**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **BRL 26830A** | | | | | | | | | | | | |
| Connacher 696 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers:Yes<br>Outcome: Yes<br>Mean age: 42.8<br>Mean weight: 100.5<br>Female/Total: 32/40 | >120% IBW | Diet: 3.35 MJ/d<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. BRL 26830A (beta adrenoreceptor agonist) start at 200 then 400 mg | 18 | 0 | 0 | (20) 100<br>(20) 101 | (16) -10 (-13.1,-6.9)<br>(16) -15.4 (-18.9, -11.9)<br>2vs1<br>-5.4 (0.8, 9.9) | | The only side effects of treatment with BRL 26830A regularly observed were shaky hands and tremulousness. Twelve patients experienced these symptoms at some time during 18 weeks. No other side effects were identified. | |
| | **Cimetidine** | | | | | | | | | | | | |
| Rasmussen 699 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 37<br>Mean weight: 95.7<br>Female/Total: 51/60 | BMI: 27-39 | Diet: Low-calorie, high fiber<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Cimetidine 200 mg TID<br>* Cross-over | 8 | NS<br>NS | 50/60 completed both periods | (30) 95.9<br>(30) 95.5 | (29) -5.9<br>(26) -5.7 *<br>2vs1<br>0.20 (-1.09, 1.48) | | Nausea/abdominal pain more frequent with cimetidine (no statistic done). | |
| | **Dexfenfluramine** | | | | | | | | | | | | |
| Guy-Grand 507 | Randomized: Yes<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>*multicenter[i] INDEX trial<br>Mean age: 40.8<br>Mean weight: 97.3<br>Female/Total: 662/822 | >120% IBW | Diet: caloric restriction not less than 1448 kj/d<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | 38<br>41 | 189 (45%)<br>150 (37%) | (418) 98.0<br>(404) 96.6 | (227) -7.5<br>(256) -9.8<br>2vs1<br>-2.30 (-3.28, -1.32) | | Tiredness, diarrhea, dry mouth, polyuria and drowsiness affected significantly more patients on dF than on placebo. | |
| | | | | | | | | | | | | | |
| Andersen 506 | Randomized: Yes<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Subgroup of INDEX trial<br>Mean age: 29.5<br>Mean weight: 99.5<br>Female/Total: 37/42 | >120% IBW | Diet: 1250 kcal<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | 0<br>0 | 8 (38%)<br>4 (19%) | subset of index trial | idem | Rate of regain 0.7 kg/mo and 0.9 kg/mo for dF and placebo. Regain of wgt SS for both groups between 6-12 mo. | No significant difference between 2 groups. | Randomization; unequal weight distribution between groups. |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Swinburn 70050 | Randomized: Unclear<br>Blinded Patient: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 45.7<br>Mean weight: 97<br>Female/Total: 57/84 | BMI 30-40 | Diet: Low fat<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Compliance: Yes | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 12 | ng | 13/97 | Weight (kg)<br>1. (42) 98.5 (94.4, 102.5)<br>2. (42) 96 (91.5, 100.5) | Weight (kg)<br>1. (42) -0.3 (-0.4, -0.2)<br>2. (42) -42.2 (-4.3, 4.0)<br><br>2vs1<br>-3.9 (-6.79, -1.01) | 12 weeks post treatment<br>1. (39) + 0.7 kg<br>2. (38) + 1.7 kg | Not given | |
| | | | | | | | | | | | | | |
| Mathus-Vliegen 390 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Subgroup of INDEX trial (?)<br>Mean age: 35.9<br>Mean weight: 110.7<br>Female/Total: 64/75 | >135% IBW | Diet: low-calorie (1000 kcal less)<br>Exercise: none<br>Behavioral: none | None | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | 0<br>0 | 3 (8%)<br>7 (19%) | (39) 110.3<br>(36) 111.2 | (36) - 8<br>(36) - 10.7<br><br>p=ns | *2 months follow-up off drug wgt regain 2.8 kg and 1.0 kg in dF and placebo | | Dutch eating behavior increased in placebo (need to restrain their eating more in order to achieve same weight loss). |
