

### Electronic Supplementary Table 1. Medline search strategy

(canagliflozin[Title/Abstract] OR dapagliflozin[Title/Abstract] OR ertugliflozin[Title/Abstract] OR henagliflozin[Title/Abstract] OR licogliflozin[Title/Abstract] OR enavogliflozin[Title/Abstract] OR remogliflozin[Title/Abstract] OR empagliflozin[Title/Abstract] OR ertugliflozin[Title/Abstract] OR ipragliflozin[Title/Abstract] OR enavogliflozin[Title/Abstract] OR luseogliflozin[Title/Abstract] OR remogliflozin[Title/Abstract] OR tofogliflozin[Title/Abstract] OR bexagliflozin [Title/Abstract] OR sotagliflozin [Title/Abstract] OR SGLT1[Title/Abstract] OR SGLT-2i[Title/Abstract] OR SGLT inhibitors[Title/Abstract] OR sodium glucose cotransporter inhibitors[Title/Abstract] OR albiglutide[Title/Abstract] OR dulaglutide[Title/Abstract] OR exenatide[Title/Abstract] OR liraglutide[Title/Abstract] OR lixisenatide[Title/Abstract] OR semaglutide[Title/Abstract] OR GLP-1 agonist[Title/Abstract] OR GLP agonist[Title/Abstract] OR glucagon like peptide agonist[Title/Abstract]) AND (PCOS[Title/Abstract] OR polycystic ovarian syndrome[Title/Abstract]).

**Electronic Supplementary Table 2. Summary of studies obtained from Clinicaltrials.gov related to SGLT2is and GLP-1 RAs in PCOS.**

| <b>NCT Number</b> | <b>Interventions</b>                                                                     | <b>Primary Outcome Measures</b>                             | <b>Secondary Outcome Measures</b>                                                                                                                                                                                                                                                                                                                              | <b>Other Outcome Measures</b>                               | <b>Age group</b> | <b>Phases of clinical trial</b> | <b>Sample size</b> | <b>Study Design</b>    | <b>Locations</b> |
|-------------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|------------------|---------------------------------|--------------------|------------------------|------------------|
| NCT05646199       | Metformin and Semaglutide injection                                                      | Weight loss (kg), Changes in weight from baseline, 28 weeks | Changes in body fat percentage (28 weeks); Free androgen index; Changes in Free androgen index (%); (28 weeks); Blood pressure and changes in blood pressure (mmHg) (28 weeks); Pulse rate and Changes in pulse rate (beats per minute) (28 weeks); Glucose tolerance: Changes in glucose reading (mmol/l) at 2 hours following 75g of oral glucose (28 weeks) | None                                                        | adults           | II/III                          | 60                 | Randomized, open-label | UK               |
| NCT05702905       | Metformin Hydrochloride ; Semaglutide injection; Semaglutide and Metformin Hydrochloride | Percentage change in bodyweight (12 weeks);                 | HOMA-IR (12 weeks); testosterone level (12 weeks); androstenedione level (12 weeks); Free androgen index (12 weeks)                                                                                                                                                                                                                                            | Depression score by self-rating depression scale (12 weeks) | adults           | IV                              | 75                 | Randomized, open-label | China            |

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|             | ; calorie-restricted diet; and physical exercise     | proportion of patients with weight reduction of at least 5% (12 weeks) |                                                                                                                                                                                                                                                                                                                          |      |                     |      |    |                        |       |
| NCT04973891 | Canagliflozin combined with metformin; and metformin | Body mass index and changes in body mass index (3 months)              | Total testosterone and changes in total testosterone (Three months); androstenedione and changes in androstenedione (Three months); Dehydroepiandrosterone sulfate and changes in dehydroepiandrosterone sulfate (Three months); Sex hormone-binding globulin and changes in sex hormone-binding globulin (Three months) | None | adults              | I/II | 52 | Randomized, open-label | China |
| NCT05819853 | Semaglutide injection                                | Change in ovulation frequency (6-10 months)                            | Change in Whole Body Insulin Sensitivity (10 months); Change in ovarian morphology (10 months)                                                                                                                                                                                                                           | None | Children and adults | III  | 80 | Non-randomized         | USA   |

|             |                              |                                                                 |                                                                               |                                                                                                                                                                                                                                                                                                                                                              |       |    |    |                                   |          |
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|             |                              | ; urinary<br>progeste<br>rone<br>metabol<br>ites (14<br>months) |                                                                               |                                                                                                                                                                                                                                                                                                                                                              |       |    |    |                                   |          |
| NCT01899430 | Liraglutide<br>and metformin | Change<br>in body<br>weight<br>(12<br>weeks)                    | Change in body mass<br>index (12 weeks); waist<br>circumference (12<br>weeks) | changes in<br>fasting<br>glucose (12<br>weeks);<br>changes in<br>fasting<br>concentratio<br>n of insulin<br>(12 weeks);<br>changes in<br>blood<br>concentratio<br>ns of<br>luteinizing<br>hormone<br>(12 weeks);<br>changes in<br>blood<br>concentratio<br>ns of<br>follicle-<br>stimulating<br>hormone<br>(12 weeks);<br>change in<br>blood<br>concentratio | adult | IV | 32 | Rando<br>mized,<br>open-<br>label | Slovenia |

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|  |  |  |  | n of<br>testosterone<br>(12 weeks);<br>change in<br>blood<br>concentratio<br>n in<br>androstened<br>ione (12<br>weeks);<br>change in<br>blood<br>concentratio<br>ns of sex<br>hormone-<br>binding<br>globulin (12<br>weeks);<br>change in<br>blood<br>concentratio<br>n of<br>dehydroepia<br>ndrosterone<br>sulfate (12<br>weeks) |  |  |  |  |  |
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| NCT05200793 | Empagliflozin, Linagliptin and Metformin | luteinizing hormone (3-6 months) ; follicle-stimulating hormone (3-6 months) ; free androgen index, total testosterone and sex hormone binding globulin (3-6 months) ; transvaginal ultrasonography : disappearance | Fasting blood glucose level; Total cholesterol, Low density lipoprotein, very low density lipoprotein, high density lipoprotein, and triglycerides; atherogenic index I, II; and Interleukin 6 or Toll Like receptor 2 (3-6 months) | None | adult | IV | 75 | Randomized, open-label | Egypt |
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|             |                                | of PCOS (3-6 months); menstrual diaries (3-6 months) |                                                                                                                                                                                                                                                                                                                                                                                                                              |      |       |    |    |                        |       |
| NCT04700839 | SGLT2 inhibitors and Metformin | HOMA-IR (3 months)                                   | Waist/hip ratio; Waist Circumference; Hip Circumference; Menstrual cycles; fasting blood-glucose; postprandial blood-glucose; fasting serum insulin; postprandial insulin; alanine aminotransferase; aspartate aminotransferase; uric acid; serum creatinine; low-density lipoprotein cholesterol; high-density lipoprotein cholesterol; total cholesterol; triglyceride; total testosterone; luteinizing hormone; follicle- | None | adult | IV | 68 | Randomized, open-label | China |

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|             |                                       |                                               | stimulating hormone; estradiol; prolactin; metabonomics; Ferriman-Gallwey score; acne score, male pattern baldness, number of participants with treatment-related adverse events; body mass index; sex hormone binding globulin; free testosterone; dehydroepiandrosterone and androstenedione (3 months)                                           |      |       |    |    |                        |       |
| NCT04876027 | GLP-1 Ras and calorie restricted diet | Changes in visceral adipose tissue (12 weeks) | menstrual frequency; systolic blood pressure; diastolic blood pressure; fasting plasma glucose; postprandial plasma glucose; fasting insulin; postprandial insulin; glycosylated hemoglobin A1c; HOMA-IR; alanine aminotransferase; aspartate aminotransferase; total cholesterol; Triglycerides; high-density lipoprotein cholesterol; low-density | None | adult | IV | 68 | Randomized, open-label | China |

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|  |  |  | lipoprotein cholesterol;<br>creatinine; serum uric<br>acid; luteinizing<br>hormone; follicle-<br>stimulating hormone;<br>pituitary prolactin; total<br>testosterone; free<br>testosterone; sex<br>hormone binding<br>globulin;<br>androstenedione;<br>dehydroepiandrosterone<br>sulfate, controlled<br>attenuation parameter;<br>liver stiffness<br>measurement; total body<br>fat; total fat mass; total<br>lean mass; and change in<br>subcutaneous adipose<br>tissue (12 weeks). |  |  |  |  |  |  |
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| NCT04029272 | DRUG:<br>Metformin DR<br>UG: Exenatide<br>2 MG | Change<br>in body<br>weight<br>(12<br>weeks) | Proportion of subjects<br>who lost at least 5% of<br>their body weight;<br>change in body mass<br>index; change in waist<br>circumference; change<br>in hip circumference;<br>changes in lipid<br>accumulation product;<br>changes in Visceral<br>obesity index; changes<br>in blood pressure;<br>changes in Blood<br>Glucose and Insulin;<br>Changes in total<br>cholesterol; Changes in<br>serum triglyceride;<br>Changes in high-density<br>lipoprotein cholesterol;<br>Changes in low-density<br>lipoprotein cholesterol;<br>Changes in<br>lipoprotein(a); Changes<br>in apolipoprotein a1;<br>Changes in<br>apolipoprotein B;<br>Changes in free fatty<br>acid; Changes in high<br>sensitivity C reactive<br>protein(hsCRP);<br>Frequency of menstrual<br>cycle; Changes in<br>testosterone, | None | adult | IV | 80 | Rando<br>mized,<br>open-<br>label | China |
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|-------------|-----------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|-------|--------|----|------------------------|-----|
|             |                             |                                                                       | dehydroepiandrosterone sulfate, luteinizing hormone, follicle stimulating hormone, LH/FSH ratio, changes in acne severity score; changes in ovarian volume; and changes in follicular number of 2-9mm in diameter (12 weeks) |      |       |        |    |                        |     |
| NCT03008551 | Empagliflozin and metformin | Endothelial function measured by reactive hyperaemia index (3 months) | Inflammatory markers; HOMA-IR; body weight; blood pressure; lipid profile; free androgen index; endothelial function measured by microparticles; and quality of life questionnaire                                           | None | adult | II/III | 40 | Randomized, open-label | UK  |
| NCT06222437 | Semaglutide                 | Compliance of the therapy (4 weeks)                                   | Body weight; numbers of days with exercise changes (4 weeks)                                                                                                                                                                 | None | adult | I      | 85 | Non-randomized         | USA |

|             |                                   |                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                      |      |       |                |     |                               |       |
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| NCT04213677 | Dapagliflozi and placebo          | Change s in insulin resistance; HOMA-IR; changes in serum androge n level (12 weeks) | Change in area under a curve of glucose and insulin during the oral glucose tolerant test; change in serum free testosterone, serum sex hormone binding globulin, total testosterone, dehydroepiandrosterone-sulfate, androstenedione, luteinzing hormone, waist circumference, liver fat assessed by liver fibroscan, change in ovulation rate, body weight, and glucose (12 weeks) | None | adult | III            | 165 | Rando mized, quadru ple-blind | China |
| NCT05966792 | SGLT2 inhibitors and metformin    | Menstrual cycles (6 months)                                                          | HOMA-IR, serum Nod-like receptor protein 3, serum Interleukin-1 beta, serum Interleukin-18, luteinizing hormone, follicle-stimulating hormone, prolactin, estradiol, progesterone, total testosterone, and antimullerian hormone (6 months)                                                                                                                                          | None | adult | Not applicable | 80  | Rando mized, open-label       | China |
| NCT03151005 | Metformin-GLP-1 Receptor Agonist, | Assess ment of Reprod uctive                                                         | Basic Vital Signs; body mass index; alanine transaminase; blood pressure; systolic blood                                                                                                                                                                                                                                                                                             | None | adult | IV             | 70  | Rando mized, triple-blind     | China |

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|-------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-----|-----|-------------------------------------|----------|
|             | Metformin-<br>Oral<br>Contraceptive                                           | Function<br>s and<br>leutinizi<br>ng<br>hormon<br>e (12<br>weeks) | pressure; reproductive<br>function; testosterone<br>(12 weeks)                |                                                                                                                                                                                                                                                            |       |     |     |                                     |          |
| NCT06405178 | Metformin,<br>Dapagliflozin,<br>Dapagliflozin/<br>Metformin,<br>and Letrozole | Pregnan<br>cy,<br>serum<br>HCG<br>positive<br>(3<br>cycles)       | None                                                                          | None                                                                                                                                                                                                                                                       | adult | III | 500 | Rando<br>mized,<br>single-<br>blind | Egypt    |
| NCT02187250 | metformin,<br>liraglutide,<br>roflumilast                                     | change<br>in body<br>weight<br>(12<br>weeks)                      | change in body mass<br>index, changes in waist<br>circumference (12<br>weeks) | changes in<br>fasting<br>concentratio<br>ns of<br>glucose,<br>fasting<br>concentratio<br>n of insulin,<br>luteinizing<br>hormone,<br>follicle-<br>stimulating<br>hormone,<br>testosterone,<br>androstened<br>ione, sex<br>hormone-<br>binding<br>globulin, | adult | IV  | 45  | Rando<br>mized,<br>open-<br>label   | Slovenia |

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|             |                             |                                                                                                                                                          |                                                             | dehydroepiandrosterone sulfate (12 weeks) |       |     |    |                             |       |
| NCT06576375 | Dapagliflozin and Metformin | Luteinizing hormone, Follicle-stimulating hormone, Free androgen index, Total testosterone, Transvaginal ultrasonography, Menstrual diaries (3-6 months) | Metabolic parameters and fasting blood glucose (3-6 months) | None                                      | adult | III | 70 | Randomized, quadruple-blind | Egypt |

|             |                                                      |                                  |                                                                     |                                                                                                                                                                                                                      |       |     |     |                        |          |
|-------------|------------------------------------------------------|----------------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-----|-----|------------------------|----------|
| NCT01911468 | Metformin, liraglutide and metformin and liraglutide | change in body weight (12 weeks) | change in body mass index; change in waist circumference (12 weeks) | changes in fasting concentrations of glucose, insulin, luteinizing hormone, follicle-stimulating hormone, testosterone, androstenedione, sex hormone-binding globulin, and dehydroepiandrosterone sulfate (12 weeks) | adult | IV  | 36  | Randomized, open-label | Slovenia |
| NCT05965908 | Liraglutide and Metformin                            | Body weight loss (1 month)       | None                                                                | None                                                                                                                                                                                                                 | adult | III | 120 | Randomized, open-label | Egypt    |

