| **Study Reference**  **Quality Rating** | **Study Characteristics** | **Inclusion/Exclusion** | **CONSORT Numbers**  **Retention** | **Participant Characteristics** |
| --- | --- | --- | --- | --- |
| **Orlistat Trials** |  |  |  |  |
| Berne, 2005180  Fair | **Design:** RCT  **Location:** Sweden  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Patients with type 2 diabetes receiving treatment with metformin alone or metformin and sulphonylurea; 30-75 years old; BMI 28-40 kg/m2; hemoglobin A1c was 6.5-10%  **Exclusion:** Treatment with insulin; recent myocardial infarction; other significant peripheral vascular, cardiac, respiratory, renal, neurological, gastrointestinal, or endocrine diseases; signs of fat soluble deficiencies; taking the following medications: drugs that influence appetite, resins, fish oil supplements, and retinoids | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:** NR  **N Randomized:**  Total: 220 (221 randomized but 1 didn't ever receive drug)  IG: 111  CG: 109  **Followup (12 mo), n (%):**  Total: 190 (86.4)  IG: 96 (86.5)  CG: 94 (86.2)  **Cluster information:** NR | **Age (mean):** 59.1 (calc)  **Sex (% female):** 45.5 (calc)  **Race/Ethnicity:**  *% Caucasian:* 100  **SES (income, education):** NR  **% Hypertension:**  *% Antihypertensive drugs:* 45  **% Diabetes:** 100  **% Dyslipidemia:**  *% Lipid-lowering drugs:* 14  **Other health problems:** NR |
| Broom, 2002181  UK Multimorbidity Study  Fair | **Design:** RCT  **Location:** UK  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Men and nonpregnant women; aged 18-80 yrs; BMI ≥28 kg/m2 (both at baseline and screening visits); at least one of the following obesity-associated CV risk factors: imapired glucose tolerance (serum glucose ≥8.0 mmol/L, 2 hrs after standard 75 g OGTT), dyslipidemia (total serum cholesterol ≥5.2 mmol/L or LDL cholesterol ≥4.2 mmol/L at screening); hypertension (sitting DBP 90-105 mmHg)  **Exclusion:** Women of child-bearing age  that were lactating or not using adequate contraception; MI; coronary artery bypass graft or percutaneous transluminal coronary angioplasty within 3 months before screening; gastrointestinal surgery for weight reduction; active gastrointestinal disorders; pancreatic disease; history of post-surgical adhesions; excessive alcohol intake; substance abuse; required any drug that might alter body weight or plasma lipids; administration of systemic steroids (other than hormone-replacement therapy); concomitant pharmacotherapy for type 2 diabetes, dyslipidemia or hypertension | **N recruited or assessed for eligibility:** 737  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Single-blind placebo and mildly hypocaloric diet (600 kcal/day deficit)  Required compliance: NR  Length: 2 weeks  N (%) retained after run-in: NR Compliance used as stratification variable  **N Randomized:**  Total: 531  IG: 265  CG: 266  **N ITT:**  Total: 522  IG: 259  CG: 263  **Followup (12 mo), n (%):**  Total: 347 (65)  IG: 186 (70)  CG: 161 (61)  **Cluster information:** NR | **Age (mean):** 46.0  **Sex (% female):** 78.4 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension alone:** 21.6  **% Hypertension** **overall**: 43  **% Impaired glucose tolerance alone:** 5.0  **% Impaired glucose tolerance overall:** 17.0  **% Dyslipidemia alone:** 44.8  **% Dyslipidemia overall:** 72  **Other health problems:** Combinations of IGT, hypertension, and dyslipidemia  *Note: Characteristics for N ITT.* |
| Davidson, 1999182  Fair | **Design:** RCT  **Location:** Multiple states, US  **Recruitment Setting:** Clinical research centers  **Self-selected:** NR | **Inclusion:** Age older than 18 years; BMI 30-43 kg/m2; adequate contraception in women of childbearing potential; absence of weight loss (>4 kg) in the previous 3 months  **Exclusion:** Frequently changed smoking habits or had stopped smoking in the past 6 months; history or presence of substance abuse; excessive intake of alcohol; significant cardiac, renal, hepatic, gastrointestinal, psychiatric, or endocrine disorders; drug-treated type 2 diabetes mellitus; concomitant use of medications that alter appetite or lipid levels | **N recruited or assessed for eligibility:** NR  **N eligible:** 1187  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Controlled-energy