients 1. (83) 6.46 (6.3, 6.6) 2. (82) 6.56 (6.4, 6.7)	FBS 1. (109) -0.19 (n/a, n/a) 2. (108) -0.64 (n/a, n/a) net change: 0.45 (0.21, 0.70) FBS, in overwgt patients 1. (83) 0.26 (n/a, n/a) 2. (82) -0.92 (n/a, n/a) net change: 0.67 (0.23, -1.07)	
Darne 677	Randomized: unclear Self-selected: unclear Included: >110% IBW Hypertension Mean age: 48 Mean Weight: 86 Female/Total: 22/54	>110% IBW	Diet: yes Low-calorie energy intake decreased 1/3 Exercise: no Behavioral: no	1. Hypocaloric diet with or without antihypertensive drug therapy 2. No diet, antihypertensive therapy	1. 5/26 (19%) 2. 1/28 (3%)	Weight in kg 1. (27) -2.4 2. (21) -5.1 <u>1vs2</u> p<0.01	FBS, mmol/l 1. (28) 5.75 (5.4, 6.1) 2. (26) 5.68 (5.4, 6.0)	FBS, mmol/l 1. (27) 5.47 (5.1, 5.9) 2. (21) 5.3 (5.0, 5.6) <u>2vs1</u> -0.1 (-0.5, 0.3)	
Grimm 350 *detailed table found at the end of this section	Randomized: unclear Self-selected: unclear Included: non-overweight hypertension Mean age: 54.8 Mean Weight: 85 Female/Total: 342/902	includes non-overweight	Diet: yes 1000-1600 kcal/d Exercise: yes 600 cal/w Behavioral: yes group, qwx8, qmo	1. Placebo (salt restriction) 2. Acebutolol 400 mg/d 3. Amlodipine 5 mg/d 4. Chlorthalidone 15 mg/d 5. Doxazosin 2 mg/d 6. Enalapril 5 mg/d	2 deaths otherwise not given	Weight in kg 12 months 1. (212) -4.5 (95%CI -4.5, -4.5) 2. (119) -4.3 (95%CI -4.4, -4.2) 3. (118) -5 (95%CI -5.1, -4.9) 4. (117) -5.6 (95%CI -5.7, -5.5) 5. (123) -3.9 (95%CI -4.0, -3.8) 6. (113) -5.3 (95%CI -5.4, -5.2)	FBS, mmol/l 1. (220) 5.62 (5.5, 5.8) 2. (126) 5.62 (5.5, 5.8) 3. (121) 5.48 (5.4, 5.6) 4. (123) 5.61 (5.5, 5.8) 5. (128) 5.58 (5.4, 5.7) 6. (127) 5.68 (5.4, 5.6)	FBS, mmol/l 12 months 1. (220) -0.18 (-0.2, -0.2) 2. (126) -0.11 (-0.1, -0.1) 3. (121) -0.09 (-0.1, -0.1) 4. (123) -0.06 (-0.1, -0.1) 5. (128) -0.06 (-0.1, 0.0) 6. (127) -0.21 (-0.2, -0.2)	
	Behavioral								
Jeffery 367	Randomized: unclear Self-selected: yes Included: 14 to 32 kg	14 to 32 kg overweight	Diet: yes 1000-1500 kcal/d	1. Control 2. Standard behavioral treatment	not given	Weight in kg 1. (ns) 0.5 (n/a, n/a) 2. (ns) -3.5 (n/a, n/a)	FBS 1. (27) 5.37 (4.5, 5.4) 2,3,4,5. (131) 5.52 (5.4,	FBS 6 months 1. (27) 0.18 2.,3.,4.,5. (131) 0.01	An average weight loss of 11.8 kg or 13% of initial body weight produced