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| NCT02635386 | Exenatide once weekly, dapagliflozin, exenatide with dapagliflozin, dapagliflozin plus metformin extended release; phentermine/topiramate extended release | Oral Disposition (Insulin Sensitivity-insulin Secretion) Index (24 weeks) | Absolute body weight; changes in body mass index; percent body weight; Central Adiposity (Waist Circumference); Waist-to-Hip Ratio; Waist-to-Height Ratio; Total Fat Mass; Total Body Fat; android-gynoid ratio; trunk/leg fat ratio; fasting blood glucose; blood glucose; HOMA-IR; Matsuda Sensitivity Index; Corrected First Phase Insulin Secretion (IGI/HOMA-IR); Total Cholesterol Levels; Triglyceride levels; Total Testosterone Concentrations; Dehydroepiandrosterone Sulfate; Free Androgen Index; systolic blood pressure; diastolic blood pressure (24 weeks) |      | adult | III | 119 | Randomized, single-blind | USA |
| NCT00344851 | Metformin, exenatide, combined metformin and exenatide                                                                                                     | Menstrual Cyclicity (24 weeks)                                            | BMI, WHR, FAI (T/SHBG), DHEAS, lipids, abdominal girth, HOMA-IR, composite insulin sensitivity index, pancreatic $\beta$ -cell                                                                                                                                                                                                                                                                                                                                                                                                                                             | None | adult | II  | 60  | Randomized, open-label   | USA |

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|-------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-------|----|-----|------------------------|----------|
|             |                                             |                                                                                                                                              | function, and insulinogenic index (24 weeks)                                                                                             |                                                                                                                                   |       |    |     |                        |          |
| NCT03383068 | Acarbose, exenatide, orlistat and metformin | Pregnancy rate (24 weeks)                                                                                                                    | Improvement of absorption rate, stillborn foetus rate, hyperandrogenism, free androgen index, blood glucose, and triglyceride (24 weeks) | None                                                                                                                              | adult | IV | 160 | Randomized, open-label | China    |
| NCT03353948 | Liraglutide with metformin, and metformin   | In-vitro fertilization pregnancy rates (14 days), changes in BMI, (12 weeks), cumulative pregnancy rates, number of all pregnancies (1 year) | Oocyte nuclear maturation (2 days), embryo quality (day 3-6)                                                                             | changes in fasting concentrations of glucose, insulin, testosterone, androstenedione, and sex hormone-binding globulin (12 weeks) | adult | IV | 30  | Randomized, open-label | Slovenia |

|             |                                           |                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |                         |     |     |                        |         |
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| NCT05952882 | Liraglutide with metformin, and metformin | Absolute Body Weight, change in Percent Body Weight (12 weeks) | Body Mass Index, Waist Circumference, Waist-to-Hip Ratio, Waist-to-Height Ratio, total Fat Mass Evaluated, Total Body Fat, Visceral Fat Level, Total lean body mass, insulin, HOMA-IR, Matsuda Insulin Sensitivity Index, SI OGTT, Total Cholesterol Levels, High Density Lipoprotein Cholesterol Triglyceride Levels, Low Density Lipoprotein Cholesterol, Systolic Blood Pressure, Diastolic Blood Pressure, Menstrual Cycle Frequency, Free Androgen Index, Sex Hormone Binding Globulin, Adrenal Dehydroepiandrosterone Sulfate 17(OH)-progesterone, Androstenedione, Progesterone, Luteinizing Hormone (LH), Follicle Stimulating Hormone Ovary Volume, |  | adults and older adults | III | 188 | Randomized, open-label | Vietnam |
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|  |  |  | Spontaneous Pregnancy Rate, Assisted Reproductive Therapy Pregnancy Rate, Cumulative Pregnancy Rate, Total dosage gonadotropin, number of retrieved oocytes/patient, number of mature (MII) oocytes/patient, Fertilization rate, Oocyte degeneration rate, Immaturity rate, number of embryos on day 5/patient, number of blastocysts/patient, Blastulation rate, No. of transferred embryos, Pregnancy rate per cycle, Pregnancy rate per Embryo Transfer, Implantation rate, Number of cancelled fresh Embryo Transfer (ET) because of hyperstimulation risk, Cryopreservation, number of cryopreserved embryos/patient (12 weeks); and ectopic Pregnancy Rate, |  |  |  |  |  |  |
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|  |  |  | Stillbirth Rate, Abortion Rate, Gestational Diabetes Mellitus Rate, Gestational hypertensive disorder Rate, Live Birth Rate, Type of Delivery Method, (24 months) |  |  |  |  |  |  |
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| NCT02073929 | Liraglutide and placebo | Change in Endogenous Thrombin Potential and Area under curve in a Thrombin Generation Test (26 weeks) | Percent Change in Plasma Level of Plasminogen Activator Inhibitor -1 (26 weeks) | Change in plasma level of adrenomedullin, atrial natriuretic peptide, copeptin, high sensitivity C-reactive protein, bleeding pattern, percent liver fat content, body composition, ovarian volume, and serum anti-Mullerian hormone (26 weeks) | adult | IV | 72 | Randomized, quadruple-blind | Denmark |
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| NCT03480022 | Liraglutide and placebo | Absolute body weight and free androgen index (32 weeks) | Body Mass Index, Change in Percent Body Weight, proportion of patients with at least 5% weight loss and 10% Body weight loss, abdominal adiposity, waist-to-hip ratio, change in central adiposity, waist-to-height ratio, total fat mass, total body fat, android-gynoid ratio, trunk/leg fat ratio, menstrual cycle frequency, total testosterone concentrations, adrenal Dehydroepiandrosterone Sulfate, fasting blood glucose, mean blood glucose, fasting HOMA-IR, Matsuda Insulin Sensitivity Index, insulin secretion- insulin sensitivity index total cholesterol levels, high density lipoprotein cholesterol, triglyceride, triglyceride and glucose index, systolic blood pressure, and diastolic |  | adult | III | 88 | Randomized, quadruple-blind | USA |
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|             |                                          |                             | blood pressure (32 weeks).                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                         |       |    |     |                        |       |
| NCT06742710 | Liraglutide and metformin, and metformin | Live birth rate at delivery | Clinical pregnancy rate of single cycle frozen embryo transfer, viable intrauterine pregnancy, newly diagnosed diabetes or gestational diabetes at 28 weeks of pregnancy, pregnancy outcome and complications, rate of miscarriage, multiple pregnancies, pregnancy induced hypertension, preeclampsia, HELLP syndrome, prematurity, macrosomia, induction of labour, prolonged duration of labour, caesarean section, assisted delivery, and peripartum increased blood loss; birth weight | Weight, glycosylated hemoglobin, number of menstrual cycles, free testosterone index, drug-related adverse reactions, anxiety, depression, quality of life, major congenital abnormalities (upto six weeks after birth) | adult | IV | 890 | Randomized, open-label | China |

|             |                             |                                                                                                                     |                                                                                                                                              |  |                     |        |     |                        |          |
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|             |                             |                                                                                                                     | for gestational age, Apgar scores, other perinatal outcomes at delivery                                                                      |  |                     |        |     |                        |          |
| NCT06140108 | Empagliflozin and metformin | Irregular menstruations assessment (3 months)                                                                       | Body weight, systolic blood pressure, lipid profile, glycosylated hemoglobin, fasting blood-glucose, and diastolic blood pressure (3 months) |  | Children and adults | II/III | 70  | Randomized, open-label | Pakistan |
| NCT03352869 | Exenatide and metformin     | Improvement of intravenous blood glucose from impaired glucose regulation to normal glucose regulation, and insulin | Improvement of hyperandrogenism, improvement of blood lipid, improvement of fatty liver (12 weeks)                                           |  | adult               | IV     | 183 | Randomized, open-label | China    |

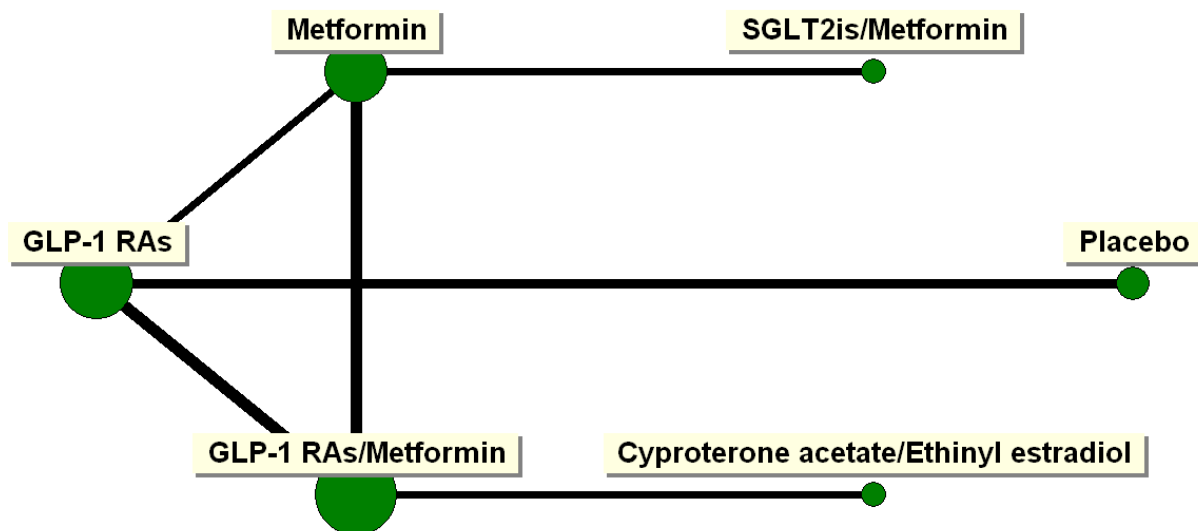
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|             |                                  | secretion of islet $\beta$ -cell (12 weeks)                                |                                                                                                                                                  |                                                                                |                     |        |     |                        |       |
| NCT06256289 | Canagliflozin and metformin      | Liver steatosis index, and changes in the liver steatosis index (12 weeks) | Liver stiffness index, body composition, selection of proteomics markers, selection of metabolomics markers, gut microbiota diversity (12 weeks) |                                                                                | adult               | IV     | 50  | Randomized, open-label | China |
| NCT03919929 | Semaglutide and weight loss diet | Change in Hepatic Fat Fraction, Change in Weight (12 weeks)                | Change in Rate of De Novo Lipogenesis, change in whole body insulin sensitivity, and change in adipose insulin sensitivity (12 weeks)            | Evaluation of Mitochondrial function, change in Free Androgen Index (12 weeks) | Children and adults | II/III | 60  | Randomized, open-label | USA   |
| NCT05601336 | Dapagliflozin, metformin, and    | Ovulation, Cumulative                                                      | Body weight changes, changes of Menstrual cycle, fasting blood                                                                                   |                                                                                | adults              | III    | 200 | Randomized,            | Egypt |

|  |                                    |                                                              |                                                                                                                             |  |  |  |  |                |  |
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|  | dapagliflozin<br>with<br>metformin | e rate of<br>pregnan<br>cy, and<br>HCG<br>test (3<br>months) | sugar, free androgen<br>index, total testosterone,<br>lipid profile, alanine<br>transminase, and side<br>effects (3 months) |  |  |  |  | open-<br>label |  |
|--|------------------------------------|--------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|--|--|----------------|--|

**Electronic Supplementary Table 3. Summary of findings and grading the pooled estimates for key outcome measures.**

| <b>Comparisons with placebo/metformin</b>                                                                                                                                                                                                                                                                     | <b>WMD (95% CI)</b>  | <b>Quality of evidence</b>               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|------------------------------------------|
| Menstrual frequency with GLP-1 RAs compared to placebo                                                                                                                                                                                                                                                        | 3.58 (3.54, 4.16)    | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Menstrual frequency with GLP-1 RAs/metformin compared to placebo                                                                                                                                                                                                                                              | 3.95 (3.48, 4.42)    | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| BMI change with GLP-1 RAs compared to placebo                                                                                                                                                                                                                                                                 | -2.01 (-2.16, -1.85) | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| BMI change with SGLT2is/metformin compared to placebo                                                                                                                                                                                                                                                         | -1.5 (-2.7, -0.3)    | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Percent fat mass changes with GLP-1 RAs compared to placebo                                                                                                                                                                                                                                                   | -0.87 (-1.07, -0.67) | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Post-interventional fat mass with GLP-1 RAs/SGLT2is compared to placebo                                                                                                                                                                                                                                       | -3.2 (-3.98, -2.42)  | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Post-interventional FAI with SGLT2is compared to placebo                                                                                                                                                                                                                                                      | -1 (-1.6, -0.39)     | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Post-interventional FAI with GLP-1 RAs compared to placebo                                                                                                                                                                                                                                                    | -0.4 (-0.75, -0.05)  | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Post-interventional FAI with SGLT2is compared to GLP-1 RAs                                                                                                                                                                                                                                                    | -0.57 (-0.97, -0.18) | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Changes in total testosterone with GLP-1 RAs compared to placebo                                                                                                                                                                                                                                              | -6.32 (-8, -4.64)    | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Changes in total testosterone with SGLT2is compared to GLP-1 RAs                                                                                                                                                                                                                                              | -3.74 (-5.94, -1.55) | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| Post-interventional LDL cholesterol with SGLT2is compared to GLP-1 RAs                                                                                                                                                                                                                                        | -0.2 (-0.33, -0.07)  | ⊕⊕⊕⊕; <b>Very low</b> <sup>1, 2, 3</sup> |
| 1- Downgraded one level for including studies with high risk of bias; 2- Downgraded one level for serious limitations in the precision of the estimates; 3- Downgraded one level as publication bias could not be assessed/ruled out; <b>Very low:</b> We have very little confidence in the effect estimate. |                      |                                          |

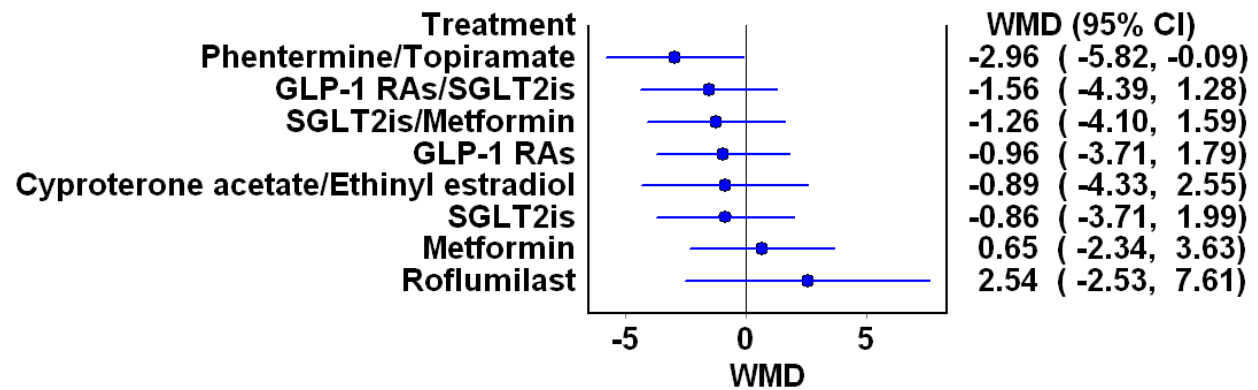
Electronic Supplementary Figure 1. Network plot for changes in BMI.