| | | | | | | | | | | | | | |
| Herwig 70037 | Randomized: Yes<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 42<br>Mean weight:<br>Female/Total: 52/60 | >120% IBW | Diet: LCD 1500<br>Exercise: No<br>Behavioral: No | None | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | ng | 18/60 | BMI (upper body obesity)<br>1. (8) 36.7 (30, 43)<br>2. (12) 35.1 (31, 39)<br><br>BMI (lower body obesity)<br>1. (6) 35.9 (29, 43)<br>2. (16) 34 (30, 38) | Weight loss (upper body obesity)<br>1. (8) –4.7 (-7.1, -2.3)<br>2. (12) –14.2 (-15.6, 12.8)<br><br>2vs1<br>–9.5 (-11.19, -7.81)<br><br>Weight loss (lower body obesity)<br>1. (6) –2.6 (-5, -0.16)<br>2. (16) –11.1 (-12.7, -9.6)<br><br>2vs1<br>-8.5 (-10.14, -6.86) | | Tiredness, headache, diarrhea, sleep disturbances, dry mouth and polyuria. Reported more often in the dF group. | In the patients with UBO waist circumference was reduced more than hip circumference and the ratio waist to hip circumference declined. In the patients with LBO both circumferences were lowered to same extent so that WHR did not change. |
| | | | | | | | | | | | | | |
| Pfohl 393 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 38.5 | >120% IBW | Diet: 1200-1500<br>Exercise: no<br>Behavioral: no | none | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | ng | 9 (38%)<br>5 (21%) | (24) 97<br>(24) 96 | (15) -9.6 (-13.2, -6.0)<br>(19)-10.9 (-14.7, -7.1)<br>2vs1<br>-1.3 (-4.87, 2.27) | (11) -2.1<br>(11) 1.5 | not described | |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean weight: 96.5<br>Female/Total: 38/48 | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| Bremer 386 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 49.4<br>Mean weight: 83.3<br>Female/Total: 15/26<br>*dyslipidemic patients | poor outcome to wgt loss programs | Diet: Low-fat diet<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Education: Yes<br>Wgt loss: No | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 12 | 0<br>3 | 0<br>3 (25%) | (14) 86.8<br>(12) 79.3 | (14) -2.5<br>(12) -4.2<br>2vs1<br>-1.70 (-8.65, 5.25) | | 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. | |
| | | | | | | | | | | | | | |
| Finer 746 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 35.7<br>Mean weight: 107.6<br>Female/Total: 39/45 | BMI >35 ($kg/m^2$) | Diet: 60-70% of total caloric needs (VLCD +snacks)<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Compliance: Yes<br>Education: NS<br>Wgt loss: Yes (25%) | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 26 | 0<br>0 | 6 (27%)<br>7 (30%) | (22) 107.3<br>(23) 107.9 | (16) 2.9<br>(16) -5.8<br>2vs1<br>-8.70 (-9.52, -7.87) | | Reported to be minor (no more details). | |
| | | | | | | | | | | | | | |
| Manning 414 | Randomized: Unclear<br>Blinded Patients: No<br>Providers: No<br>Outcome: No<br>Mean age: 55.6<br>Mean weight: ng<br>Female/Total: 101/205<br>* Type II diabetes | BMI 28-45 ($kg/m^2$) | Diet: ADA diet except control<br>Exercise: No<br>Behavioral: yes group qmox24 then q2mo | None | 1. Control<br>2. Clinic visit<br>3. Home and clinic visit<br>4. Behavioral therapy<br>5. Dexfenfluramine 15 mg BID | 12 of dF | NS<br>NS<br>NS<br>NS<br>15 | 0/58<br>13/37 (35%)<br>7/35 (20%)<br>17/38 (45%)<br>7/37 (19%) | N/A | End of tx<br>N/A<br>(37) -1.59<br>(35) -1.69<br>(38) -1.20<br>(37) -3.40 | 6 mo f/u 1y f/u<br>N/A (58) 1.2<br>(37) -2.30 (37) -1.21<br>(35) -1.30 (35) -1.14<br>(38) -1.21 (38) -1.82<br>(37) -3.13 (37) -2.75 | Cephalgia, drowsiness, insomnia, fatigue and dry mouth. | |
