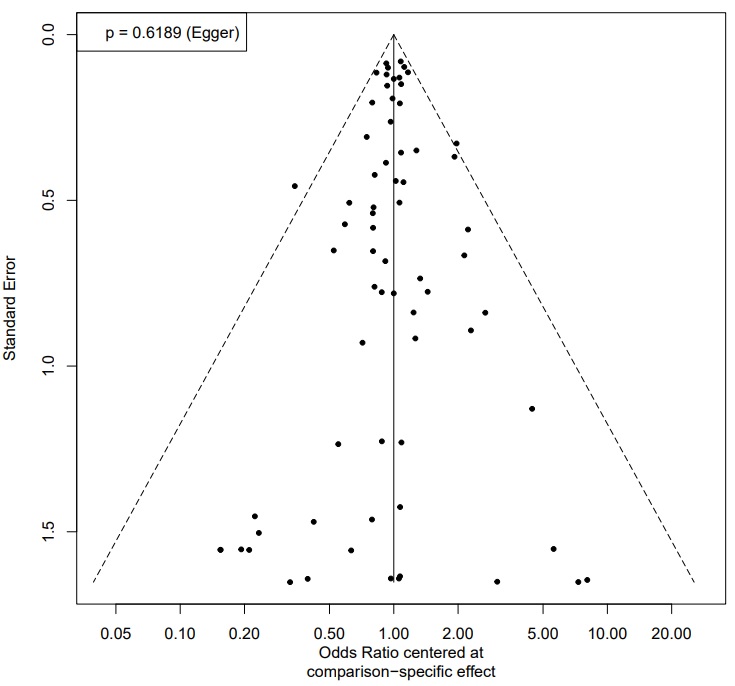
Supplemental Table 1. searching keywords

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| **(((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((((Teriparatide) OR (hPTH (1-34))) OR (Human Parathyroid Hormone (1-34))) OR (Parathar)) OR (Teriparatide Acetate)) OR (Forteo)) OR (Abaloparatide)) OR (tymlos)) OR (BA058)) OR (Denosumab)) OR (Xgeva)) OR (AMG 162)) OR (Prolia)) OR (Alandronate)) OR (4-Amino-1-Hydroxybutylidene 1,1-Biphosphonate)) OR (Aminohydroxybutane Bisphosphonate)) OR (MK-217)) OR (MK 217)) OR (MK217)) OR (Alendronate Monosodium Salt, Trihydrate)) OR (Alendronate Sodium)) OR (Fosamax)) OR (Amino-1-hydroxypropane-1,1-diphosphonate)) OR (Amino 1 hydroxypropane 1,1 diphosphonate)) OR (AHPrBP)) OR (Aminopropanehydroxydiphosphonate)) OR (Amidronate)) OR ((3-Amino-1-hydroxypropylidene)-1,1-biphosphonate)) OR (Aminohydroxypropylidene Diphosphonate)) OR (1-Hydroxy-3-aminopropane-1,1-diphosphonic acid)) OR (1 Hydroxy 3 aminopropane 1,1 diphosphonic acid)) OR (Pamidronic Acid)) OR (Pamidronate Monosodium)) OR (Pamidronate Calcium)) OR (Pamidronate Disodium)) OR (Aredia)) OR (Pamidronate)) OR (Zoledronic acid)) OR (2-(Imidazol-1-yl)-1-hydroxyethylidene-1,1-bisphosphonic acid)) OR (CGP 42446A)) OR (CGP-42446)) OR (CGP 42446)) OR (CGP42446)) OR (CGP-42'446)) OR (CGP42'446)) OR (CGP 42'446)) OR (Zometa)) OR (Zoledronic Acid Anhydrous)) OR (Zoledronate)) OR (Ibandronate)) OR (1-Hydroxy-3-(methylpentylamino)propylidenebisphosphonate)) OR ((1-Hydroxy-3-(methylpentylamino)propylidene)bisphosphonate)) OR (Ibandronate Sodium Anhydrous)) OR (Boniva)) OR (Bonviva)) OR (Ibandronate Sodium)) OR (Ibandronic Acid, Sodium Salt, Monohydrate)) OR (RPR 102289A)) OR (RPR-102289A)) OR (RPR102289A)) OR (Bondronat)) OR (BM 21.0955)) OR (BM 210955)) OR (BM-21.0955)) OR (BM21.0955)) OR (BM-210955)) OR (BM210955)) OR (1-Hydroxy-2-(3-pyridyl)ethylidene diphosphonate)) OR (Atelvia)) OR (Risedronate Sodium)) OR (2-(3-pyridinyl)-1-hydroxyethylidene-bisphosphonate)) OR (2-(3-pyridinyl)-1-hydroxyethylidenebisphosphonate)) OR (Risedronic Acid, Monosodium Salt)) OR (Actonel)) OR (Risedronate)) OR (Bisphosphonate Risedronate Sodium)) OR (Risedronate Sodium, Bisphosphonate)) OR (Sodium, Bisphosphonate Risedronate)) OR (AMG 785)) OR (AMG785)) OR (AMG-785)) OR (evenity)) OR (romosozumab-aqqg)) OR (CDP 7851)) OR (CDP7851)) OR (CDP-7851)) OR (Acid, Clodronic)) OR (Dichloromethane Diphosphonate)) OR (Diphosphonate, Dichloromethane)) OR (Dichloromethylenebisphosphonate)) OR (Dichloromethanediphosphonic Acid)) OR (Acid, Dichloromethanediphosphonic)) OR (Dichloromethylene Biphosphonate)) OR (Biphosphonate, Dichloromethylene)) OR (Dichloromethylene Diphosphonate)) OR (Diphosphonate, Dichloromethylene)) OR (Cl2MDP)) OR (Dichloromethanediphosphonate)) OR (Clodronate)) OR (Clodronate Disodium)) OR (Disodium, Clodronate)) OR (Clodronate Sodium)) OR (Sodium, Clodronate)) OR (Bonefos)) OR (SERMs)) OR (Estrogen Receptor Modulators, Selective)) OR (Selective Estrogen Receptor Modulator)) OR (SERM)) OR (Estrogen Receptor Modulator, Selective)) OR (Therapy, Hormone Replacement)) OR (Hormone Replacement Therapies)) OR (Replacement Therapies, Hormone)) OR (Therapies, Hormone Replacement)) OR (Replacement Therapy, Hormone)) OR (Estrogen Replacement Therapies)) OR (Replacement Therapies, Estrogen)) OR (Therapies, Estrogen Replacement)) OR (Therapy, Estrogen Replacement)) OR (Replacement Therapy, Estrogen)) OR (Estrogen Replacement)) OR (Estrogen Replacements)) OR (Replacements, Estrogen)) OR (Replacement, Estrogen)) OR (Postmenopausal Hormone Replacement Therapy)) OR (Hormone Replacement Therapy, Post-Menopausal)) OR (Hormone Replacement Therapy, Post Menopausal)) OR (Estrogen Progestin Replacement Therapy)) OR (Estrogen Progestin Combination Therapy))** |
| **(((((((((((((((((((((((((((((((((((((((((((randomized controlled trial) OR (controlled clinical trial)) OR (randomized)) OR (randomly)) OR (RCTs)) OR (Clinical Trials, Randomized)) OR (Trials, Randomized Clinical)) OR (Controlled Clinical Trials, Randomized)) OR (controlled trial, randomized)) OR (randomised controlled study)) OR (randomised controlled trial)) OR (randomized controlled study)) OR (trial, randomized controlled)))))))** |
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Paroxysmal)) OR (Fibrillation, Paroxysmal Atrial)) OR (Fibrillations, Paroxysmal Atrial)) OR (Paroxysmal Atrial Fibrillations)) OR (Heart Failure)) OR (Cardiac Failure)) OR (Heart Decompensation)) OR (Decompensation, Heart)) OR (Heart Failure, Right-Sided)) OR (Heart Failure, Right Sided)) OR (Right-Sided Heart Failure)) OR (Right Sided Heart Failure)) OR (Myocardial Failure)) OR (Congestive Heart Failure)) OR (Heart Failure, Congestive)) OR (Heart Failure, Left-Sided)) OR (Heart Failure, Left Sided)) OR (Left-Sided Heart Failure)) OR (Left Sided Heart Failure)) OR (Heart Failure, Diastolic)) OR (Diastolic Heart Failures)) OR (Heart Failures, Diastolic)) OR (Diastolic Heart Failure)) OR (Heart Failure, Systolic)) OR (Heart Failures, Systolic)) OR (Systolic Heart Failures)) OR (Systolic Heart Failure)) OR (Atherosclerosis)) OR (Atheroscleroses)) OR (Atherogenesis)) OR (Coronary Artery Disease)) OR (Artery Disease, Coronary)) OR (Artery Diseases, Coronary)) OR (Coronary Artery Diseases)) OR (Disease, Coronary Artery)) OR (Diseases, Coronary Artery)) OR (Coronary Arteriosclerosis)) OR (Arterioscleroses, Coronary)) OR (Coronary Arterioscleroses)) OR (Atherosclerosis, Coronary)) OR (Atheroscleroses, Coronary)) OR (Coronary Atheroscleroses)) OR (Coronary Atherosclerosis)) OR (Arteriosclerosis, Coronary)) OR (Artery Disease, Carotid)) OR (Artery Diseases, Carotid)) OR (Carotid Artery Disease)) OR (Carotid Artery Disorders)) OR (Artery Disorder, Carotid)) OR (Artery Disorders, Carotid)) OR (Carotid Artery Disorder)) OR (Disorders, Carotid Artery)) OR (Arterial Diseases, Carotid)) OR (Arterial Disease, Carotid)) OR (Carotid Arterial Disease)) OR (Carotid Arterial Diseases)) OR (Carotid Atherosclerosis)) OR (Carotid Atheroscleroses)) OR (Carotid Atherosclerotic Disease)) OR (Atherosclerotic Diseases, Carotid)) OR (Carotid Atherosclerotic Diseases)) OR (Atherosclerotic Disease, Carotid)) OR (Internal Carotid Artery Diseases)) OR (Arterial Diseases, Internal Carotid)) OR 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Diseases)) OR (Disease, Valvular Heart)) OR (Diseases, Valvular Heart)) OR (Heart Disease, Valvular)) OR (Heart Diseases, Valvular)) OR (Valvular Heart Disease)) OR (Mitral Valve Insufficiency)) OR (Insufficiency, Mitral Valve)) OR (Valve Insufficiency, Mitral)) OR (Mitral Valve Regurgitation)) OR (Regurgitation, Mitral Valve)) OR (Valve Regurgitation, Mitral)) OR (Mitral Regurgitation)) OR (Regurgitation, Mitral)) OR (Mitral Valve Incompetence)) OR (Incompetence, Mitral Valve)) OR (Valve Incompetence, Mitral)) OR (Mitral Incompetence)) OR (Incompetence, Mitral)) OR (Mitral Insufficiency)) OR (Insufficiency, Mitral)) OR (Tricuspid Valve Insufficiency)) OR (Insufficiency, Tricuspid Valve)) OR (Valve Insufficiency, Tricuspid)) OR (Tricuspid Valve Regurgitation)) OR (Regurgitation, Tricuspid Valve)) OR (Valve Regurgitation, Tricuspid)) OR (Tricuspid Valve Incompetence)) OR (Incompetence, Tricuspid Valve)) OR (Valve Incompetence, Tricuspid)) OR (Tricuspid Incompetence)) OR (Incompetence, Tricuspid)) OR (Tricuspid Regurgitation)) OR (Regurgitation, Tricuspid)) OR (Pulmonary Embolism)) OR (Pulmonary Embolisms)) OR (Embolism, Pulmonary)) OR (Embolisms, Pulmonary)) OR (Pulmonary