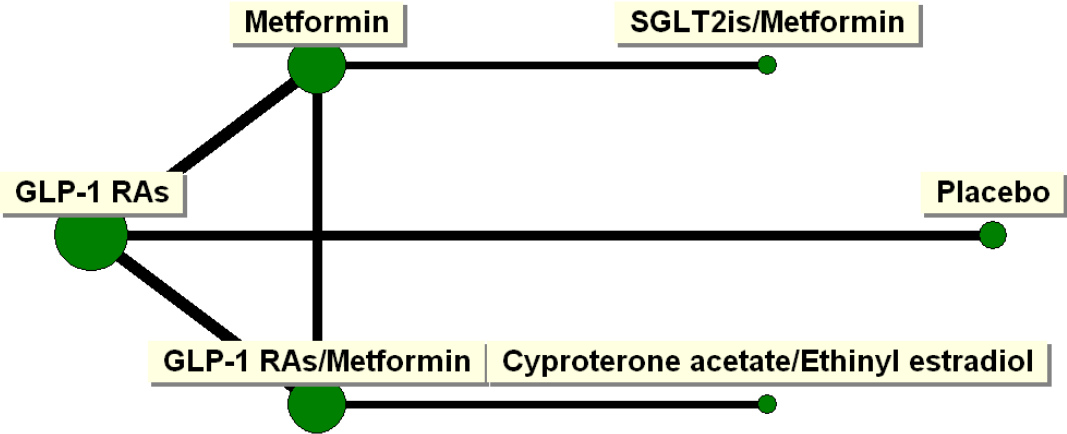
GLP-1 RAs, metformin and GLP-1 RAs/metformin were the most evaluated interventions for changes in BMI.

Green circles represent the relative numbers of studies evaluating the specific interventions and the thickness of lines represents the relative numbers of studies evaluating the connected interventions.

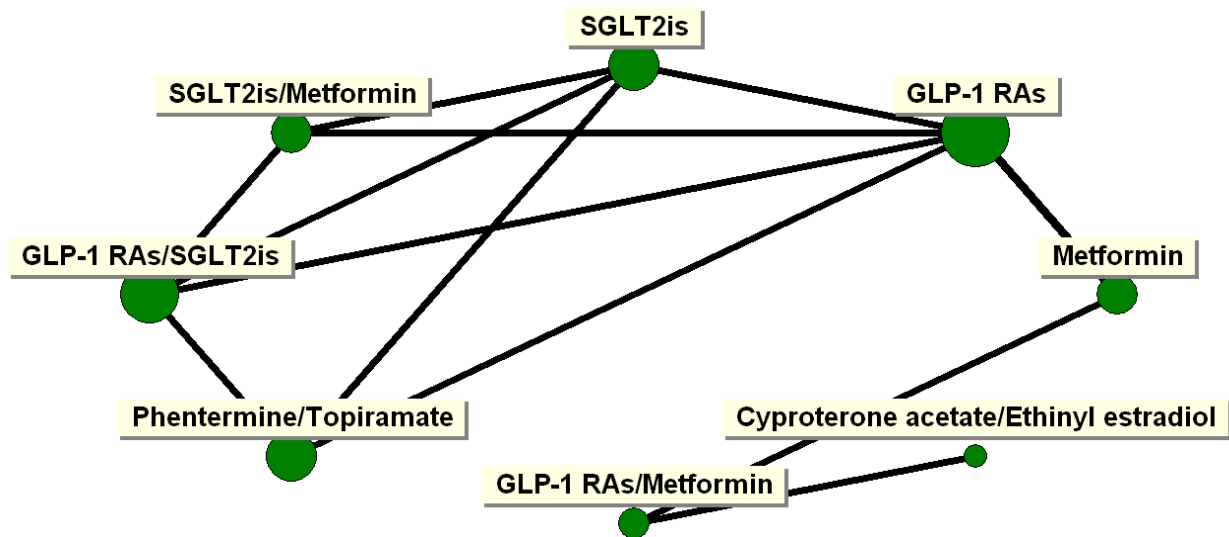
Electronic Supplementary Figure 2. Forest plot for postinterventional BMI between the interventions.



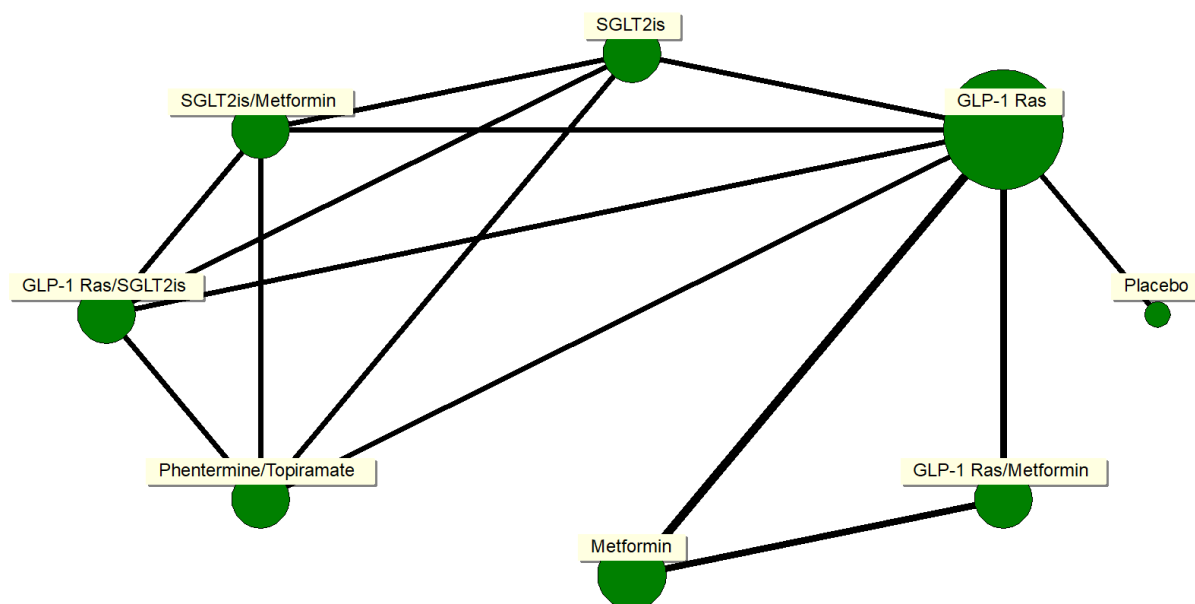
Electronic Supplementary Figure 3. Network plot for changes in body weight.



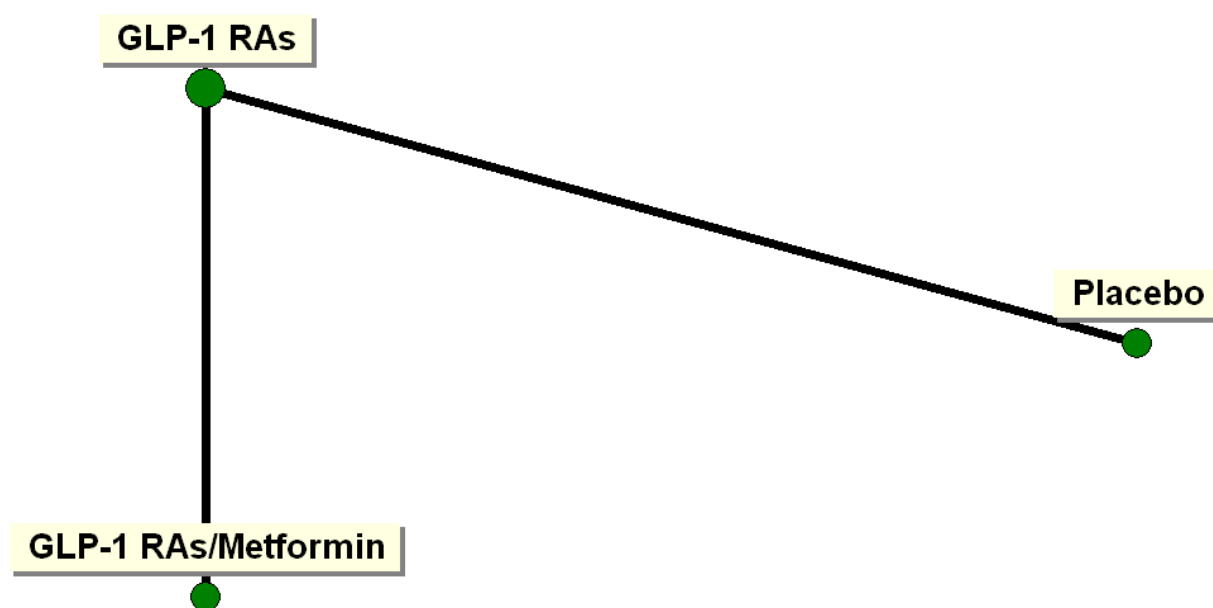
Electronic Supplementary Figure 4. Network plot for post-interventional WHR.



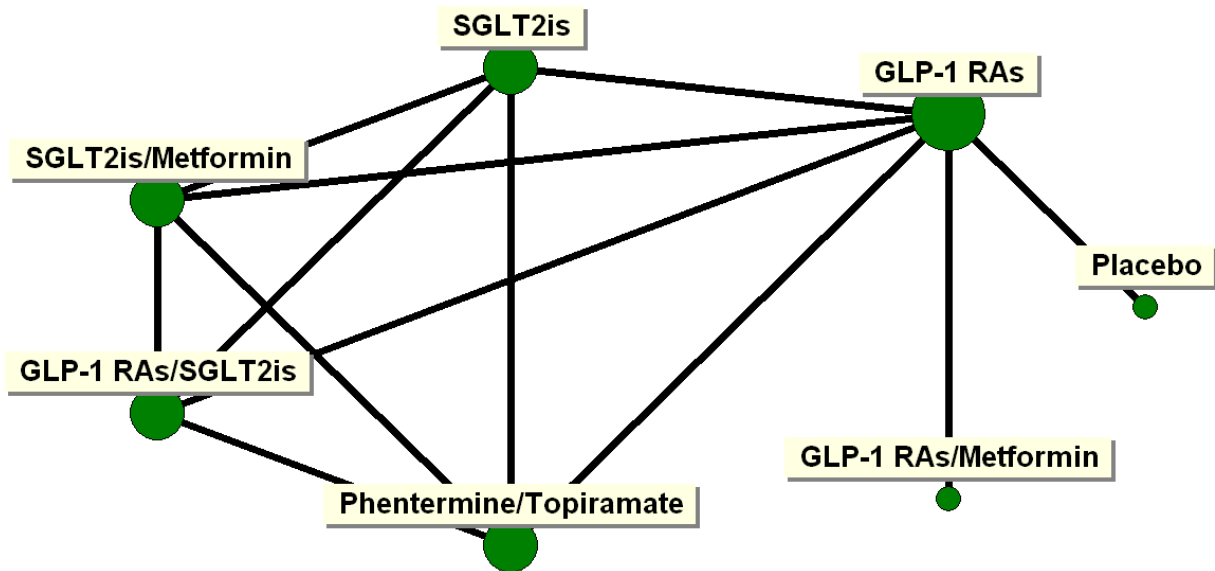
Electronic Supplementary Figure 5. Network plot for post-interventional percent fat mass.