| | | | | | | | | | | | | | |
| Mathus-Vliegen 391 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 36.5<br>Mean weight: 109<br>Female/Total: 35/42 | >120% IBW | Diet: 1000 kcal less<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 52 | 0<br>0 | 3 (17%)<br>4 (24%) | (18) 110.57<br>(17) 107.43 | (18) -8.63<br>(17) -12.84<br>2vs1<br>-4.21 (-13.21, 4.79) | 60 wks<br>(18) 0.82<br>(17) 3.24 | | |
| | | | | | | | | | | | | | |
| Breum 745 | Randomized: Unclear<br>Blinded Patients: no<br>Providers: no<br>Outcome: no | ng | Diet: .1625 kcal/d<br>Exercise: no<br>Behavioral: no | none | 1. Placebo<br>2. Dexfenfluramine 30 mg qd | 56 | 0 | ng | (5?) 105<br>(5?) 88.6 | ( 5?) -9.3<br>( 5?) -14.6 | 14 months<br>(5?) 0.8<br>(5?) 2.9<br>2vs1 $p<0.05$ | not reported | |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean age: 32.8<br>Mean weight: 96.8<br>Female/Total: 10/10 | | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| O'Connor 392 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 40.2<br>Mean weight: 96.4<br>Female/Total: 31/51 | BMI 30-40 ($kg/m^2$) | Diet: 1200 to 1500<br>Exercise: none<br>Behavioral: none | Education: Yes<br>Compliance Assessment: No<br>Weight loss: No | 1. Placebo<br>2. Dexfenfluramine 15 mg BID | 24 | 0<br>0 | 4 (14%)<br>3 (10%) | (24) 100<br>(27) 93.3 | (24) -4.9 (-6.8,-3.0)<br>(27) - 9.7 (-12.0,-7.4)<br><br>2vs1<br>-4.8 (-6.9, 2.73) | 12 months<br>(14) -6.2 (-9.0, -3.4)<br>(20) -6.0 (-9.3, -2.7)<br>2vs1<br>0.2 (-2.79, 3.19) | Diarrhea, ↓appetite, fatigue, headache more common in dF (NS) significantly more nausea, dry mouth, dizziness with dF | |
| | | | | | | | | | | | | | |
| Pedrinola 711 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: ng<br>Mean weight: 87.1<br>Female/Total: 24/33 | not specified | Diet: 1000 kcal/d<br>Exercise: encouraged<br>Behavioral: none | Diet: 1000 kcal/d<br>Wgt loss: No<br>Pill count: No | 1. Fluoxetine 20 mg at breakfast and lunch and placebo at night<br>2. Fluoxetine 20 mg at breakfast and lunch and dexfenfluramine 15 mg at night | 32 | 4<br>0 | 7 (35%)<br>0 (0%) | Weight (kg) at end of run-in phase<br>1. (13) 87.8<br>2. (20) 86.7 | Weight (kg)<br>1. (13) 81.4<br>2. (20) 73<br><br>2vs1<br>–7.30 (–13.53, -1.07) | Weight (kg) at 2 months<br>1. (13) 85<br>2. (20) 81<br><br>2vs1<br>-2.90 (-10.05,4.25)<br><br>Weight (kg) at 4 months<br>1. (13) 84<br>2. (20) 78<br><br>2vs1<br>-4.90 (-11.39,1.59)<br><br>Weight (kg) at 6 months<br>1. (13) 83<br>2. (20) 75<br><br>2vs1<br>-6.90 (-13.17,-0.63) | Adverse events:<br>Somnolence in the first 2 weeks of treatment was the most common complaint (20% and 28% in group 1 and 2). This side effect disappeared spontaneously after 15 days of continuous medication.<br>Headache was reported in 16% in group 1 and 18% in group 2. Diarrhea was more common (11%) in group 2 affecting mostly male patients.<br>No significant difference occurred between groups for changes in vital signs. | |
| | **Ephedrine** | | | | | | | | | | | | |
| Astrup 697 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 35.5<br>Mean weight: 94.8<br>Female/Total: 155/180 | 120-180% IBW | Diet: 1000 kcal<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Caffeine 200 mg TID<br>3. Ephedrine 20 mg TID<br>4. Ephedrine 20 mg + Caffeine 200 mg TID | 24 (12. 16. 20) | 0<br>2<br>1<br>3 | 10 (22%)<br>10 (22%)<br>10 (22%)<br>10 (22%) | (45) 96.9 (92, 101.7)<br>(45) 94.0 (91, 97)<br>(45) 93.7 (89.7, 97.7)<br>(45) 94.6 (90.5, 98.7) | (35) -13.2 (-15.5,-10.9)<br>(35) -11.5 (-13.6, 9,.4)<br>(35) -16.3, -12.3)<br>(35) -16.6 (-18.9, -14.3)<br>4vs1<br>p<0.02<br>3vs1 | | Significantly more patients in the ephedrine/caffeine group than in placebo reported at least one symptom.<br>Withdrawal symptom seemed more frequent in EC (headache, tiredness) and ephedrine. | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | p>0.2<br>2vs1<br>p>0.2 | | | |