Thromboembolisms)) OR (Pulmonary Thromboembolism)) OR (Thromboembolism, Pulmonary)) OR (Thromboembolisms, Pulmonary)) OR (Venous Thrombosis)) OR (Phlebothrombosis)) OR (Phlebothromboses)) OR (Thrombosis, Venous)) OR (Thromboses, Venous)) OR (Venous Thromboses)) OR (Deep Vein Thrombosis)) OR (Deep Vein Thromboses)) OR (Thromboses, Deep Vein)) OR (Vein Thromboses, Deep)) OR (Vein Thrombosis, Deep)) OR (Deep-Venous Thrombosis)) OR (Deep-Venous Thromboses)) OR (Thromboses, Deep-Venous)) OR (Thrombosis, Deep-Venous)) OR (Deep-Vein Thrombosis)) OR (Deep-Vein Thromboses)) OR (Thromboses, Deep-Vein)) OR (Thrombosis, Deep-Vein)) OR (Thrombosis, Deep Vein)) OR (Deep Venous Thrombosis)) OR (Deep Venous Thromboses)) OR (Thromboses, Deep Venous)) OR (Thrombosis, Deep Venous)) OR (Venous Thromboses, Deep)) OR (Venous Thrombosis, Deep)))** |

Supplemental Table 2. Characteristics of the studies included in the NMA

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | NCT Number | Number of participants | Age (mean) | Gender | Underlying disease | Trial duration (weeks) | Intervention | CVD event |
| E Michael Lewiecki, 2018 (BRIDGE) | NCT02186171 | 163 | 72.1 | M | osteoporosis | 52 | Romosozumab | 14 |
|  |  | 82 |  |  |  |  | Placebo | 4 |
| Ki-Hyun Baek, 2021 | NCT02791516 | 34 | 67.5 | F | postmenopausal osteoporosis | 26 | Romosozumab | 1 |
|  |  | 33 |  |  |  |  | Placebo | 0 |
| Felicia Cosman, 2016 (FRAME) | NCT01575834 | 3589 | 70.9 | F | postmenopausal osteoporosis | 52 | Romosozumab | 72 |
|  |  | 3591 |  |  |  |  | Placebo | 64 |
|  | NCT02016716 | 241 | 67.7 | F | postmenopausal osteoporosis | 26 | Romosozumab | 3 |
|  |  | 53 |  |  |  |  | Placebo | 0 |
| Kenneth G Saag, 2017 (ARCH) | NCT01631214 | 2047 | 74.3 | F | postmenopausal osteoporosis | 52 | Alendronate | 60 |
|  |  | 2046 |  |  |  |  | Romosozumab | 69 |
| Bente L Langdahl, 2017 (STRUCTURE) | NCT01796301 | 218 | 71.5 | F | postmenopausal osteoporosis | 52 | Teriparatide | 2 |
|  |  | 218 |  |  |  |  | Romosozumab | 11 |
| Paul D Miller, 2016 (ACTIVE) | NCT01343004 | 1642 | 68.8 | F | postmenopausal osteoporosis | 78 | Abaloparatide/Teriparatide | 26 |
|  |  | 821 |  |  |  |  | Placebo | 15 |
| Felicia Cosman, 2017 | NCT01657162 | 558 | 68.5 | F | postmenopausal osteoporosis | 78 | Abaloparatide | 14 |
|  |  | 581 |  |  |  |  | Placebo | 17 |
|  | NCT00439244 | 137 | 65 | F | postmenopausal osteoporosis | 52 | Zoledronic acid | 4 |
|  |  | 138 |  |  |  |  | Placebo | 3 |