diet (30% intake as fat and energy, prescribed as 1.3 BMR − 2100 to 3360 kj/d), placebo capsules  Required compliance: ≥75% placebo capsules taken  Length: 4 weeks  N (%) retained after run-in: 892 (75.1)  **N Randomized:**  Total: 892  IG: 668  CG: 224  **N ITT:**  Total: 880  IG: 657  CG: 223  **Followup (12 mo), n (%):**  Total: 591 (66.3)  IG: 458 (68.6)  CG: 133 (59.4)  *24 mo data not given because high attrition*  **Cluster information:** NR | **Age (mean):** 43.5 (calc)  **Sex (% female):** 84.2 (calc)  **Race/Ethnicity:**  *% White:* 80.8 (calc)  *% Black:* 14.0 (calc)  *% Hispanic:* 4.2 (calc)  *% Other:* 1.0 (calc)  **SES (income, education):** NR  **% Hypertension:**  *% DBP>90 mmHg*  *Untreated:* 5.9 (calc)  *Treated:* 2.5 (calc)  **% Diabetes:** 4.1  **% Dyslipidemia:**  *% Abnormal LDL level (>129.9 mg/dL):* 33.1 (calc)  *% Abnormal HDL level (<.9 mmol/L):* 14.4 (calc)  *% Abnormal triglycerides level (>98.2 mg/dL):* 9.2 (calc)  **Other health problems:** Impaired glucose tolerance  \* Characteristics for N ITT |
| Derosa, 2003183  Fair | **Design:** RCT  **Location:** Italy  **Recruitment Setting:** Database from the Clinica Medica II at the University of Pavia  **Self-selected:** N | **Inclusion:** Obese (BMI>30 kg/m2); aged >40 years; severe hypercholesterolemia (TC≥240 mg/dL); normotensive (SBP<140 mmHg and DBP<90 mmHg); nonsmokers; normal thyroid function; not taking diuretics or beta-blockers  **Exclusion:** NR | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Controlled-energy diet (1500 kcal, 54% carbohydrates, 24% proteins, 22% lipids (6% saturated), 108 mg cholesterol, and 35 g fiber); placebo  Required compliance: NR  Length: 4 weeks  N (%) retained after run-in: NR Degree of weight loss in compliance trial used for stratification  **N Randomized:**  Total: 99  IG-O: 27  IG-F: 24\*  IG-OF: 25\*  CG: 23  Total (IG-O + CG): 50  **Followup (12 mo), n (%):**  Total (IG-O + CG): 48 (96.0)  IG-O: 25 (92.6)  CG: 23 (100)  **Cluster information:** N/A  \*IG-F (fluvastatin) & IG-OF (orlistat + fluvastatin) are not included in remainder of abstraction. | **Age (mean):** 52.0 (calc)  **Sex (% female):** 52 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Derosa, 2010215  Good | **Design:** RCT  **Location:** Italy  **Recruitment Setting:** University medical centers  **Self-selected:** N | **Inclusion:** Caucasian; type II diabetic patients; aged 18 years or older; BMI ≥30 kg/m2; uncontrolled type II diabetes (glycated hemoglobin >8.0%) in therapy with different oral hypoglycemic agents or insulin  **Exclusion:** History of ketoacidosis; unstable or rapidly progressive diabetic retinopathy, nephropathy, or neuropathy; impaired hepatic function; impaired renal function; severe anemia; serious cardiovascular disease or cerebrovascular conditions within 6 months before study enrollment; women pregnant or breastfeeding or of childbearing potential and not taking adequate contraceptive precautions | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:** NR  **N Randomized:**  Total: 254  IG: 126  CG: 128  **Followup (12 mo), n (%):**  Total: 234 (92.1)  IG: 113 (89.7)  CG: 121 (94.5)    **Cluster information:** NR | **Age (mean):** 52.5 (calc)  **Sex (% female):** 49.6 (calc)  **Race/Ethnicity:**  *% White:* 100  **SES (income, education):** NR  **% Hypertension:** 71.7  **% Diabetes:** 100  **% Dyslipidemia:**  *% Hypercholesterolemia:* 35.0  *% Hypertriglyceridemia:* 3.1  *% Combined dyslipidemia:* 17.3  **Other health problems:** NR |
| Finer, 2000184  James, 1997290  Fair | **Design:** RCT  **Location:** UK  **Recruitment Setting:** Local advertisement or GP referral  **Self-selected:** Mixed | **Inclusion:** Obese (BMI 30-43 kg/m2); 18 years or older  **Exclusion:** Weight loss of more than 4 kg in the 3 months before screening; history of any serious systemic disease, including diabetes; uncontrolled hypertension; previous gastrointestinal surgery for weight reduction; history of post-surgical adhesions; history or presence of cancer; psychiatric or neurological disorder requiring chronic medications or liable to prejudice patient compliance; evidence of alcohol or substance abuse; bulimia or evidence of laxative abuse; pregnancy or lactation (women of