| | | | | | | | | | | | | | |
| Daly<br>697 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 35<br>Mean weight: 96.7<br>Female/Total: 22/29 | ng | Diet: Yes<br>Exercise: no<br>Behavioral: no | none | 1. Placebo<br>2. Ephedrine 150 mg/d + Caffeine 150 mg/d + ASA 330 mg/d | 8 | ng | 2<br>3 | (13) 100.1<br>(11) 93.3 | ( 13) -0.7<br>( 11) -2.2<br>2vs1<br>-1.50(-2.66, -0.14) | | ECA group: 3/11 complained of transient jitteriness, 2 complained of dry mouth and 2 of constipation.<br>Placebo group 1/13 complained of jitteriness, 2 of dry mouth and one of constipation.<br>There was no difference in frequency of any of these side effects and in both ECA and placebo groups side effects, tended not to persist.<br>Part II<br>Side effects: 3/8 complained of transient dry mouth with ECA while none did with placebo but there was no significant difference in frequency of any side effects. | |
| | | | | | | | | | | | | | |
| Pasquali<br>747 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 28.7<br>Mean weight: 83.9<br>Female/Total: 10/10 | NS | Diet: NS<br>Exercise: none<br>Behavioral: none | none | 1. Placebo cross-over to ephedrine 50 mg TID<br>2. Ephedrine cross-over to placebo | 8 | 0<br>0 | 0<br>0 | All (10) 83.5 | (10) -0.64<br>(10) -2.41(-2.12, -1.42)<br>* no comparison for parallel | | Incidence very rare with few reporting mild agitation, insomnia, palpitation, giddiness, while taking ephedrine. | |
| | **Fenfluramine/Phentermine** | | | | | | | | | | | | |
| Craighead<br>478 | Randomized: Unclear<br>Blinded Patients: no<br>Providers: no<br>Outcome: no | ng | Diet: 1000-1200<br>Exercise: no<br>Behavioral: yes group weekly | none | 1. Waiting list control<br>2. Physician's office medication control | 24 | ng | 0<br>1 (10%)<br>7 (17%)<br>1 (2%) | (10) 93.5<br>(6) 82.2<br>(32) 91.6<br>(25) 95.6 | (10) 1.3 (-1.6, 4.2)<br>(6) -6 (-10.4, -1.6)<br>(32) -10.9 (-12.9, -8.9)<br>(25) -14.5 (-16.8, | (32) -9 (-11.7, -6.3)<br>(25) -6.3 (-9.3, -3.2)<br>(23) -4.6 (-7.9, -1.3) | not reported | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean age: ng<br>Mean weight: 93.8<br>Female/Total: 120/120 | | | | 3. Behavior therapy<br>4. Fenfluramine 120 mg/d start at 120 mg then 120 mg<br>5.Behavioral + Fenfluramine | | | 3 (9%) | (23) 98.1 | -12.2)<br>(23) -15.3 (-17.8, -12.8)<br><u>4vs3</u><br>-3.80 (-5.69, -1.51)<br><u>5vs3</u><br>-4.40 (-6.57, -2.23)<br><u>5vs4</u><br>-0.80 (-3.13, 1.53) | | | |
| | | | | | | | | | | | | | |
| Wadden 71267 | Randomized: Unclear<br>Blinded Patients: no<br>Providers: no<br>Outcome: no<br>Mean age: 47.0<br>Mean weight: 97.6<br>Female/Total: 26/26 | Not defined | Diet: 1200 kcal<br>Exercise: yes<br>Behavioral: yes<br>LEARN Manual | No | 1. Fenfluramine 60mg/d plus phentermine 15mg/d with infrequent but structured physician visits<br>2. Fenfluramine 60mg/d plus phentermine 15mg/d with frequent group behavior modification | 52 | None | None | <u>Weight</u> (kg)<br>1. (13) 98.5 (89, 108)<br>2. (13) 96.7 (90.4, 103) | <u>Weight loss</u><br>1. (13) -13.9 (-19.7, -8)<br>2. (13) -15.4 (-20, -10.6) | Not given | Most frequent complaints: fatigue, drowsiness, diarrhea, poor concentration | |
| | | | | | | | | | | | | | |