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
	overweight, multiple failed attempts Mean age: 37.5 Mean Weight: 98.7 Female/Total: 22/54		Exercise: yes 2 and 5 1000 kcal/w Behavioral: yes group, qw x20, qmo	3. Standard behavioral treatment plus food provision 4. Standard behavioral treatment plus monetary incentive 5. Standard behavioral treatment plus food provision plus monetary incentive		3. (ns) -6 (n/a, n/a) 4. (ns) -3 (n/a, n/a) 5. (ns) -6 (n/a, n/a) <u>Weight in kg</u> 12 months 1. (ns) 0 (n/a, n/a) 2. (ns) -4 (n/a, n/a) 3. (ns) -8 (n/a, n/a) 4. (ns) -5 (n/a, n/a) 5. (ns) -8 (n/a, n/a) <u>Weight in Kg</u> 12 months 1. (28) -1.5 2.,3.,4.,5. (131) -7.5 <u>Weight in kg</u> 120 weeks 1. (27) 0.6 (-1.5, 2.7) 2. (24) -1.4 (-4.4, 1.6) 3. (34) -2.2 (-4.5, 0.1) 4. (34) -1.6 (-3.5, 0.3) 5. (34) -1.6 (-3.8, 0.6) <u>Weight in kg</u> 120 weeks 1. (28) -1.2 2.,3.,4.,5. (131) -6.0	5.7) <u>Insulin levels</u> 1. (27) 169 (142.5, 195.5) 2.,3.,4.,5.(129) 161 (143.9, 178)	<u>FBS, men</u> 6 months 2.,3.,4.,5. (ns) -0.14 <u>FBS, women</u> 6 months 2.,3.,4.,5. (ns) -0.17 <u>Insulin levels</u> 6 months 1. (27) 49.5 2.,3.,4.,5. (129) -28.7 p=ns <u>Insulin levels, men</u> 6 months 2.,3.,4.,5. (ns) -26.5 <u>Insulin levels, women</u> 6 months 2.,3.,4.,5. (ns) -30.9 <u>FBS</u> 12 months 1. (ns) 0.14 2.,3.,4.,5. (ns) -0.22 p=ns <u>Insulin levels</u> 12 months 1. (ns) 16.5 2.,3.,4.,5. (ns) -17.9 p=ns <u>FBS, men</u> 12 months 2.,3.,4.,5. (ns) -0.31 <u>FBS, women</u> 12 months 2.,3.,4.,5. (ns) -0.13 <u>Insulin levels, men</u> 12 months 2.,3.,4.,5. (ns) -28.7 <u>Insulin levels, women</u> 12 months 2.,3.,4.,5. (ns) -5.7 <u>FBS</u> 120 weeks 1. (ns) 0.34 2.,3.,4.,5. (ns) 0.05	significant and persistent improvements in Tg, HDL, SBP, DBP, WHR, fasting insulin. The only exception is FBS which returned to baseline. Adjusting for baseline values and changes in BMI were sufficient to remove gender differences.

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
								<u>Insulin levels</u> 120 weeks 1. (ns) 10.8 2.,3.,4.,5. (ns) -20.8 <u>FBS, men</u> 120 weeks 2.,3.,4.,5. (ns) -0.08 <u>FBS, women</u> 120 weeks 2.,3.,4.,5. (ns) 0.19 <u>Insulin levels, men</u> 120 weeks 2.,3.,4.,5. (ns) -23.7 <u>Insulin levels, women</u> 120 weeks 2.,3.,4.,5. (ns) -17.2	
Glasgow 482	Randomized: unclear Self-selected: yes Included: diabetes, >60 years old Mean age: 67 Mean Weight: 186.3	includes non-overweight	Diet: 500 kcal less than EER Exercise: yes aerobic 4x/week Behavioral: yes group, 10 sessions	1. Immediate Intervention (self-management training session) 2. Delayed intervention (3 month delay)	1. 0 2. 0.5%	<u>Weight in lb</u> 1. (52) -5.8 2. (49) -3.5* *at 6 months	<u>HgbAc</u> 1. (52) 6.8 (6.4, 7.2) 2. (49) 7.4 (6.9, 7.9)	<u>HgbAc</u> 1. (52) 6.3 (5.9, 6.7) 2. (49) 7 (6.6, 7.4) <u>2vs1</u> 0.1 (-0.4, 2.6) <u>HgbAc</u> 6 months 1. (49) 6.7 (6.2, 7.2) 2. (49) 6.4 (6.0, 6.8) <u>2vs1</u> -0.9 (-1.4, -0.4) *end of treatment for group 2 since start was 3 months later	
Wing 492	Randomized: unclear Self-selected: yes Included: diabetes Spouses required to be >115% IBW Mean age: 52.4 Mean Weight: 221	% desirable weight >20% IBW	Diet: 1200-1500 Exercise: yes aerobic 5x week Behavioral: yes group, qwx 12, q2w	1. Behavioral weight loss program alone 2. Behavioral weight loss program together with spouse		<u>Weight in lb</u> 1. (23) -19.9 (95%CI -27.8, -12.0) 2. (20) -19.1 (95%CI -24.3, -13.9) <u>Weight in lb</u> 52 weeks 1. (23) -11.6 (95%CI -21.5, -1.7) 2. (20) -7 (95%CI -12.5, -1.5)	<u>HgbAc</u> 1. (23) 10.3 (95%CI 9.4,11.2) 2. (20) 9.5 (95%CI 8.4,10.6) <u>FBS</u> 1. (23) 226 (95%CI 192.3,259.7) 2. (20) 205 (95%CI 171.3,238.7)	<u>HgbAc</u> 1. (23) -2.1 (95%CI -3.0, -1.2) 2. (20) -1.2 (95%CI -2.1, -0.3) <u>FBS</u> 1. (23) -64 (95%CI -99.9, -28.1) 2. (20) -50 (95%CI -74.3, -25.7)	