childbearing potential were allowed to enter the study if using adequate contraceptive precautions); post-menopausal women who had been amenorrhoeic for less than 1 year; taken drugs capable of influencing body weight, resins for lipid-lowering, anti-coagulants, digoxin or lipid-soluble vitamin supplements within the previous month | **N recruited or assessed for eligibility:** NR  **N eligible:** 267  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo and low-calorie diet  Required compliance: Taking 75% of capsules  Length: 4 weeks  N (%) retained after run-in: 228 (85.4) Stratified by weight loss during run in  **N Randomized:**  Total: 228  IG: 114  CG: 114  **Followup (12 mo), n (%):**  Total: 139 (61.0)  IG: 66 (57.9)  CG: 73 (64.0)  **Cluster information:** NR | **Age (mean):** 41.5 (calc)  **Sex (% female):** 88.5 (calc)  **Race/Ethnicity:**  *% White:* 94.9  *% Black:* 1.4  *% Other:* 3.7  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Hanefeld, 2002187  Fair | **Design:** RCT  **Location:** Germany  **Recruitment Setting:** Centers (primary care physicians and outpatient clinics)  **Self-selected:** NR | **Inclusion:** Aged 18-70 years; BMI ≥28 kg/m2; HbA1c 6.5-11%; diagnosis of type 2 diabetes treated with sulphonylureas for at least two months before screening or were diagnosed with type 2 diabetes but not yet treated with antidiabetic medication  **Exclusion:** Diabetes patients treated with drugs other than sulphonylureas; treated with medications known to effect body weight, serum lipids or vitamins; proliferative retinopathy or papilloedema; uncontrolled hypertension (DBP>120 mmHg); hypo- or hyper-thyroidism; secondary or type I diabetes; cardiac insufficiency (NYHA III/IV); presence or history of cancer or any significant appetite, renal, hepatic, gastrointestinal, psychiatric, immunological, or metabolic disorders; pregnant, lactating, or of childbearing potential and not taking adequate contraceptive measures | **N recruited or assessed for eligibility:**  **N eligible:** 492  **N excluded:**  **N refused or other reason:**  **Pre-randomization compliance trial**  Description: Placebo and diet  Required compliance:NR  Length: 4 weeks  N (%) retained after run-in: 383 (77.8)  **N Randomized:**  Total: 383  IG: 195  CG: 188  **N ITT:**  IG: 189  CG: 180  **Followup (12 mo), n (%):**  Total: 264 (68.9)  IG: 133 (68.2)  CG: 131 (69.7)  **Cluster information:** NR | **Age (mean):** 56.2 (calc)  **Sex (% female):** 50.9 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** 100  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Hauptman, 2000189  Fair | **Design:** RCT  **Location:** Multiple states, US  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Obese (BMI 30-44 kg/m2); aged >18 years  **Exclusion:** Women who were pregnant, lactating, or of childbearing potential and not taking adequate contraceptive measures; weight loss of more than 4 kg during the previous 3 months; history of significant cardiac, renal, hepatic, or gastrointestinal disorders; uncontrolled hypertension or any other clinically significant condition; gastrointestinal surgery for weight-reducing purposes; bulimia or laxative and/or substance abuse; abnormal laboratory measures (values ≥10% greater than the reference value for the normal range sufficient to require medical followup by the study physician); changes in smoking habits in the previous 6 months; use of any drug that might influence body weight or food intake during the 8 weeks before screening | **N recruited or assessed for eligibility:** NR  **N eligible:** 796  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo and reduced-energy diet (same as in study)  Required compliance: 75% compliance, determined by counting capsules returned  Length: 4 weeks  N (%) retained after run-in: 635 (79.8)  **N Randomized:**  Total: 635  IG1 (60 mg): 213  IG2 (120 mg): 210  CG: 212  (Use IG2 in MA)  **Followup (12 mo), n (%):**  Total: 427 (67.2)  IG1: 154 (72.3)  IG2: 151 (71.9)  CG: 122 (57.5)  **Cluster information:** NR | **Age (mean):** 42.5 (calc)  **Sex (% female):** 78.3  **Race/Ethnicity:**  % White: 90.9  % Black: 6.8  % American Indian: 0.2  % Hispanic: 1.9  % Other: 0.3  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Hill, 1999190  Fair | **Design:** RCT  **Location:** Multiple sites, US  **Recruitment Setting:** Clinical research centers  **Self-selected:** NR | **Inclusion:** Men and women aged ≥18 years; BMI 28-43 kg/m2; had to lose ≥8% of their initial body weight in run in  **Exclusion:** Ever had significant medical disorders; uncontrolled hypertension; recurrent nephrolithiasis; symptomatic cholelithiasis; active gastrointestinal disorders; type 2 diabetes; pancreatic disease; cancer; pregnant or lactating; history of presence of substance abuse; eating disorders; excessive alcohol intake; significantly abnormal laboratory test results; previous gastrointestinal surgery for weight reduction; history of postsurgical adhesions; had not taken any medications known to influence body weight, appetite, or lipid concentrations during the 8 weeks prior to screening | **N recruited or assessed for eligibility:** NR  **N eligible:** 1313  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Hypoenergetic diet (deficit of 4180 kJ/day with goal 0.5-1.0 kg/wk; 30% fat, 50% carb, 20% protein) with no pharmacologic intervention. Included dietary counseling, 4 session behavioral modification (UM's Wise Weighs) program, and encouraged to increase physical activity (brisk walking 20-30 min 5 times/wk)  Required compliance: Lose ≥8% of initial body wt  Length: 6 months  N (%) retained after run-in: 729 (55.5)  **N Randomized:**  Total: 729  IG1 (30 mg): 187  IG2 (60 mg): 173  IG3 (120 mg): 181  CG: 188  **Followup (12 mo), n (%):**  Total: 537 (73.7)  IG1: 140 (74.9)  IG2: 133 (76.9)  IG3: 126 (69.6)  CG: 138 (73.4)  **Cluster information:** NR | **Age (mean):** 46.3 (calc)  **Sex (% female):** 84.0 (calc)  **Race/Ethnicity:**  % White: 88.3 (calc)  % Black: 5.8 (calc)  % Hispanic: 4.9 (calc)  % Other: 1.0 (calc)  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR  *Note: Characteristics captured at beginning of run-in period (-6 months), not at randomization. Also, 9 participants appear to be missing in the characteristics table (720 participants total, yet 729 completed the run-in period).* |
| Hollander, 1998191  Fair | **Design:** RCT  **Location:** 12 centers, US  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Aged >18 years; drug compliance ≥70% during 5-week placebo run-in; HbA1c of 6.5-10%, fasting plasma glucose level of 5.6-12.2 mmol/l at the end of the 4th week of the run-in; blood levels of fat-soluble vitamin above the lower limit of the normal reference range; BMI 28-40 kg/m2; were on oral hypoglycemic drug therapy for at least 6 months before the study; stable plasma glucose level on a second-generation sulfonylurea agent as the only hypoglycemic agent at entry  **Exclusion:** Pregnant; lactating; of child-bearing potential and not using contraception; any clinically relevant condition that might affect study outcomes; complications associated with diabetes; weight loss of >4 kg during the previous 3 months; history of recurrent hephrolithiasis or symptomatic cholelithiasis; gastrointestinal surgery for weight reducing purposes; history of bulimia or laxative abuse; had taken any drug that might influence body weight or plasma lipids during the 8 weeks before the study initiation | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo and mildly hypocaloric(-500 kcal) weight loss diet (~30% calories from fat, 50% from carbohydrate, and 20% from protein, with a maximum of 300 mg/day of cholesterol)  Required compliance: ≥70% drug compliance  Length: 5 weeks  N (%) retained after run-in: 322 (82.4 (calc)) (322 of 391)  **N Randomized:**  Total: 322  IG: 163  CG: 159  **Followup (12 mo), n (%):**  Total: 254 (79)  IG: 139 (85)  CG: 115 (73)  **Cluster information:** NR | **Age (mean):** 55.1 (calc)  **Sex (% female):** 48.9 (calc)  **Race/Ethnicity (calc):**  *% White:* 87.5  *% Black:* 6.9  *% Hispanic:* 3.1  *% Other:* 2.5  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Krempf, 2003193  Fair | **Design:** RCT  **Location:** France  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Aged 18-65 years; BMI ≥28  **Exclusion:** Serious eating disorders; type I or type II diabetes; pregnant or lactating; smoking ≥1 pack/day or intention to stop smoking during the trial; previous surgical treatment for obesity; known or suspected