| Weintraub 748 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 35<br>Mean weight: ng<br>Female/Total: ng | >130-180% IBW | Diet: 900-1800<br>Exercise: n<br>Behavioral: no | Diet: Yes<br>Pill count: no<br>Education: ng<br>Wgt loss: no | 1. Placebo<br>2. Fenfluramine 20 mg tid<br>3. Phentermine 30 mg qd<br>4. Phentenmine 15 mg qam + Fenfluramine 30 mg qpm | 16 | ng | 10 (50%)<br>10 (50%)<br>8 (40%)<br>8 (38%) | not given | (20) -4.4 (-6.3, -2.5)<br>(20) -7.5 (-10.0, -5.0)<br>(20) -10 (-12.5, -7.5)<br>(21) -8.4 (-10.7, -6.1)<br><br><u>4vs1</u><br>-4.00 (-6.05, -1.95)<br><u>4vs3</u><br>1.60 (-0.72, 3.92)<br><u>4vs2</u><br>-0.90 (1.148, -3.22) | | Patients in groups 2 and 3 had statistically significantly more complaints than those receiving placebo not with the combo.<br>Combo group reported significantly fewer cardiovascular and CNS complaints than the phentermine participants ($p<0.05$). Group 2 and 3 had statistically more cardiovascular and CNS complaints than the placebo group. Again there was no difference | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | between combo and placebo.<br>Number of patients complaining of dry mouth, palpitations, CNS<br>at week 6: group 1: 10 group 2: 17 group 3: 18 group 4: 14<br>at week 20 group 1: 2 group 2: 6 group 3: 10 group 4: 6. | |
| | | | | | | | | | | | | | |
| Weintraub 593 | Randomized: Yes<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 40<br>Mean weight: 33.4 mg/kg$^2$<br>Female/Total: 90/121 | >130-180% IBW | Diet: 1000-1800<br>Exercise: 900 cal/wk<br>Behavioral: Yes group weekly | Diet: Yes<br>Pill count: NG<br>Education: Yes<br>Wgt loss: no | 1. Placebo<br>2. Fenfluramine extended release 60 mg + Phentermine 15 mg<br><br><u>Second Double-blind</u><br>1. Placebo<br>2. Fenfluramine 60 mg, Phentermine 15 mg<br>weeks 156-190 | 28<br><br>28 | ng<br><br>ng | 5/54<br>4/62<br><br>overall 1/52 | (59) 94<br>(62) 93.7*<br>*estimate from graph | (54) -4.6 (-6.2, -3.0)<br>(58)-14.3 (-16.1, -12.5)<br><br><u>Weeks 0-190</u><br>(24) -2.1 (-4.6, 0.4)<br>(27) -5.9 (-8.8, -3.0)<br><br><u>2vs1</u> p<0.01 | After cessation of medication<br><u>Weight in kg</u> 0-210 wks<br>(48) -1.4 (-3.4, 0.6) | Dry mouth was the most important and troublesome adverse effect reported.<br>GI complaints were also more common in group 2.<br>Number of moderate and severe adverse effects were greater throughout study period in active therapy vs placebo.<br>Withdrawal symptoms: none of the participants reported signs and symptoms of a withdrawal reaction during cessation. | |

**Femoxitine/Fluoxetine**

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bitsch 750 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>* Multicenter<br>Mean age: 47.9<br>Mean weight: ng<br>Female/Total: 43/53 | >120% IBW | Diet: 1200 kcal/d<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Femoxetine 300 mg BID | 16 | 0<br>3 | 11 (42%)<br>9 (33%) | N/A | (26) -6.7<br>(27) -7.9<br><u>2vs1</u><br>-1.20 (-3.14, 0.74) | | Most side effects were reported in 1st 2 wks (24 vs 4 in placebo). Dry mouth was the only difference. | |
| | | | | | | | | | | | | | |
| Goldstein 752 | Randomized: Unclear<br>Blinded Patients: Yes | BMI >=25 | Diet: caloric restriction to lose | none | 1. Placebo<br>2. Fluoxetine 60 mg | 52<br>(20) | 19<br>41 | 120 (53%)<br>131 (57%) | (228) 99.2<br>(230) 100.3 | (107) -1.2 (-2.3, -0.1)<br>(105) -1.7 (-3.4, -0.04) | | Fluoxetine group had significantly more side | |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Providers: Yes<br>Outcome: Yes<br>Mean age: 43<br>Mean weight: 99.7<br>Female/Total: 366/458 | | 0.45 kg/w<br>Exercise: none<br>Behavioral: none | | qd | | | | | 2vs1<br>-0.5 (-1.91, 0.91) | | effects such as asthma, GI symptoms, nervousness, tremor, amnesia, thirst, sleep disorders. | |