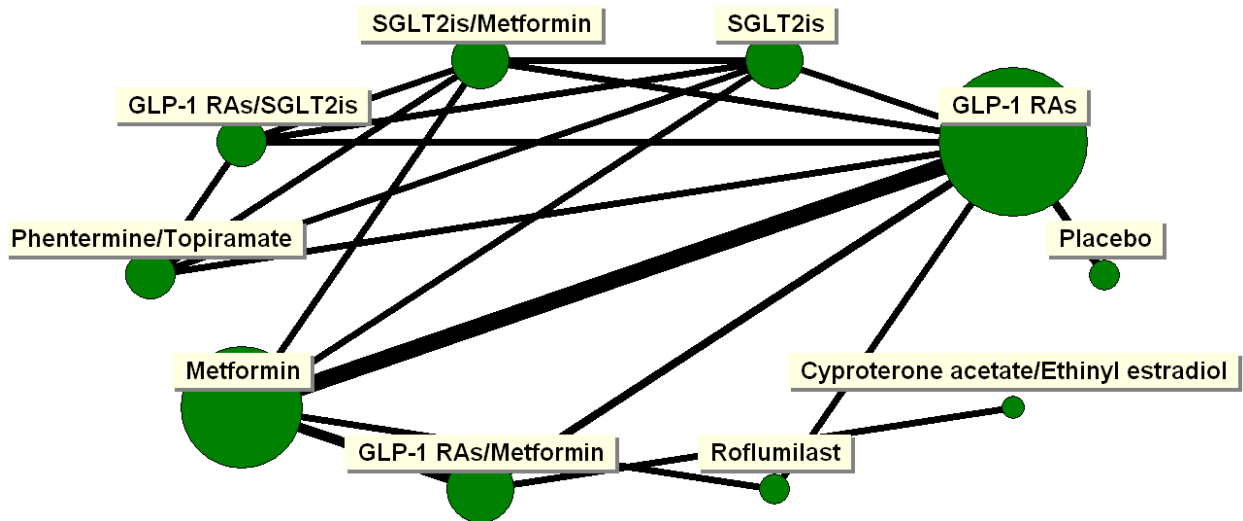
Electronic Supplementary Figure 6. Network plot of interventions evaluating changes in VAT mass.



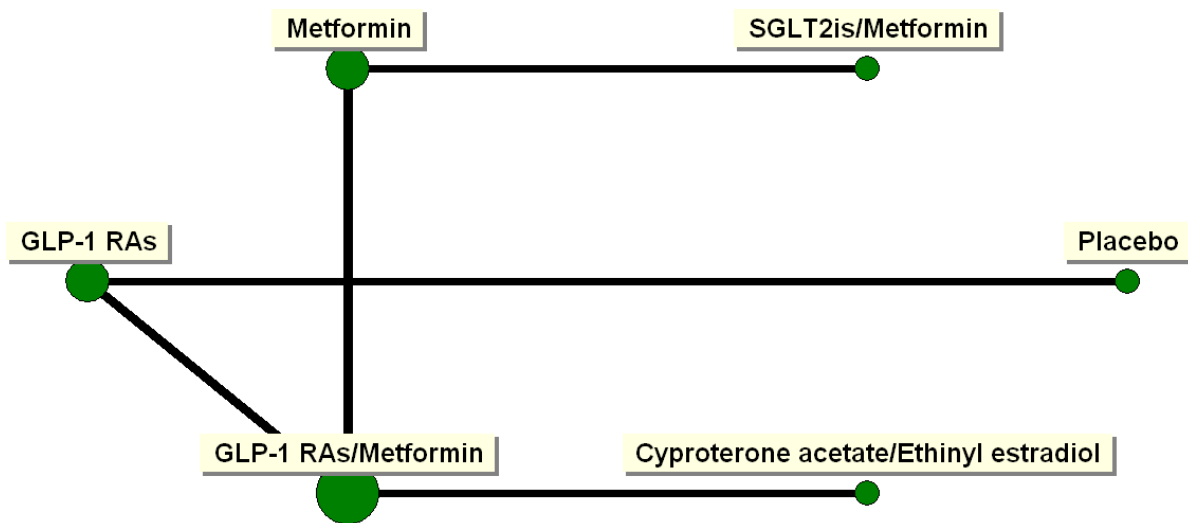
Electronic Supplementary Figure 7. Network plot of interventions evaluating post-intervention AGF ratio values.



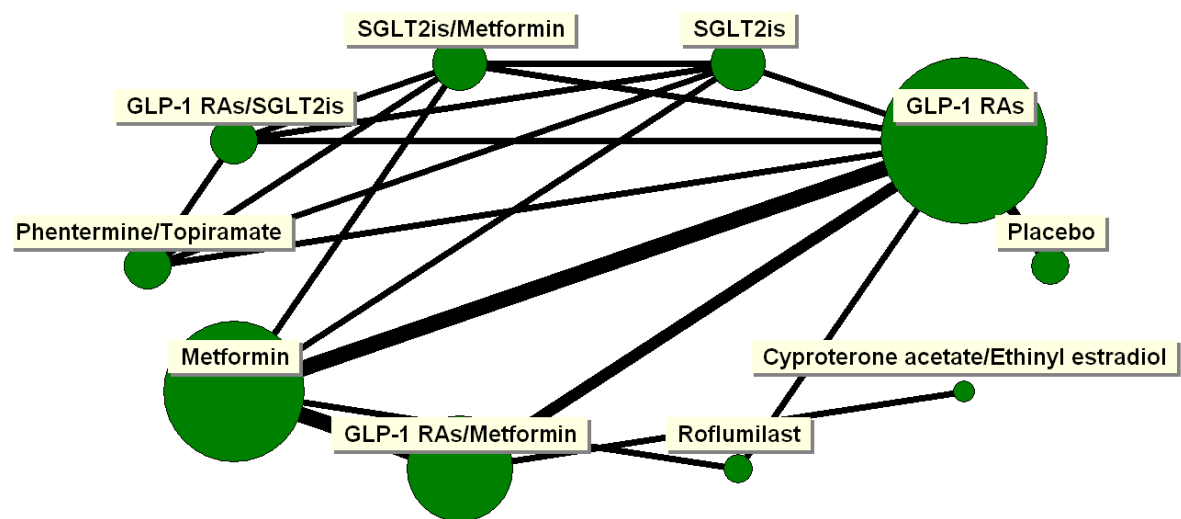
Electronic Supplementary Figure 8. Network plot for post-intervention FAI.



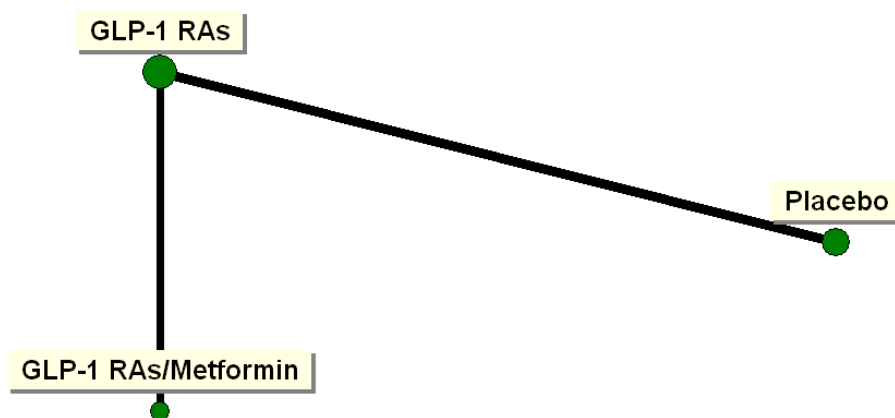
Electronic Supplementary Figure 9. Network plot for changes in the serum total testosterone.



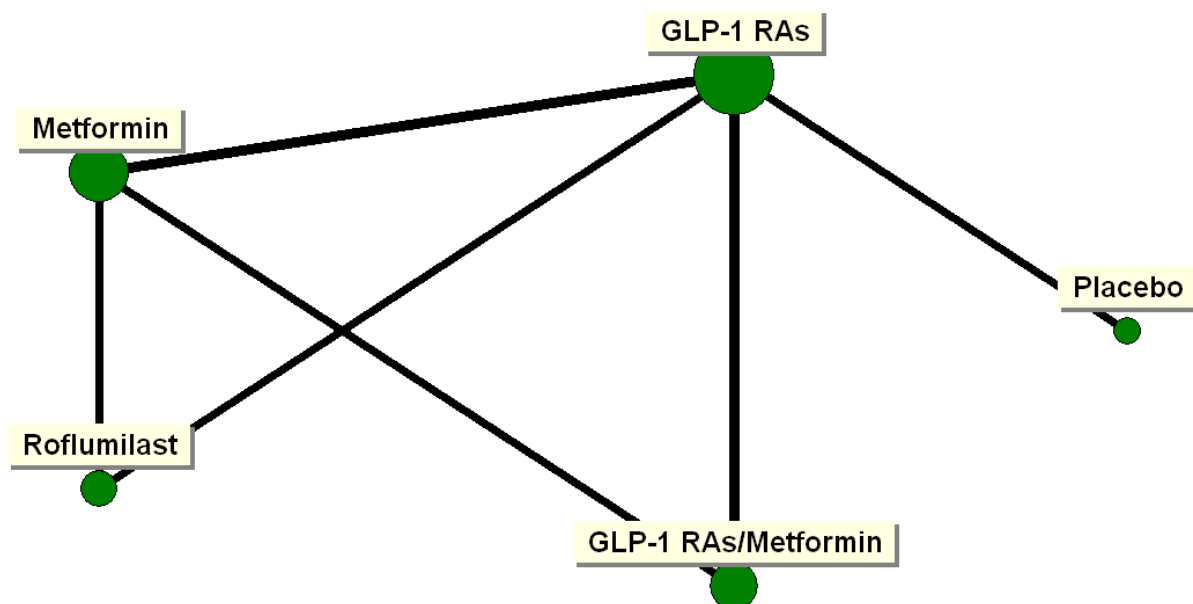
Electronic Supplementary Figure 10. Network plot for post-interventional testosterone.



Electronic Supplementary Figure 11. Network plot for changes in free testosterone.



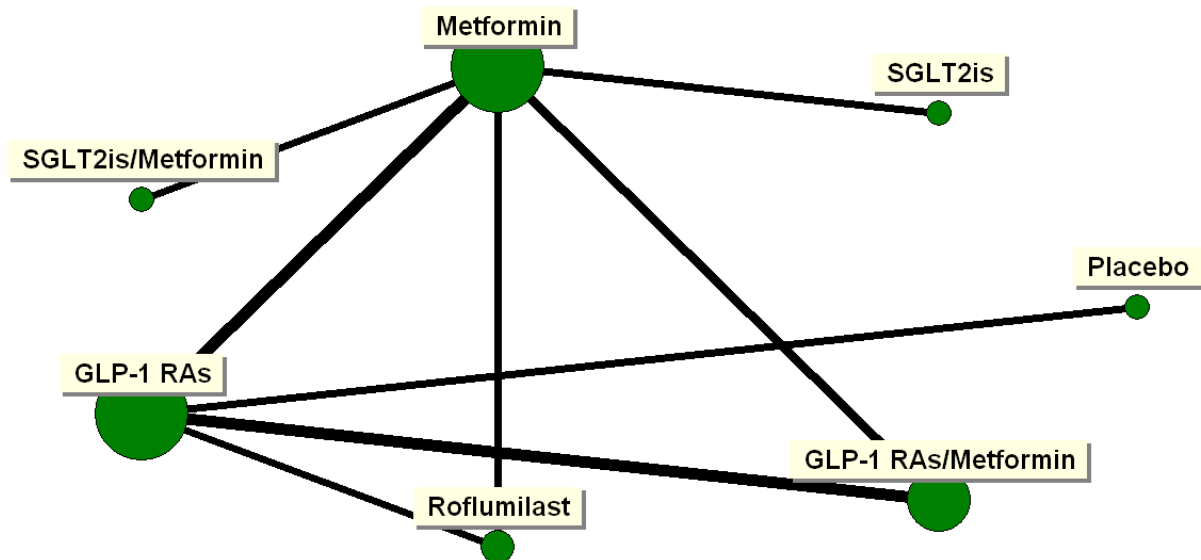
Electronic Supplementary Figure 12. Network plot for changes in post-interventional free testosterone.



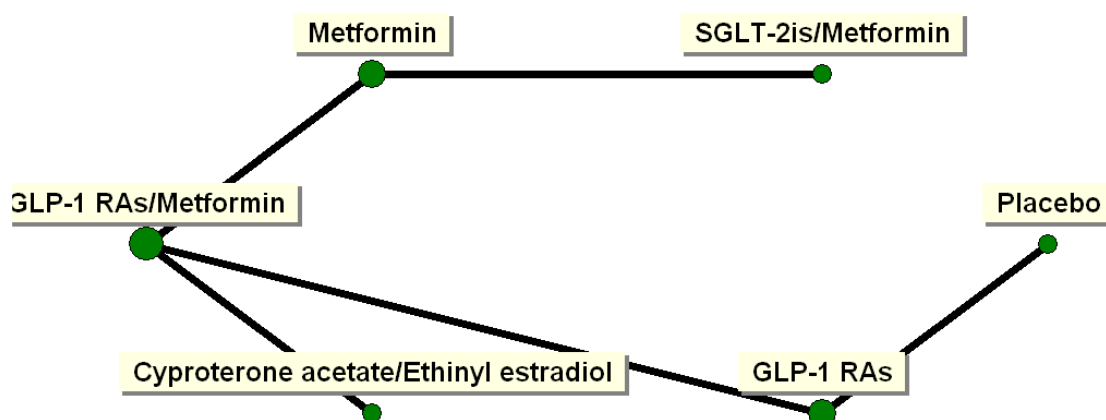
Electronic Supplementary Figure 13. Network plot for changes in androstenedione.