substance abuse; significant thyroid, renal, hepatic, gastrointestinal, or immune disorders; concomitant use of medications that alter body weight, appetite, or the absorption of food | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo run-in, no further information  Required compliance: NR  Length: 15 days  N (%) retained after run-in: 696 (87.4% (calc))  **N Randomized:**  Total: 696  IG: 346  CG: 350  **Followup (18 mo), n (%):**  Total: 425 (61.1) (calc)  IG: 224 (64.7) (calc)  CG: 201 (57.4) (calc)  **Cluster information:** NR | **Age (mean):** 41  **Sex (% female):** 86.4  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** 0  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Lindgarde, 2000194  Swedish Multimorbidity Study  Fair | **Design:** RCT  **Location:** Sweden  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Men and nonpregnant women; aged 18-75 yrs; BMI 28-38 kg/m2; at least one of the following obesity-associated CHD risk factors: fasting serum glucose ≥6.7 mmol/L or confirmed type 2 diabetes treated with sulphonylurea or metformin but not insulin, total serum cholesterol ≥6.5 mmol/L and/or LDL cholesterol ≥4.2 mmol/L on at least 2 occasions or prescribed lipid-lowering med, DBP ≥90 mmHg on at least 2 occasions or confirmed hypertension treated with antihypertensive medication  **Exclusion:** Women of child-bearing potential who were lactating or not using adequate contraception; MI within 3 mo prior to screening; gastrointenstinal surgery for weight reduction; active gastrointestinal disorders; pancreatic disease; history of postsurgical adhesions; excessive alcohol intake; substance abuse; required any drug that might alter body weight or plasma lipids; administration of systemic steroids (other than hormone replacement therapy) or insulin | **N recruited or assessed for eligibility:** NR  **N eligible:** 382  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: single blind placebo and mildly hypocaloric diet (-600 kcal/day deficit); minimum diet 1200 kcal; 30% fat  Required compliance: NR (weight loss used for stratification)  Length: 2 weeks  N (%) retained after run-in: 376 (98.4)  **N Randomized:**  Total: 376  IG: 190  CG: 186  **Followup (12 mo), n (%):**  Total: 323 (85.9)  IG: 159 (83.7)  CG: 164 (88.2)  **Cluster information:** NR | **Age (mean):** 53.5  **Sex (% female):** 63.6  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** 74.5  **% Diabetes:** 26.1 (type 2)  **% Dyslipidemia:** 39.9 (hypercholesterolemia)  **Other health problems:** Combinations of hypercholesterolemia, diabetes, and hypertension and with each condition alone |
| Miles, 2002197  Fair | **Design:** RCT  **Location:** US and Canada  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Patients with type 2 diabetes; 40-65 yrs; BMI 28-43 kg/m2; maintained stable weight for ≥3 mo; HbA1c between 7.5 and 12.0%; received metformin treatment at 1000-2500 mg/day for at least 6 weeks (sulfonylurea therapy in combination with metformin was permitted as long as the sulfonylurea dose was stable for 12 weeks before study entry)  **Exclusion:** Receiving insulin, thiazolidinediones, or α-glucosidase inhibitors; any clinical condition that might affect study end points, including renal, hepatic, or endocrine disorders; poorly controlled hypertension (SBP≥160 mmHg or DBP≥100 mmHg); active gastrointestinal disease; previous bariatric surgery; history of bulimia; substance abuse; use of any weight loss medications; women who were pregnant, lactating, or of child-bearing potential | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:** NR  **N Randomized:**  Total: 516  IG: 255  CG: 261  **N ITT:**  Total: 504  IG: 250  CG: 254  **Followup (12 mo), n (%):**  Total: 311 (60)  IG: 165 (65)  CG: 146 (56)  **Cluster information:** NR | **Age (mean):** 53.1 (calc)  **Sex (% female):** 48 (calc)  **Race/Ethnicity:**  *% Caucasian:* 82  *% Black:* 12  *% Other:* 6  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** 100  **% Dyslipidemia:** NR  **Other health problems:** NR |