| | | | | | | | | | | | | | |
| O'Kane 408 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 57.1<br>Mean weight: 98.7<br>Female/Total: 13/19<br>* Type II diabetes | BMI >30 | Diet: ns<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Fluoxetine 60 mg qd | 52 (24) | 0<br>2 | 1 (11%)<br>2 (29%) | (9) 99.9<br>(7) 97.2 | (9) 1.5 (0.2, 2.8)<br>(7) -4.3 (-6.0, -2.6) | | Diabetic symptoms, infection more common in placebo. GI symptoms, falls, and migraines were common with Fluoxetine. | |
| | | | | | | | | | | | | | |
| Darga 730 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 46.9<br>Mean weight: 102.9<br>Female/Total: 32/45 | ng | Diet: Yes<br>to lose 0.5 kg/wk<br>Exercise: Yes<br>Behavioral: Yes | none | 1. Placebo<br>2. Fluoxetine qd 60 mg | 52 | 0 | 6 (27%)<br>9 (64%) | (22) 100<br>(23) 105.8 | (16) -4.6<br>(14) -8.2<br>2vs1<br>-3.6 | 29 weeks<br>(ns) -5.5<br>(17) -12.3 | | |
| | | | | | | | | | | | | | |
| Marcus 734 | Randomized: Yes<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 39.2<br>Mean weight: ng<br>Female/Total: 41/45 | BMI >30 | Diet: low-calorie<br>to lose 1 lb./w<br>Exercise: yes<br>2 miles 5x<br>Behavioral: yes group q2wx10,q4w | none | 1. Placebo<br>2. Fluoxetine 60 mg qd | 52 (2 8 20 36) | 3<br>5 | 11 (52%)<br>10 (48%) | N/A | (10) +0.6(-3.0,+4.2)<br>(11)-13.9(-22.4,-5.4) | 15/21 program complete gave fu weight at 3-6 mo after study<br>1.(ns) 0 ± 2.7<br>2.(ns) 5.4 ± 4.9 | No significant differences between 2 groups for reported SE. | |
| Connolly 712 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 66<br>Mean weight: 88.3<br>Female/Total: 9/15<br>completers | BMI >29 | Diet: 1200-1600<br>Exercise: no<br>Behavioral: no | none | 1. Placebo<br>2. Fluoxetine start at 60 mg | 24 | ng | 2 (15%)<br>4 (23%) | (13) 85.1<br>(11) 92.0 | (11) 0 (-0.3, 0.3)<br>(7) -3.9 (-5.3, -2.5) | | The reporting of GI side effects was more common in the fluoxetine group and infections, mainly respiratory tract, were more common in placebo. | |
| | | | | | | | | | | | | | |
| Fernandez-Soto | Randomized: Unclear<br>Blinded Patients: Yes | ns | Diet: 1200 kcal/d<br>Exercise: none | none | 1. Fluoxetine cross-over to placebo | 12 | NS<br>NS | 5 (22%)<br>4 (21%) | N/A | (18) -7.31/ (18) -4.92<br>(15) -8.55/ (15) -4.67 | | Main side effects were cephalgia, drowsiness, | |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 757 | Providers: Yes<br>Outcome: Yes<br>Mean age: 39<br>Mean weight: 35.9<br>Female/Total: 39/39 | | Behavioral: none | | 2. Placebo cross-over to fluoxetine | | | | | (cross-over) | | insomnia, fatigue, and dryness of mouth (NS). | |
| | **Mianserin** | | | | | | | | | | | | |
| Cook 753 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 38<br>Mean weight: n/a<br>Female/Total: 43/45 | BMI >37 | Diet: 320<br>Exercise: no<br>Behavioral: no | none | 1. Placebo + VLCD<br>2. Mianserin 10 mg/d + VLCD | 16 | ng | ng | not given | (13) -15.5<br>(8) -15.6<br>*Given for women only<br>2vs1<br>- 0.10 (-3.99, 3.79) | | not reported | |
| | **Orlistat** | | | | | | | | | | | | |
| Drent 407 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 41.8<br>Mean weight: 83.7<br>Female/Total: 33/39 | >120-150% IBW | Diet: Low fat, 500 kcal reduced<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Pill count: Yes<br>Education: NS<br>Wgt: Yes<br>(0.5 to 4 kg) | 1. Placebo<br>2. Orlistat 50 mg TID | 12 | 0<br>1 | 2 (11%)<br>3 (15%) | | | (19) -2.1 (-3.4, -0.8)<br>(20) -4.3 (-5.9, -2.7)<br>2vs1<br>-2.2 (-3.61, 0-.78) | More GI adverse events (abdominal pain to fecal incontinence) in patients with orlistat. | |