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
								For all outcome 2vs1 p=ns HgbAc 52 weeks 1. (23) -0.7 (95%CI -1.9, 0.5) 2. (20) -0.1 (95%CI -1.0, 0.8) FBS 52 weeks 1. (23) -36 (95%CI -72.8, 0.8) 2. (20) -11 (95%CI -39.5, 17.5) For all outcome 2vs1 p=ns	
Smith 71328	Randomized: unclear Self-selected: yes Included: 120-200% desirable weight, diabetes Mean age: 62.4 Mean Weight: 34.7 kg/m ²	120-200% desirable weight	Diet: 1200-1500 30-40 g/d fat Exercise: yes encouraged Behavioral: yes group, weekly	1. Behavioral modification 2. Behavioral modification with motivational interviewing	not given	Weight (kg) 1. (10) -4.5 (-6, -2.9) 2. (6) -5.5 (-9.6, -1.4)	HbA _{1c} (overall group) 10.25 (9.1, 11.4)	HbA _{1c} 1. (10) 10.8 (8.8, 13.2) 2. (6) 9.8 (8.6, 11.4)	Self monitoring was a critical component of the program. Participants recorded daily calorie consumption and physical activity in diaries.
Muchmore 485	Randomized: unclear Self-selected: yes Included: diabetes, BMI 27.5-44 Mean age: 58.7 Mean weight: 99.1	BMI 27.5-44	Diet: yes to lose 0.5-1.0 kg/w Exercise: no Behavioral: yes LEARN program individual, qwx4,qmo	1. Behavioral therapy 2. Behavioral therapy plus self-monitoring blood glucose levels	none	Weight in kg 44 weeks 1. (8) -5.1 2 (9) -5.2 2vs1 -0.1 (-9.06, 8.8)	HgbAc 1. (11) 10.45 (9.5, 11.4) 2. (12) 10.29 (9.6, 11.0)	HgbAc 44 weeks 1. (8) 9.6 (8.1, 11.1) 2. (9) 8.75 (7.6, 9.9) 2vs1 -0.69 (-1.72, 0.34)	
Wing 493	Randomized: unclear Self-selected: unclear Included: diabetes, >120% IBW Mean age: 54 Mean weight: 98.2	>120% IBW	Diet: yes 1000 kcal less than usual Exercise: yes encouraged	1. Behavioral therapy 2. Behavioral therapy with self-monitoring blood glucose levels	10%	Weight in kg 1. (22) -8.24 (-18, 1.73) 2. (23) -4.1 (-11.63, 3.43) 2vs1 4.14 (-4.41, 12.69)	FBS, mg/dl 1. (22) 207.5 (176.2, 238.8) 2. (22) 209.2 (178.3, 240.1) HgbAc 1. (21) 10.86 (9.9, 11.8) 2. (22) 10.19 (9.1, 11.3)	FBS, mg/dl 1. (22) 210.2 (177.8, 242.6) 2. (22) 216.2 (190.2, 242.2) 2vs1 4.30 (-26.98, 35.58) HgbAc 1. (21) 10.44 (9.5, 11.4)	