| Richelsen, 2007198  Fair | **Design:** RCT  **Location:** Multiple sites, Scandinavia  **Recruitment Setting:** Clinical research centers  **Self-selected:** NR | **Inclusion:** Aged 18-65 years; BMI between 30-45 kg/m2 and a waist circumference ≥102 cm (men) or ≥92 cm (women); one or more of the following risk factors: impaired fasting glucose (plasma glucose ≥6.1 mmol/L), diet-treated type 2 diabetes (plasma glucose ≥7.0 mmol/L) or dyslipidemia (HDL cholesterol ≤0.9 mmol/L for men, ≤1.1 mmol/L for women), and/or serum triglycerides ≥2.0 mmol/L but <10.0 mmol/L  **Exclusion:** NR | **N recruited or assessed for eligibility:** NR  **N eligible:** 383  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Very-low-energy diet of 600-800 kcal/day  Required compliance: Body weight loss of ≥5%  Length: 8 weeks  N (%) retained after run-in: 309 (80.7)  **N Randomized:**  Total: 309  IG: 153  CG: 156  **Followup (36 mo), n (%):**  Total: 200 (64.7)  IG: 102 (66.7)  CG: 98 (62.8)  **Cluster information:** NR | **Age (mean):** 47.0 (calc)  **Sex (% female):** 50.8  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** 22.3  **% Dyslipidemia:**  *% Low HDL (≤0.9/1.1 mmol/L):* 43.4  *% High triglycerides (>2.0 mmol/L):* 59.2  **Other health problems:** Impaired fasting glucose  *Characteristics reported for -2 months* |
| Rossner, 2000199  Fair | **Design:** RCT  **Location:** 14 centers, Europe  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Aged ≥18 years; BMI 28-43 kg/m2  **Exclusion:** Pregnant, lactating, or of childbearing potential but not taking adequate contraceptive measures; any clinically significant condition other than obesity that might affect the outcome of the study; lost >4 kg during the previous 6 months; undergone GI surgery for weight reducing purposes; had a history of post-surgical adhesions or of bulimia or laxative abuse; taken any drug that might influence body weight or serum lipids during 8 weeks before screening; uncontrolled hypertension, drug-treated DM, or history or presence of symptomatic cholelithiasis | **N recruited or assessed for eligibility:** NR  **N eligible:** 783  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo plus nutritionally balanced diet that was designed to cause a 600-kcal daily energy deficit and to supply about 30% of energy as fat  Required compliance: 75% assessed by proportion of capsules taken  Length: 4 weeks  N (%) retained after run-in: 729 (93.1) (calc)  **N Randomized:**  Total: 729 (calc)  IG1 (60 mg): 242  IG2 (120 mg): 244  CG: 243  **Followup (12, 24 mo), n (%):**  *12 mo*  Total: 524 (71.9) (calc)  IG1: 185 (76.4) (calc)  IG2: 181 (74.2) (calc)  CG: 158 (65.0)  *24 mo*  Total: 435 (59.7) (calc)  IG1: 140 (57.9) (calc)  IG2: 159 (65.2) (calc)  CG: 136 (56.0)  **Cluster information:** NR | **Age (mean):** 44.2 (calc)  **Sex (% female):** 82.3 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:**  % DBP ≥90 mmHg: 21.6  **% Diabetes:** NR  **% Dyslipidemia:**  % LDL cholesterol ≥3.362 mmol/L: 53.3  **Other health problems:** NR  NOTE: Reported for 718 subjects only (assume that this excluded the subjects who had no followup assessments, n=11) |
| Sjostrom, 1998200  Fair | **Design:** RCT  **Location:** Multi-center, Europe  **Recruitment Setting:** Hospital waiting lists and local advertising  **Self-selected:** Mixed | **Inclusion:** Obese (BMI 28-47 kg/m2) men and women; aged 18 years and over; using adequate contraception (women of child-bearing age)  **Exclusion:** Serious diseases, including uncontrolled hypertension and pharmacologically treated diabetes; weight loss of more than 4 kg in the 3 months before screening; surgery for weight reduction; history of post surgical adhesions, bulimia, or laxative abuse; use of any drug that might have influenced body weight or plasma lipids in the month before study entry; drug or alcohol abuse | **N recruited or assessed for eligibility:** 937  **N eligible:** 743  **N excluded:** 194  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Placebo TID with meals and hypo-caloric diet with -600 kcal/day from total estimated energy expenditure (1.3 times BMR) (roughly 30% of energy from fat); minimum 1200 kcal/day  Required compliance: 75% compliance calculated from number of capsules returned  Length: 4 weeks  **N (%) retained after run-in:** 688 (92.6)  **N Randomized:**  Total: 688  IG: 345  CG: 343  **N ITT:**  Total: 683  IG: 343  CG: 340  **Followup (12 mo), n (%):**  Total: 544 (79)  IG: 284 (82)  CG: 260 (76)  (Not clear if randomly reassigned at 12 mo)  **Cluster information:** NR | **Age (mean):** 44.8 (calc)\*  **Sex (% female):** 83.0 (calc)\*  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** NR  **% Dyslipidemia:** NR  **Other health problems:** NR  *\* Characteristics from ITT participants* |