| Drent 710 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 44<br>Mean weight: 92<br>Female/Total: 107/186 | BMI: 27.8-35 for men and 27.3-35 for women<br>WHR: >=0.9 for men and >=0.8 for women | Diet: Low-fat with 500 kcal restriction<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Pill count: Yes<br>Education: Yes<br>Wgt loss to be enrolled: No | 1. Placebo<br>2. Orlistat 30 mg qd<br>3. Orlistat 60 mg BID<br>4. Orlistat 90 mg QID | 12 | NS<br>NS<br>NS<br>NS | 6 (13%)<br>5 (10%)<br>3 (7%)<br>5 (11%) | 1. (46) 90.0 (86.6, 93.4)<br>2. (48) 92.1 (88.5, 95.7)<br>3. (45) 92.6 (88.4, 96.3)<br>4. (47) 94.1 (90.31, 97.9) | (46) -2.98 (-3.75, -2.21)<br>(48) -3.61 (-4.37, -2.85)<br>(45) -3.69 (-4.48, -2.90)<br>(47) -4.74(-4.9,-4.6)<br>*Intention to treat analysis<br>4vs1<br>-1.76 (-2.30, -1.22)<br>3vs1<br>-0.71 (-1.48, 0.0)<br>2vs1<br>-0.63 (-1.38, 0.12) | | | |
| | **Phenylpropanolamine** | | | | | | | | | | | | |

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**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Schteingart 512 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 37.8<br>Mean weight: 79.9<br>Female/Total: 85/101 | 115-145% overweight | Diet: 1200 kcal<br>Exercise: none<br>Behavioral: none | Diet: Yes<br>Pill count: Yes<br>Education: NS<br>Wgt loss: No | 1. Placebo<br>2. Phenylpropanolamine 75 mg qd | 12 | 1<br>1 | 23 (46%)<br>15 (29%) | (50) 84.8<br>(51) 78.8 | (28) -1.07 (-1.9, -0.2)<br>(36) -2.59 (-3.3, 1.9)<br>2vs1<br>-1.52 (-3.52, 0.48) | 20 weeks<br>(12) -0.39 (-2.4, 1.6)<br>(24) -5.1 (-8.2, -2.0) | No details other than 2 drop-out secondary to nausea. | |
| **Phentermine** | | | | | | | | | | | | | |
| Williams 509 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 67.5<br>Mean weight: 73.6<br>completers<br>Female/Total:all | >25% IBW | Diet: 1000 kcal<br>Exercise: No<br>Behavioral: No | Diet: No<br>Pill Count: No<br>Education: No<br>Wgt Loss: No | 1. Placebo<br>2. Phentermine 30 mg | 24 | 1<br>4 | 4 (27%)<br>4 (27%) | not given | Weight in kg 24 weeks<br>1. (ng) -4.5<br>2. (11) -6.3<br><br>2vs1 p=ns | Weight in kg at 3 months<br>1. (11) -2.6 (95%CI n/a, n/a)<br>2. (11) -5.8 (95%CI n/a, n/a)<br><br>2vs1 p<0.05 | Nausea or vomiting occurred in 3 patients taking phentermine; one patient in each group had CNS side effects. | There was some improvement in correlation of weight loss with pain-free range of movement and analgesic count when those with severe radiological change were excluded.<br>The average individual scores plotted against weight loss showed a correlation of 0.45 with statistical significance. The patients with knee disease showed a stronger correlation (r=0.66) with clinical score than did those with hip disease. |
| **Sibutramine** | | | | | | | | | | | | | |
| Bray 510 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 43.5<br>Mean weight: 96.2<br>Female/Total: ng | BMI 30-40 kg/m$^2$ | Diet: 1200-1500 kcal<br>Exercise:<br>3-5 kcal/min<br>Behavioral:<br>written material given | Diet: Yes<br>Pill count: No<br>Education: No<br>Wgt loss: No | 1. Placebo<br>2. Sibutramine 1 mg<br>3. Sibutramine 5 mg<br>4. Sibutramine 10 mg<br>5. Sibutramine 15 mg<br>6. Sibutramine 20 mg | 24 | ng<br>ng<br>ng<br>ng<br>ng<br>ng | overall 15% | Weight (kg), men<br>1. (ng) 111.95<br>2. (ng) 98.62<br>3. (ng) 107.80<br>4. (ng) 94.20<br>5. (ng) 109.37<br>6. (ng) 104.15<br>7. (ng) 96.05 | Weight (kg), men (completers)<br>1. (ng) 