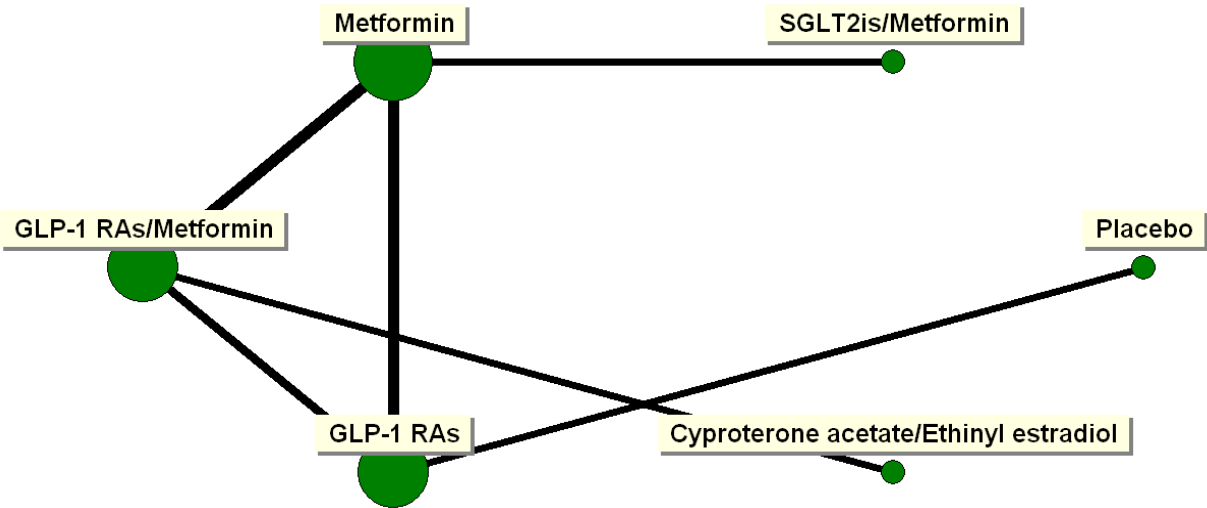
Electronic Supplementary Figure 14. Network plot for post-interventional androstenedione.



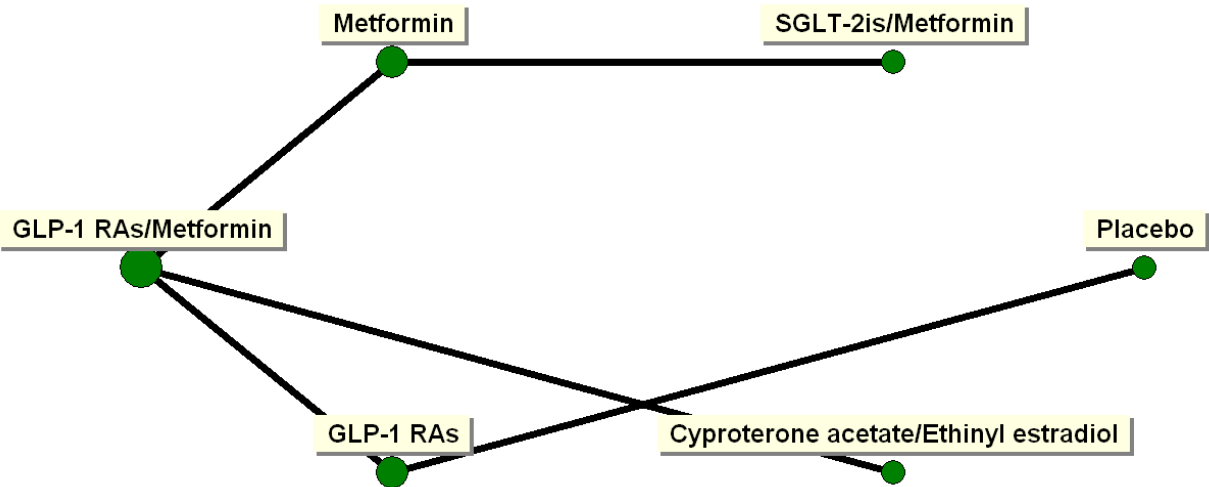
Electronic Supplementary Figure 15. Network plot for changes in LH.



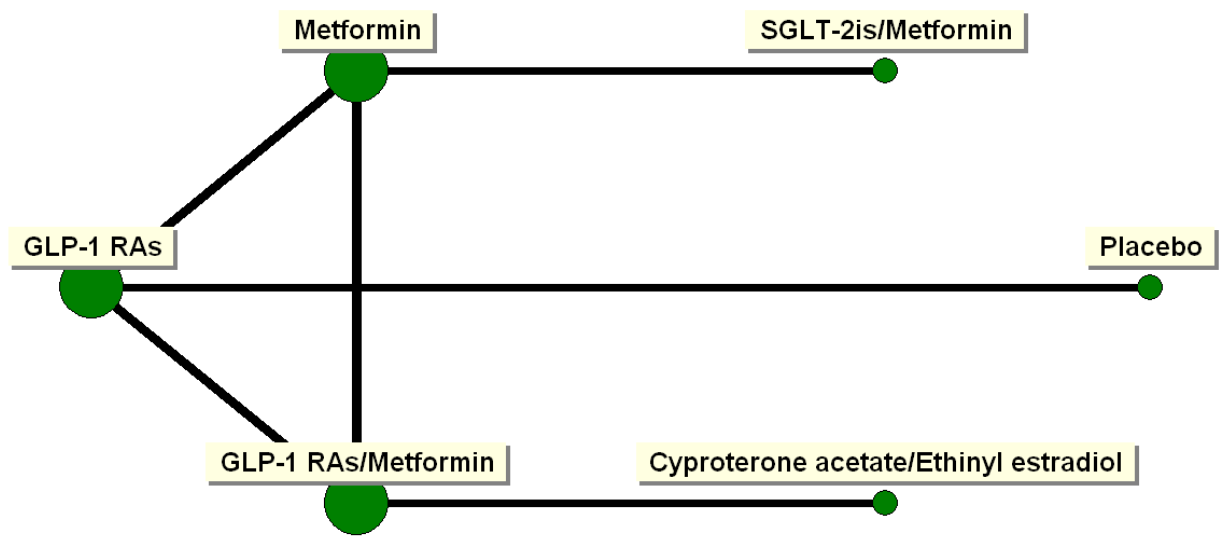
Electronic Supplementary Figure 16. Network plot for post-interventional LH.



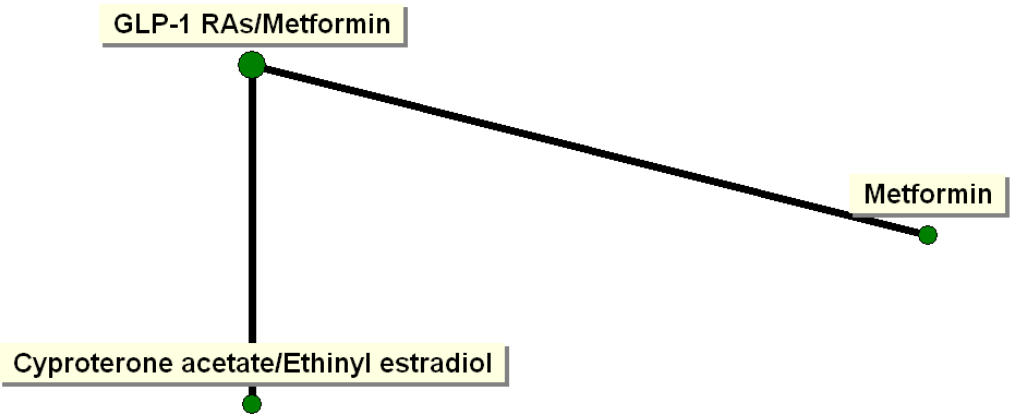
Electronic Supplementary Figure 17. Network plot for changes in FSH.



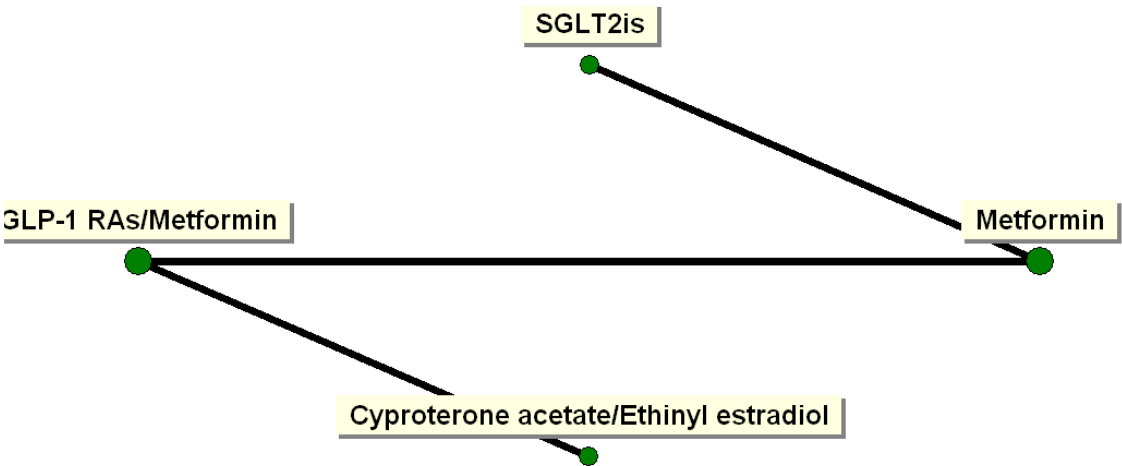
Electronic Supplementary Figure 18. Network plot for post-interventional FSH.



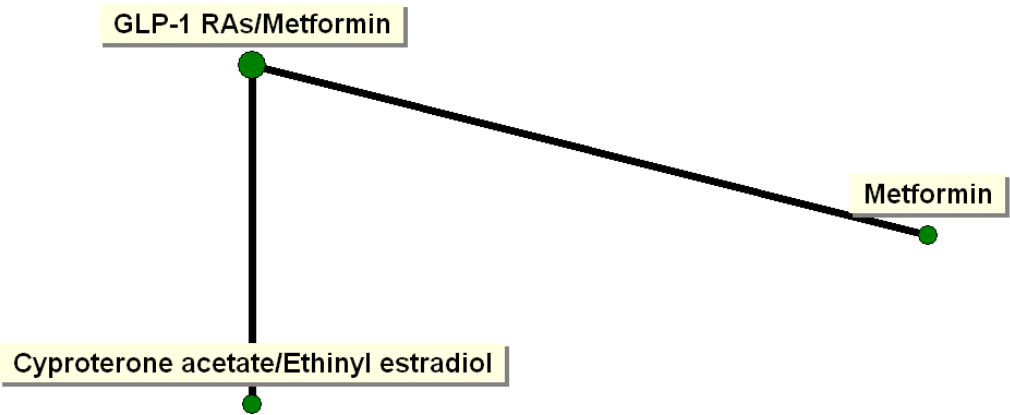
Electronic Supplementary Figure 19. Network plot for changes in estradiol



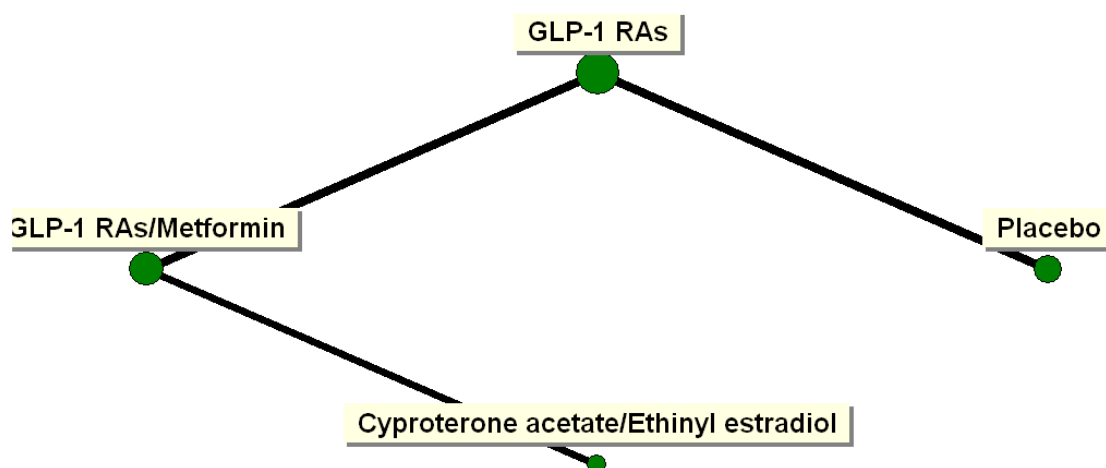
Electronic Supplementary Figure 20. Network plot for post-interventional estradiol.



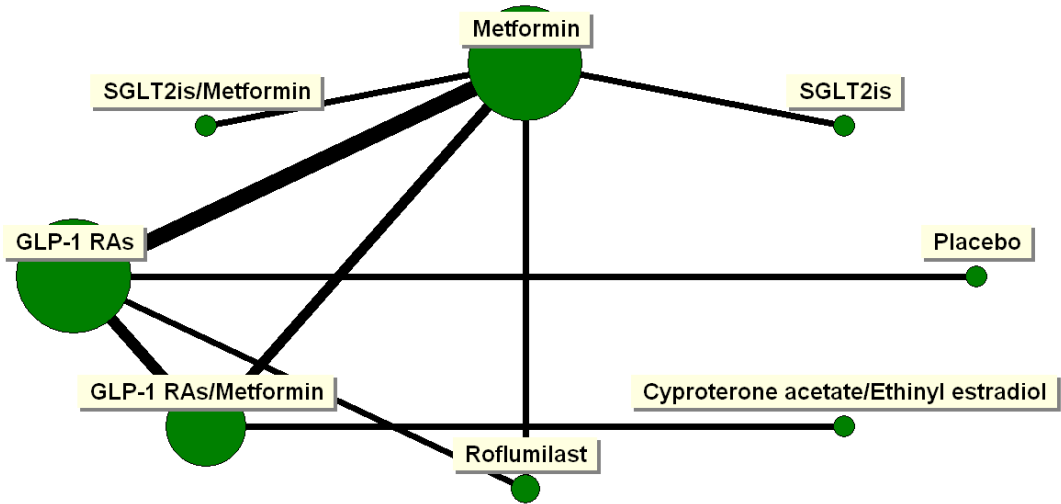
Electronic Supplementary Figure 21. Network plot for post-interventional progesterone.