| Swinburn, 2005201  Fair | **Design:** RCT  **Location:** 8 clinical research centers, Australia and New Zealand  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** Aged 40-70 years, BMI 30-50 kg/m2; One or more of the following conditions: hypercholesterolemia (serum total cholesterol >5.5mmol/l and/or LDL >3.5 mmol/L and clinically stable if on treatment), hypertension (systolic >140 mmHg and/or diastolic >90 mmHg and clinically stable if on treatment), and/or Type-2 diabetes treated with dietary modification or any oral hypoglycemic agent for 6+ months and clinically stable (glycated hemoglobin: 6.5-10%)  **Exclusion:** History of significant cardiac, renal, hepatic, gastrointestinal, or endocrine disorders; uncontrolled hypertension; previous gastrointestinal surgery for weight reduction; history of post-surgical adhesions; smoking; history or presence of substance abuse, bulimia, type-1 diabetes, psychiatric disorders, or active gastrointestinal disease | **N recruited or assessed for eligibility:** 352  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:**  Description: Single blind placebo lead-in period with advice on reducing dietary fat and increasing physical activity levels  Required compliance: NR  Length: 4 weeks  N (%) retained after run-in: NR  **N Randomized:**  Total: 339  IG: 170  CG: 169  **Followup (12 mo), n (%):**  Total: 269 (79.4) (calc)  IG: 132 (77.6 (calc))  CG: 137 (81.1 (calc))  **Cluster information:** NR | **Age (mean):** 52.2 (calc)  **Sex (% female):** 56.9 (calc), significantly greater in CG  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** 56.6 (calc)  **% Diabetes:**  *% Type 2 diabetes:* 26.8 (calc)  **% Dyslipidemia:**  *% Hypercholesterolemia:* 65.5 (calc)  **Other health problems:** 10 year risk CV disease |
| Torgerson, 2004202  Torgerson, 2001291  XENDOS  Fair | **Design:** RCT  **Location:** 22 medical centers, Sweden  **Recruitment Setting:** Newspaper advertisements  **Self-selected:** Y | **Inclusion:** Aged 30-60 years; BMI ≥30 kg/m2; nondiabetic glucose tolerance (2-hour whole blood glucose <10.0 mmol/L and fasting whole blood glucose <6.7 mmol/L); IGT (fasting whole blood glucose <6.7 mmol/L and 2-hour whole blood glucose 6.7-10.0 mmol/L)  **Exclusion:** Diabetes; ongoing and active cardiovascular and gastrointestinal disease; change in body weight >2 kg between screening and baseline examinations; SBP >165 mmHg or DBP >105 mmHg on the same 2 consecutive visits; MI within 6 months; symptomatic cholelithiasis; gastrointestinal surgery for weight reduction; peptic ulcer; active pancreatic disease; malignancy; significant psychiatric or neurologic disorder; abuse or previous participation in any trial of orlistat | **N recruited or assessed for eligibility:** 20,401  **N eligible:** 3373  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:** NR  **N Randomized:**  Total: 3305  IG: 1650  CG: 1655  **Followup, n (%):**  *12 mo*  Total: 2746 (83.1) (calc)  IG: 1478 (calc) (89.6)  CG: 1268 (calc) (76.6)  *48 mo*  Total: 1414 (42.8%)  IG: 850 (52%) , ITT 1640 (99.4 (calc))  CG: 564 (34%), ITT 1637 (98.9 (calc))  **Cluster information:** NR | **Age (mean):** 43.3 (calc)  **Sex (% female):** 55.2 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:** 0  **% Dyslipidemia:** NR  **Other health problems:** NR |
| **Metformin Trials** |  |  |  |  |
| Fontbonne, 1996185  BIGPRO  Fair | **Design:** RCT  **Location:** France  **Recruitment Setting:** NR  **Self-selected:** NR | **Inclusion:** High waist-to-hip ratio (≥0.95 for men, ≥0.80 for women); men aged 35-60 years; women aged 40-65 years  **Exclusion:** Ischemic cardiovascular disease (diagnosed before inclusion or detected by ECG required for inclusion; diabetes (diagnosed before inclusion or by OGTT at inclusion); heavy chronic medical treatment; serious life-threatening medical conditions; psychiatric disorders; impaired renal function (plasma creatinine ≥15 mg/dL) | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial:** NR  **N Randomized:**  Total: 457  IG: 227  CG: 230  **Followup (12 mo), n (%):**  Total: 324 (70.9)  IG: 164 (72.2)  CG: 160 (69.6)  **Cluster information:** NR | **Age (mean):** 49.5  **Sex (% female):** 66.7 (calc)  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:**  *% With antihypertensive treatment:* 33.0 (calc)  **% Diabetes:**  *% Abnormal glucose tolerance:* 21.5  **% Dyslipidemia:** NR  **Other health problems:** NR  *Characteristics at baseline are for those for participants who complete study; Also present baseline characteristics of subjects present and absent at 12 months* |