0.24<br>2. (ng) -6.43<br>3. (ng) -6.98<br>4. (ng) -7.3<br>5. (ng) -7.68<br>6. (ng) -9.3<br>7. (ng) -12.29 | Weight (kg), lost 5% at 30 weeks<br>1. (ng) 8%<br>2. (ng) 25%<br>3. (ng) 28%<br>4. (ng) 40%<br>5. (ng) 48%<br>6. (ng) 45%<br>7. (ng) 58% | Adverse events:<br>There was statistically significant difference in the reported number of adverse events with increasing drug doses. The reported adverse events which were possibly drug related | During the 6 week following dc of sibutramine, there was a regain in body weight which was most rapid in those who lost the most weight and least rapid in the placebo |

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| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 7. Sibutramine 30 mg | | | | Weight (kg), women<br>1. (ng) 92.02<br>2. (ng) 95.76<br>3. (ng) 90.91<br>4. (ng) 87.21<br>5. (ng) 89.67<br>6. (ng) 90.90<br>7. (ng) 91.0 | 7vs1 p<0.001<br><br>Weight (kg), women (completers)<br>1. (ng) -0.75<br>2. (ng) -2.96<br>3. (ng) -2.87<br>4. (ng) -6.19<br>5. (ng) -6.89<br>6. (ng) -7.3<br>7. (ng) -8.24<br><br>7vs1 p<0.001<br>6vs1 p<0.001<br>5vs1 p<0.001<br>4vs1 p<0.001<br><br>Weight (kg), lost 5%<br>1. (ng) 13%<br>2. (ng) 33%<br>3. (ng) 28%<br>4. (ng) 64%<br>5. (ng) 52%<br>6. (ng) 63%<br>7. (ng) 62%<br><br>Weight (kg), lost 10%<br>1. (ng) 0%<br>2. (ng) 8%<br>3. (ng) 16%<br>4. (ng) 16%<br>5. (ng) 28<br>6. (ng) 38%<br>7. (ng) 35% | Weight (kg), lost 10% at 30 weeks<br>1. (ng) 0%<br>2. (ng) 8%<br>3. (ng) 12%<br>4. (ng) 12%<br>5. (ng) 20<br>6. (ng) 21%<br>7. (ng) 31% | included dry mouth, decreased appetite, constipation and insomnia. These were generally mild.<br><br>Investigators terminated 14 subjects/173; 11/4 were in group 5 or higher. One subject was terminated early for mild hypertension. | and 1 mg dose groups.<br><br>There were 23 non-responders across all treatment groups. Of those whose weight remained stable or increased, 6 were in group 1, 4 in group 2, 7 in group 3, 2 in group 4, 1 in group 5, 2 in group 6, 1 in group 7. |
| | **Testosterone** | | | | | | | | | | | | |
| Marin 698 | Randomized: Unclear<br>Blinded Patients: No<br>Providers: No<br>Outcome: No<br>Mean age: 50.8<br>Mean weight: 95.6 | BMI >25 | Diet: ns<br>Exercise: none<br>Behavioral: none | none | 1. Placebo<br>2. Testosterone Decanoate 80 mg BID | 32 | 0<br>0 | 1 (8%)<br>1 (9%) | (12) 95.8<br>(11) 95.5 | (12) -0.2<br>(11) -1.4<br>2vs1<br>-1.20 (-8.03, 5.63) | | Side effects: a statistically significant enlargement of the prostate was found in the testosterone group. PSA unchanged. | |

**Question 13D. What is the evidence that pharmacotherapy interventions effect a change in weight?**

| Reference | Design | Overweight defined as: | Adjuvant therapy | Run-in Phase | Intervention | Length (F/U) | Drop out Side effects | Drop-out Total #(%) | Baseline Weight (n) mean (95%CI) kg | Mean weight change (n) mean (95% CI) | Weight Regain | Side effects | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Female/Total: 0/23 | | | | | | | | | | | | |
| | **Yohimbine** | | | | | | | | | | | | |
| Sax<br>755 | Randomized: Unclear<br>Blinded Patients: Yes<br>Providers: Yes<br>Outcome: Yes<br>Mean age: 42<br>Mean weight: n/a<br>Female/Total: 0/47 | >120% | Diet: 1800<br>Exercise: no<br>Behavioral: no | none | 1. Placebo<br>2. Yohimbine start at 16.2 mg then 43.2 mg | 24 | ng | 6<br>8 | not given | ( 15) -9.4<br>( 18) -8.7<br>2vs1<br>0.70 (-16.01, 17.41) | | The incidence was low in both groups. Two subjects (one in each group) developed hypertension. | |

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