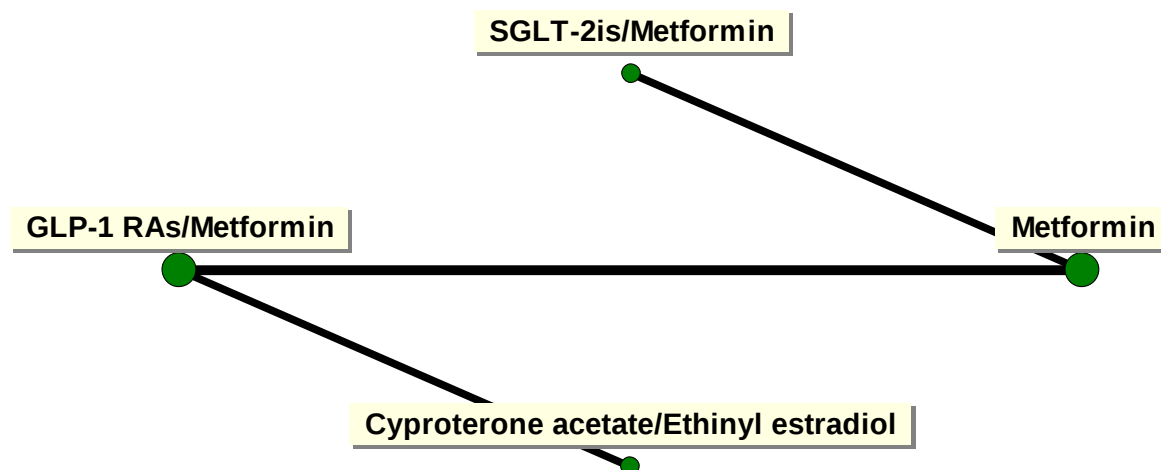
Electronic Supplementary Figure 22. Network plot for changes in SHBG.



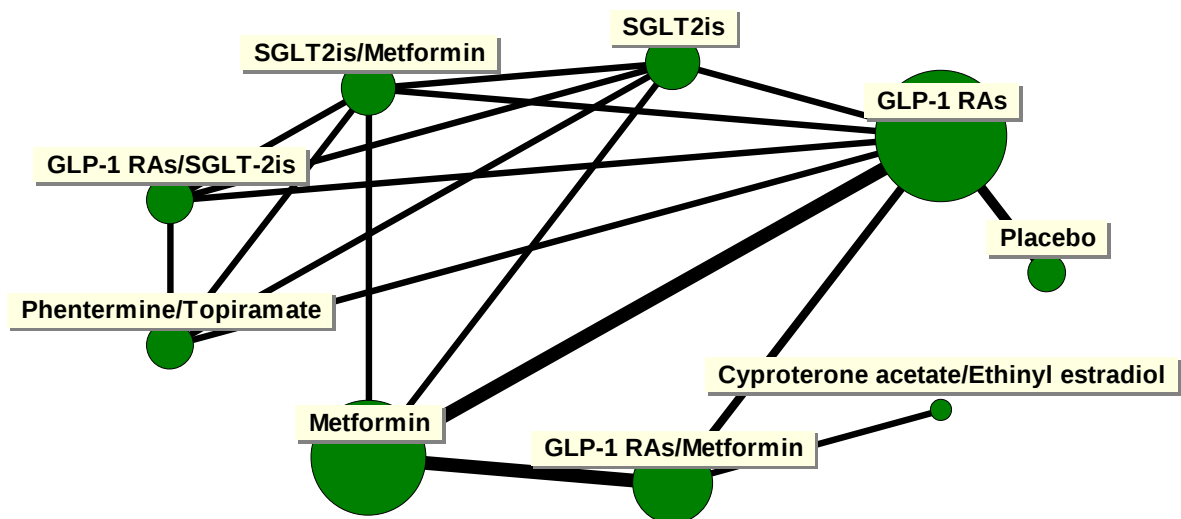
Electronic Supplementary Figure 23. Network plot for post-intervention SHBG.



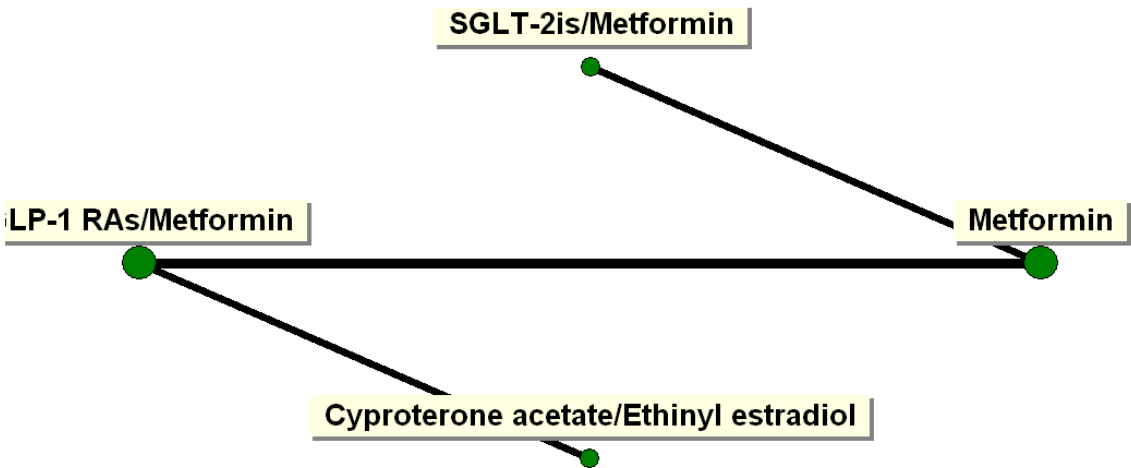
Electronic Supplementary Figure 24. Network plot for changes in total cholesterol.



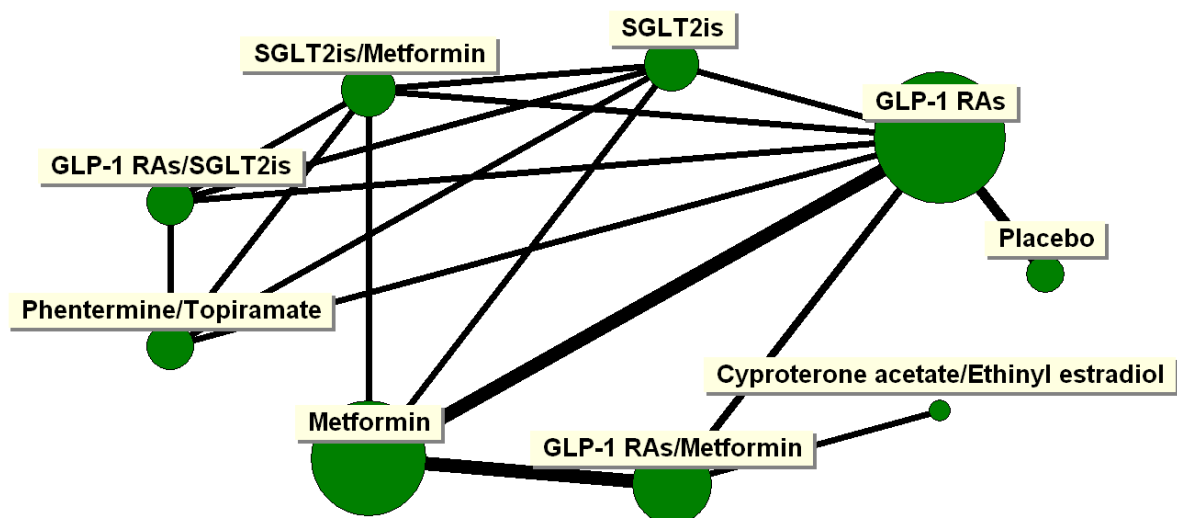
Electronic Supplementary Figure 25. Network plot for post-interventional total cholesterol.



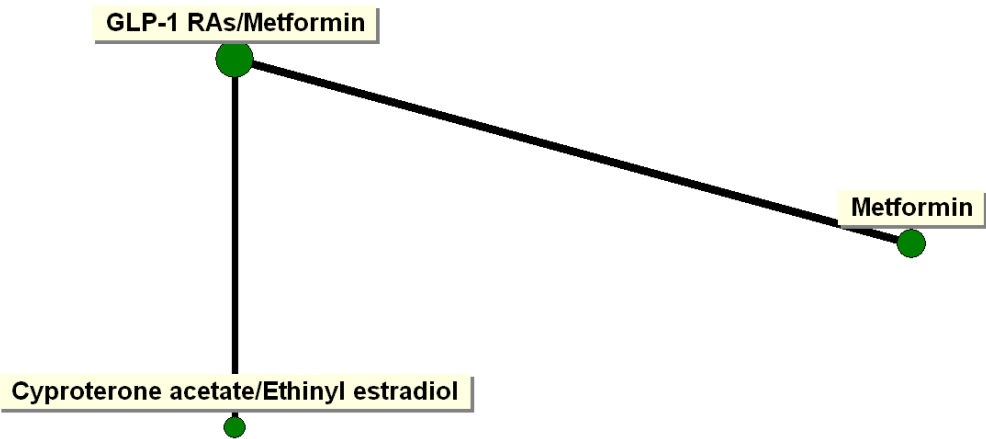
Electronic Supplementary Figure 26. Network plot for changes in LDL cholesterol.



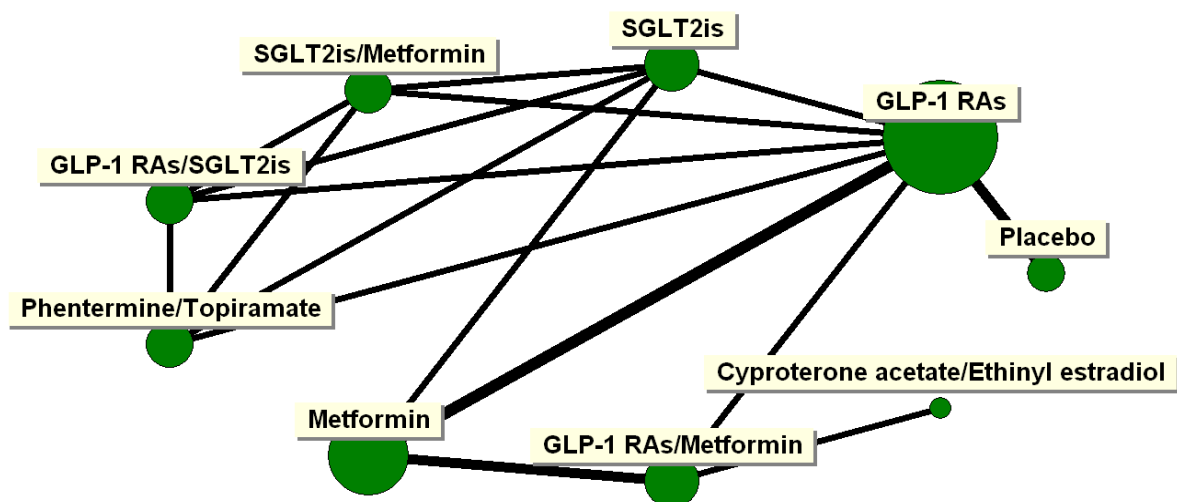
Electronic Supplementary Figure 27. Network plot for post-intervention LDL cholesterol.



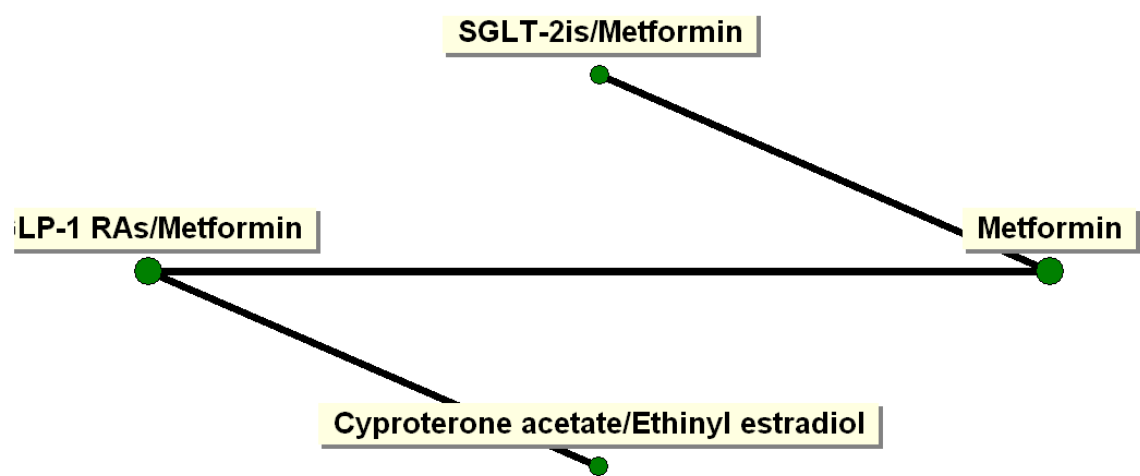
Electronic Supplementary Figure 28. Network plot for changes in HDL cholesterol.



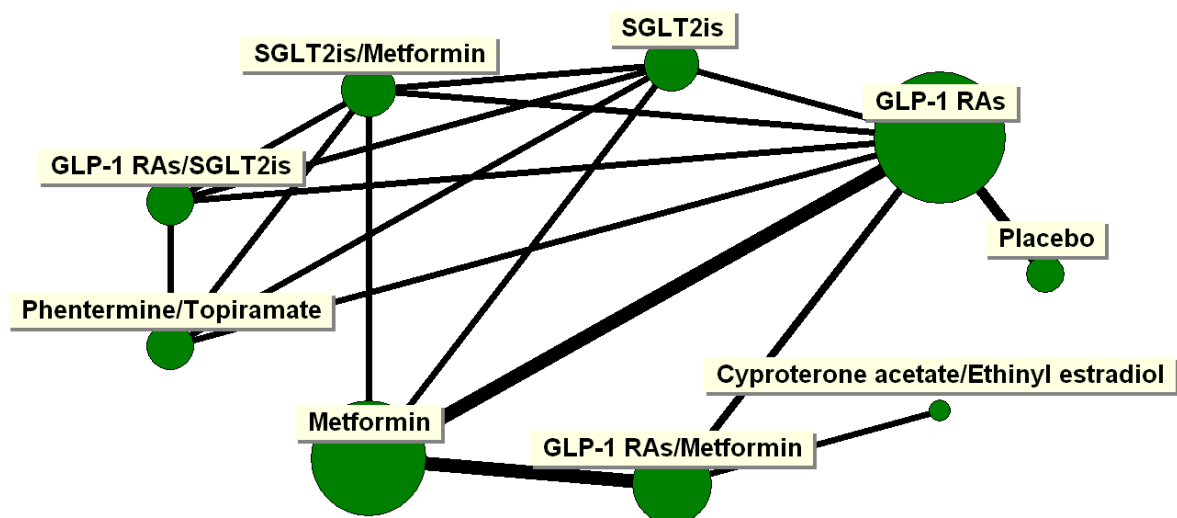
Electronic Supplementary Figure 29. Network plot for post-interventional HDL cholesterol.