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
			Behavioral: yes group, qwx12, qmo					2. (22) 10.19 (9.2, 11.2) <u>2vs1</u> 0.42 (-0.55, 1.39)	
Uusitupa 490	Randomized: unclear Self-selected: no Included: diabetes >120% IBW Mean age: 53 Mean weight: 93 kg Female/Total: ng/88	>120% IBW	Diet: yes kcal ng, low fat Exercise: no Behavioral: yes Format: unclear q2w	1. Conventional diet education 2. Intensified diet education	overall (4%)	<u>BMI</u> 1. (46) -0.8 2. (40) -1.8 <u>2vs1</u> -1.0 (-2.65,0.65)	<u>FBS</u> 1. (48) 8.9 (7.9, 9.9) 2. (40) 7.6 (6.8, 8.4) <u>HgbAc</u> 1. (48) 9 (8.2, 9.8) 2. (40) 8.4 (7.7, 9.1)	<u>FBS</u> 1. (46) 7.5 (6.8, 8.2) 2. (40) 6.2 (5.5, 6.9) <u>2vs1</u> 0 (-0.88, 0.88) <u>HgbAc</u> 1. (46) 7.5 (7.0, 8.0) 2. (40) 6.6 (6.1, 7.1) <u>-2vs1</u> -0.3 (-1.0, 0.4) <u>FBS 108 weeks</u> 1. (44) 8.2 (7.5, 8.9) 2. (38) 7.1 (6.3, 7.9) <u>2vs1</u> 0.2 (-0.70, 1.10) <u>HgbAc 108 weeks</u> 1. (44) 8 (7.5, 8.5) 2. (38) 7.2 (6.6, 7.8) <u>2vs1</u> -0.2 (-0.92, 0.52)	Both groups showed significant reductions (p<0.001) in body weight and body mass index during the run-in phase. FBS reduced markedly in both groups during the run-in phase (p<0.001). SBP and DBP levels decreased significantly in both groups during run-in phase (p<0.001). At 15 months, FBS after adjustment for baseline differences was significantly lower in group 2 (p=0.02) but the difference in HgbA1c was not significant (p=0.063). According to HGBA1c at baseline 33.3% of patients in group 2 and 28.3% in group 1 were in good metabolic control (<7.0%). At 15 months, this goal was achieved by 74.4% of patients in group 2 compared to 47.8% in group 1 (p=0.005).
Wing 694	Randomized: unclear Self-selected: unclear Included: 13.6-31.8 kg above IBW Mean age: 37.4 Mean weight: 89.8 Female/Total: 101/202	13.6-31.8 kg above IBW	Diet: yes Exercise: yes Behavioral: yes Format: group Frequency: weekly	Patients assigned to one to four groups which varied in the type of behavioral strategies use to promote adherence but not described further in this publication.	not given	<u>Weight in kg</u> men (101) -9.77 (95%CI -11.12, -8.42) women (101) -6.43 (95%CI -7.57, -5.29)	<u>FBS</u> men (101) 5.67 (95%CI 5.52, 5.82) women (101) 5.28 (95%CI 5.16, 5.40)	<u>FBS</u> men (101) -0.08 (95%CI -0.24, 0.08) women (101) 0.21 (95%CI 0.09, 0.33) <u>FBS at 6 months</u> women (16) -8.94 (95%CI -12.62, -5.26)	

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Question 24. What is the evidence that weight loss directly affects glucose tolerance?

Reference	Design/Demographics	Overweight defined as:	Adjuvant therapy	Intervention	Drop-out Total	Mean weight change (n) mean (95%CI)	Fasting Blood Sugar/Insulin levels Baseline (n) mean (95%CI)	FBS/Insulin levels change (n) mean (95%CI)	Comments
								FBS at 12months women (16) -5.67 (95%CI -9.35, -1.99)	

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