| Gambineri, 2006186  Fair | **Design:** RCT  **Location:** Italy  **Recruitment Setting:** Division of Endocrinology, S. Orsola-Malpighi Hospital  **Self-selected:** Probably not but did not state that all PCOS were assessed so could have been some volunteer recruitment through fliers, etc. | **Inclusion:** Women with polycystic ovarian syndrome (Rotterdam consensus: (*need 2 of the following*)) 1. chronic anovulation or severe oligomenorrhea/amenorrhea, 2. hirsutism or total testosterone levels of at least 0.72 ng/mL, 3. polycystic ovarian morphology at ultrasound); aged 18-45 years; BMI of at least 28 kg/m2; waist circumference of at least 88 cm; consistent with an abdominal fat distribution phenotype  **Exclusion:** Use of any medication or a significant modification in body weight within the previous 3 months or dieting; hyperprolactinemia; Cushing's syndrome; late-onset congenital adrenal hyperplasia; thyroid dysfunction; diabetes; cardiovascular, renal, or liver diseases | **N recruited or assessed for eligibility:** 140  **N eligible:** 85  **N excluded:** 55  **N refused or other reason:** 5  **Pre-randomization compliance trial:** NR | **Age (mean):** 27.0 (calc)  **Sex (% female):** 100  **Race/Ethnicity:** NR  **SES (income, education):** NR  **% Hypertension:** NR  **% Diabetes:**  *% Impaired glucose tolerance and/or impaired fasting glucose:* 33  **% Dyslipidemia:** NR  **Other health problems:**  100% Polycystic ovarian syndrome |
| Diabetes Prevention Program Research Group, 1999142  Haffner, 2005212  Orchard, 2005262  Diabetes Prevention Program Research Group, 2006210  Ratner, 2005207  Knowler, 2002206  West, 2008214  Rubin, 2005205  Ackermann, 2009211  Diabetes Prevention Program  Good | **Design:** RCT  **Location:** 27 clinical centers (research and community based), US  **Recruitment Setting:** Mass media, mail, telephone contacts, and recruitment through employment or social groups or health care systems  **Self-selected:** Assume mostly self-selected | **Inclusion:** Fasting plasma glucose 95-125 mg/dL (≤125 mg/dL in American Indian clinics); 2-hour postchallenge glucose 140-199 mg/dL after a 75 g glucose load; aged ≥25 years; BMI ≥24 kg/m2 (≥22 kg/m2 for Asian Americans)  **Exclusion:** Diabetes at baseline; medical conditions likely to limit life span and/or increase risk of intervention; conditions or behaviors likely to affect conduct of the trial; medications and medical conditions likely to confound the assessment for diabetes | **N recruited or assessed for eligibility:** NR  **N eligible:** NR  **N excluded:** NR  **N refused or other reason:** NR  **Pre-randomization compliance trial**  Description: Compliance with pill taking (placebo) and diet and exercises recordkeeping, no further detail  Required compliance: NR  Length: 3 weeks  N (%) retained after run-in: NR  **N Randomized:**  Total: 3234  IG-Metformin: 1073  IG-Lifestyle: 1079  CG: 1082  **Followup (12 mo, 36 mo), n (%):**  *12 mo*  Total: 3070 (94.9) (calc)  IG-M: 1017 (94.8 (calc))  IG-L: 1026 (95.1 (calc))  CG: 1027 (94.9 (calc))  *36 mo*  Total: 1921 (59.4) (calc)  IG-M: 626 (58.3 (calc))  IG-L: 638 (59.1 (calc))  CG: 657 (60.7 (calc))  **Cluster information:** NR | **Age (mean):** 50.6  **Sex (% female):** 67.7  **Race/Ethnicity:**  *% White:* 54.7  *% African American:* 19.9  *% Hispanic:* 15.7  *% American Indian:* 5.3  *% Asian/Pacific Islanders:* 4.4  **SES (income, education):** NR  **% Hypertension:** 29.6  **% Diabetes:** 0  **% Dyslipidemia:** 44.1% had elevated LDL or taking medication  **Other health problems:** History of stroke, revascularization, MI, MI by ECG, elevated TG, metabolic syndrome |