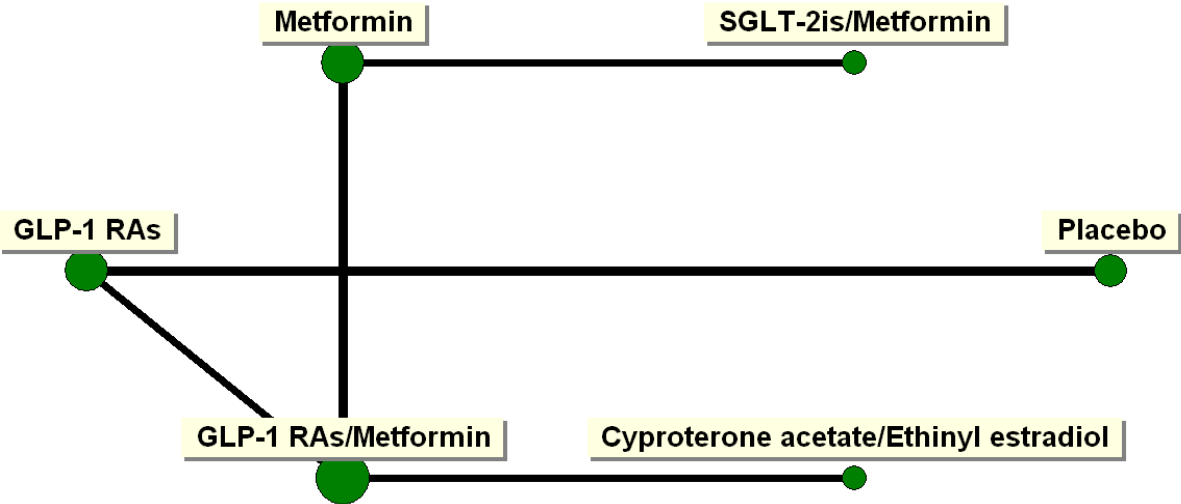
Electronic Supplementary Figure 30. Network plot for changes in triglycerides.



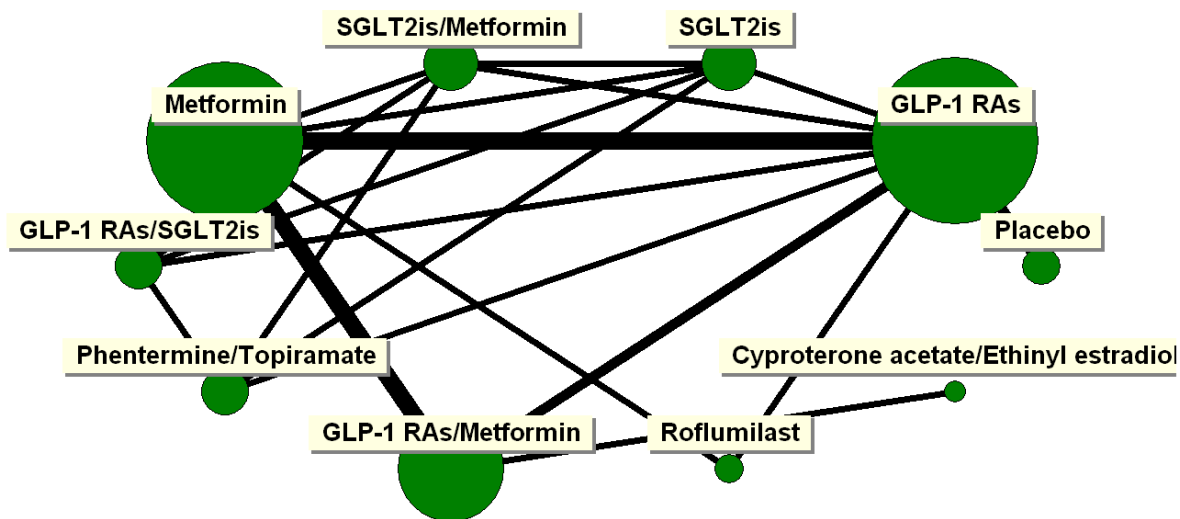
Electronic Supplementary Figure 31. Network plot for post-intervention triglycerides.



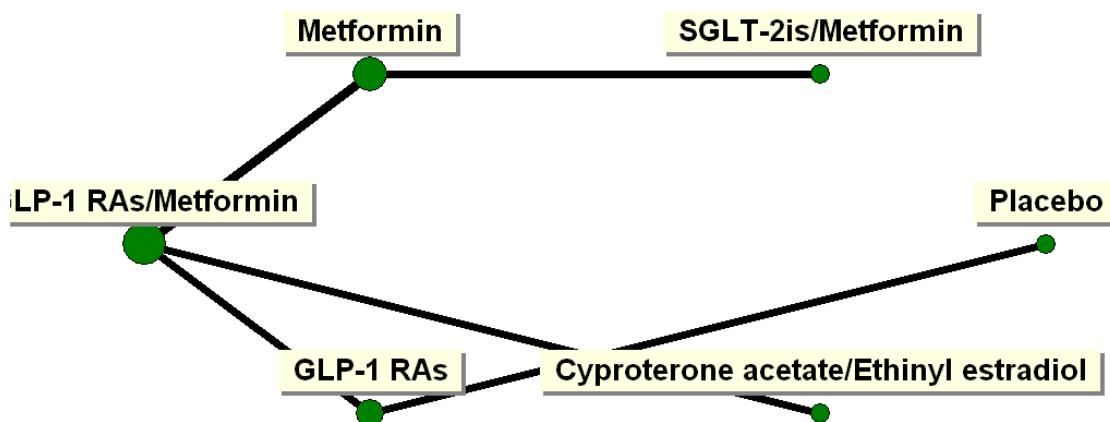
Electronic Supplementary Figure 32. Network plot for changes in HOMA-IR.



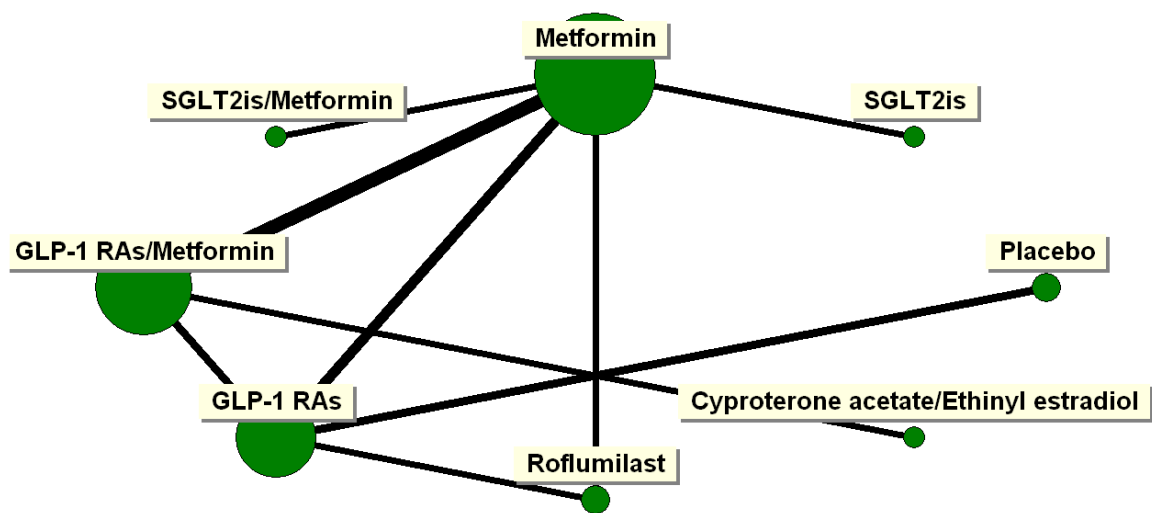
Electronic Supplementary Figure 33. Network plot for post-interventional HOMA-IR.



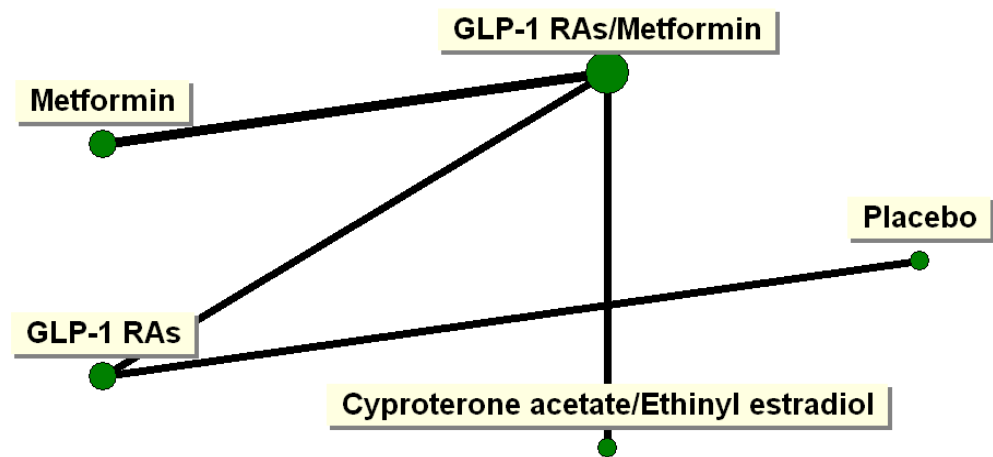
Electronic Supplementary Figure 34. Network plot for changes in fasting insulin.



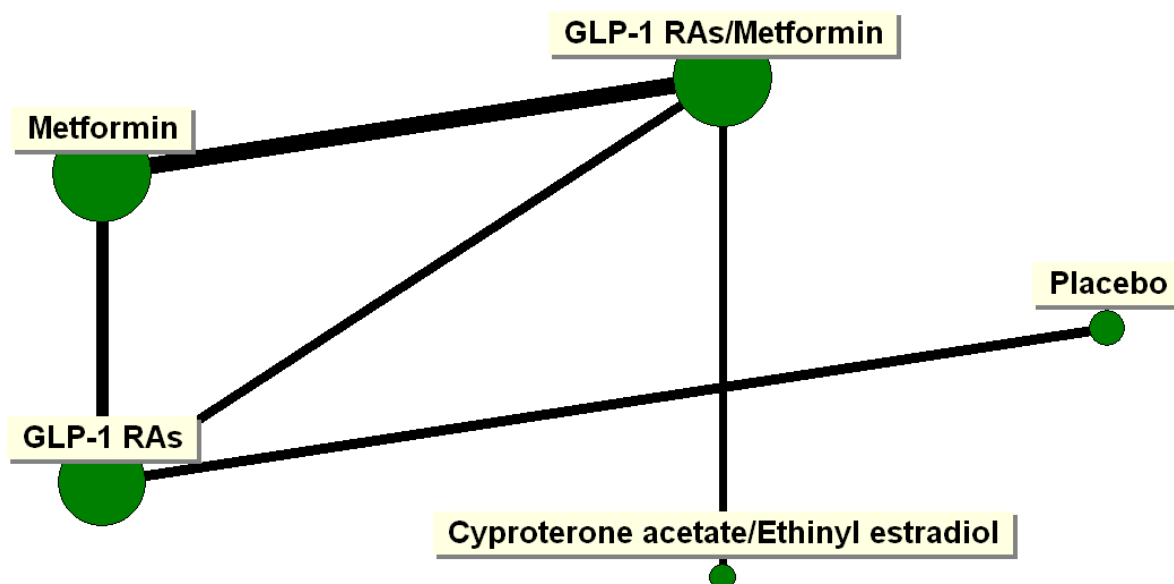
Electronic Supplementary Figure 35. Network plot for post-intervention fasting insulin.



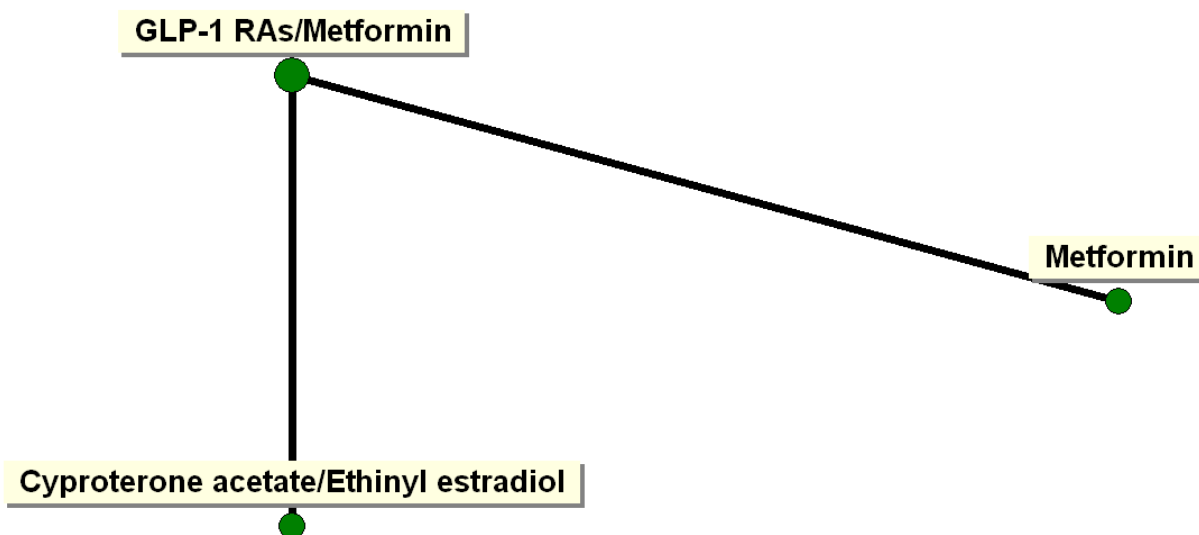
Electronic Supplementary Figure 36. Network plot for changes in two-hour insulin.



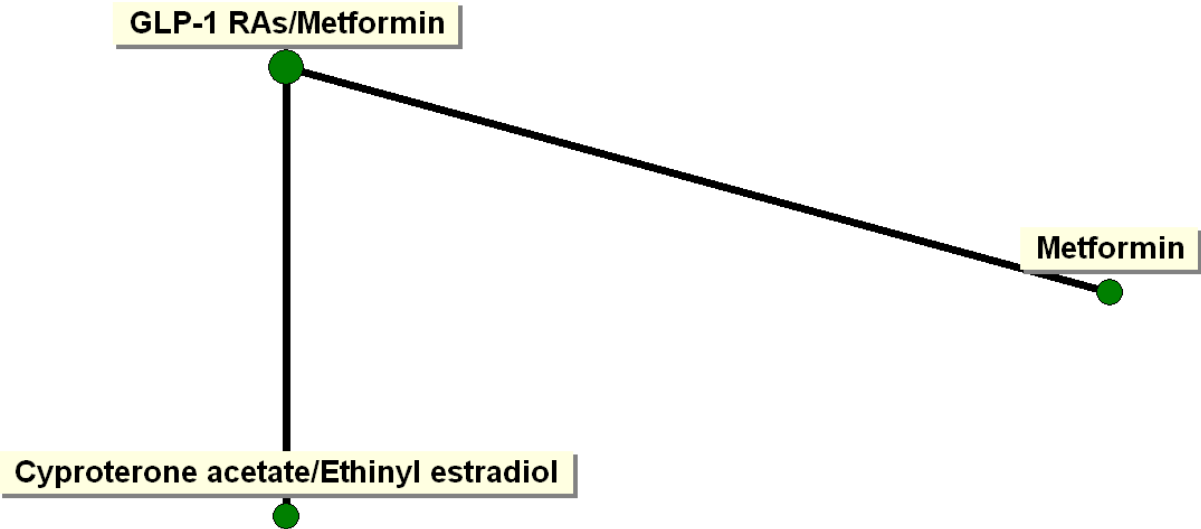
Electronic Supplementary Figure 37. Network plot for post-interventional two-hour insulin levels.



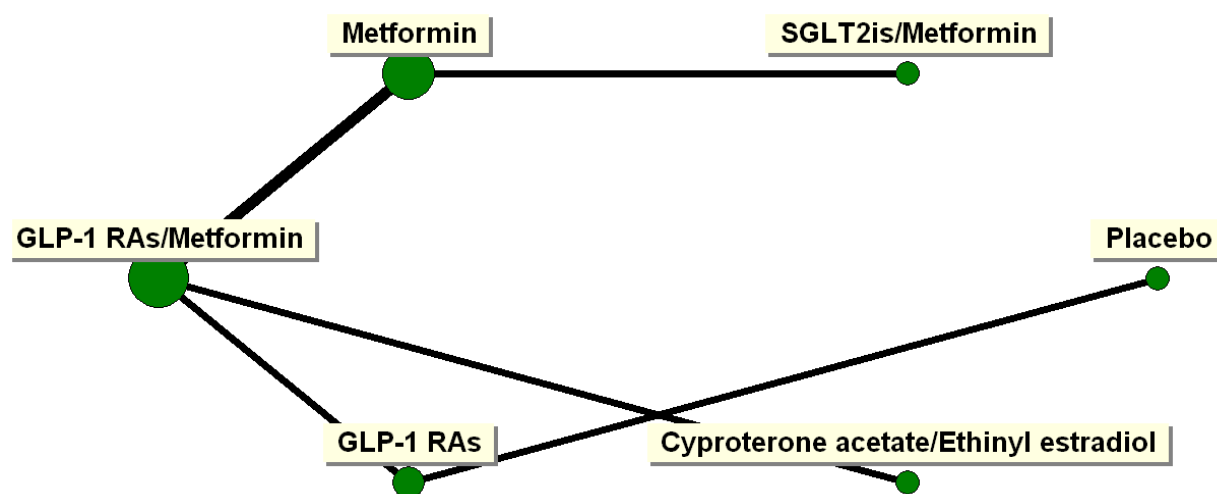
Electronic Supplementary Figure 38. Network plot for change-from-baseline HbA1c.



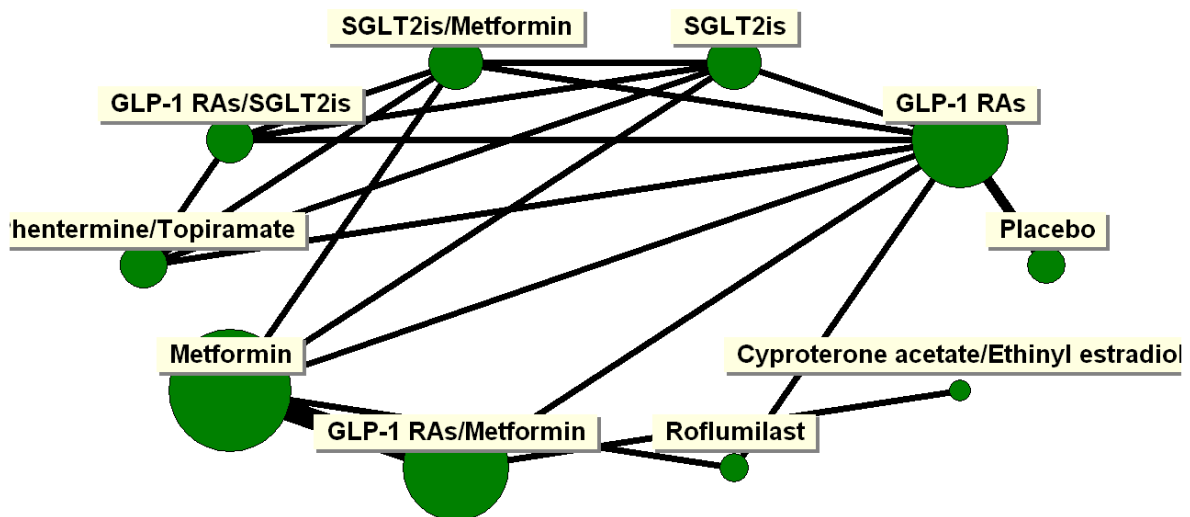
Electronic Supplementary Figure 39. Network plot for post-interventional HbA1c.



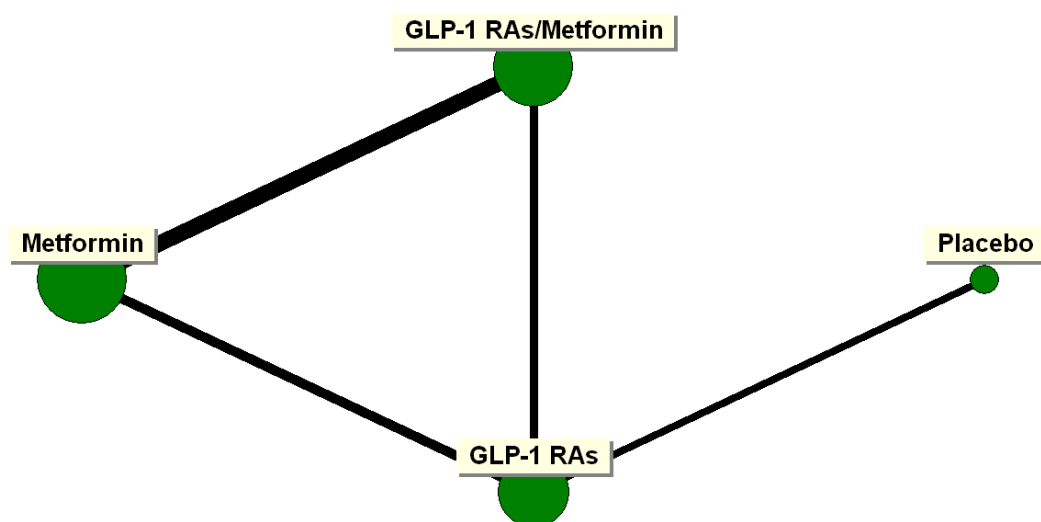
Electronic Supplementary Figure 40. Network plot for changes in fasting plasma glucose.



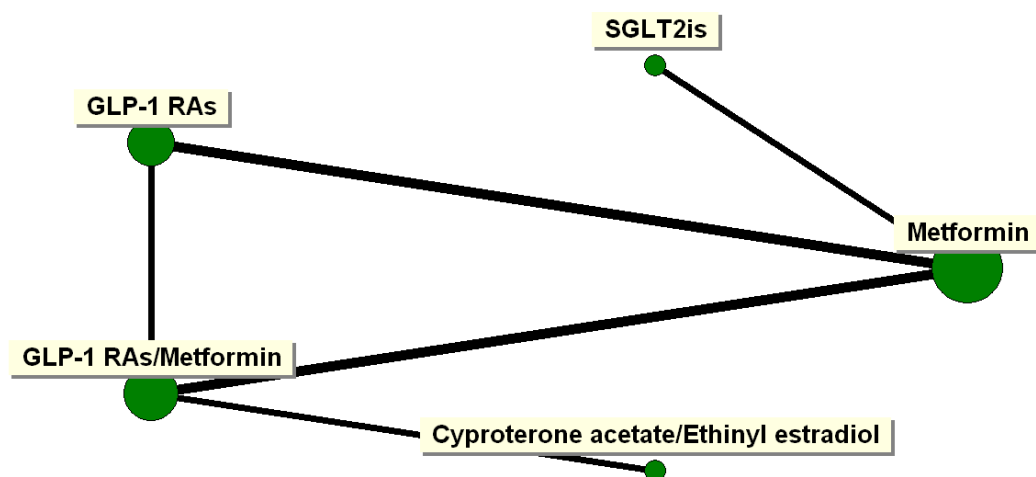
Electronic Supplementary Figure 41. Network plot for post-interventional fasting plasma glucose.



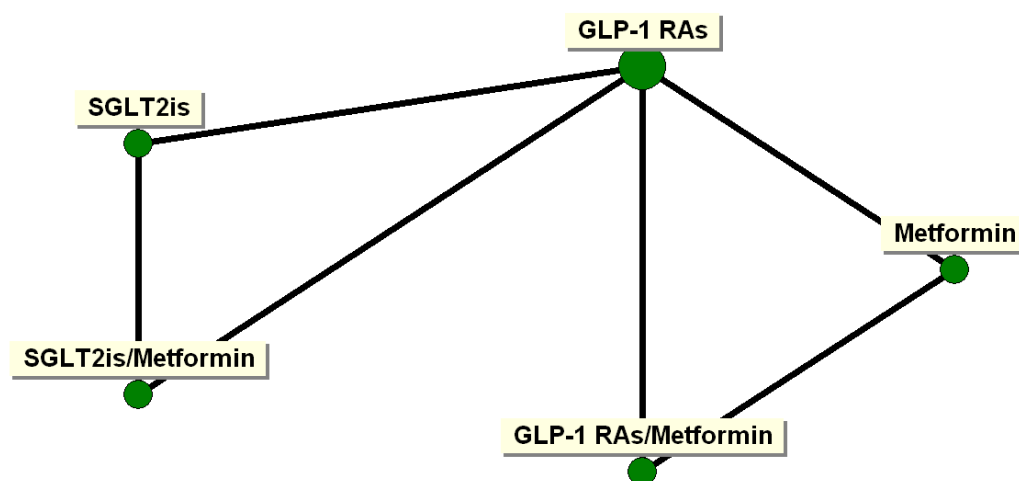
Electronic Supplementary Figure 42. Network plot for post-interventional postprandial plasma glucose.



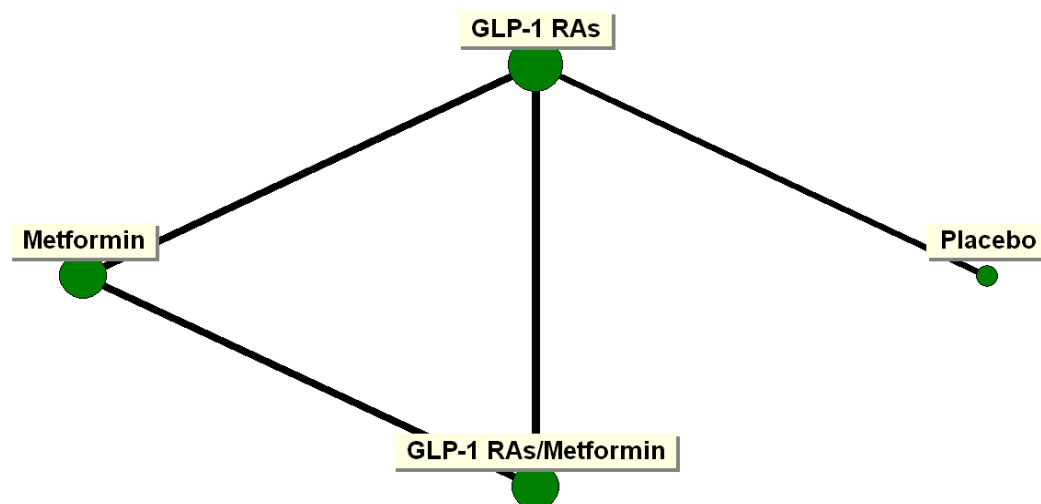
Electronic Supplementary Figure 43. Network plot for post-interventional hsCRP levels.



Electronic Supplementary Figure 44. Network plot for post-interventional ISSI.



Electronic Supplementary Figure 45. Network plot for post-interventional ISOGTT.



Electronic Supplementary Figure 46. Network plot for post-interventional adiponectin.