| David W Dempster, 2018 | NCT01753856 | 33 | 63.5 | F | postmenopausal osteoporosis | 26 | Teriparatide | 0 |
|  |  | 36 |  |  |  |  | Denosumab | 1 |
| Claus-C Glüer, 2013 | NCT00503399 | 45 | 56.3 | M | Glucocorticoid-Induced Osteoporosis | 78 | Teriparatide | 1 |
|  |  | 47 |  |  |  |  | Risedronate | 6 |
| Kenneth G Saag, 2007 | NCT00051558 | 214 | 56.7 | M/F (80.6%) | Glucocorticoid-Induced Osteoporosis | 78 | Teriparatide | 12 |
|  |  | 214 |  |  |  |  | Alendronate | 13 |
| David L Kendler, 2018 (VERO) | NCT01709110 | 683 | 72.1 | F | postmenopausal osteoporosis | 108 | Teriparatide | 34 |
|  |  | 683 |  |  |  |  | Risedronate | 30 |
|  | NCT00887354 | 111 | 76.8 | M/F (77.2%) | osteoporosis | 78 | Teriparatide | 2 |
|  |  | 113 |  |  |  |  | Risedronate | 8 |
|  | NCT00343252 | 361 | 71 | F | postmenopausal osteoporosis | 78 | Teriparatide | 6 |
|  |  | 351 |  |  |  |  | Risedronate | 20 |
| Steven R Cummings, 2009 (FREEDOM) | NCT00089791 | 3902 | 72.3 | F | postmenopausal osteoporosis | 156 | Denosumab | 351 |
|  |  | 3906 |  |  |  |  | Placebo | 129 |
| P D Miller, 2016 | NCT01732770 | 322 | 69 | F | postmenopausal osteoporosis | 52 | Zoledronic acid | 6 |
|  |  | 321 |  |  |  |  | Denosumab | 6 |
| Jung Min Koh, 2016 | NCT01457950 | 69 | 66.5 | F | postmenopausal osteoporosis | 52 | Denosumab | 1 |
|  |  | 66 |  |  |  |  | Placebo | 0 |
| Toshitaka Nakamura, 2014 (DIRECT) | NCT00680953 | 500 | 69.5 | M/F (95%) | osteoporosis | 104 | Denosumab | 11 |
|  |  | 511 |  |  |  |  | Placebo | 13 |
| C Roux, 2014 | NCT00919711 | 435 | 67.7 | F | postmenopausal osteoporosis | 52 | Risedronate | 7 |
|  |  | 435 |  |  |  |  | Denosumab | 8 |
|  | NCT02014467 | 365 | 69 | F | postmenopausal osteoporosis | 52 | Denosumab | 4 |
|  |  | 119 |  |  |  |  | Placebo | 6 |
| N Freemantle, 2012 | NCT00518531 | 124 | 65.2 | F | postmenopausal osteoporosis | 52 | Alendronate | 2 |
|  |  | 126 |  |  |  |  | Denosumab | 0 |
| Chris Recknor, 2013 | NCT00936897 | 417 | 66.7 | F | postmenopausal osteoporosis | 52 | Denosumab | 12 |
|  |  | 416 |  |  |  |  | Ibandronate | 5 |
| David L Kendler, 2010 | NCT00377819 | 251 | 67.6 | F | postmenopausal osteoporosis | 52 | Alendronate | 3 |
|  |  | 253 |  |  |  |  | Denosumab | 5 |
| S. Adami, 2008 |  | 157 | 66.9 | F | postmenopausal osteoporosis | 52 | Raloxifene | 2 |
|  |  | 172 |  |  |  |  | Placebo | 0 |
| Valery T. Miller, 1995 (PEPI) |  | 701 | 56.1 | F | postmenopausal | 156 | Estrogen+Progesterone | 15 |
|  |  | 174 |  |  |  |  | Placebo | 0 |
| Steven Boonen, 2006 |  | 541 | 69.2 | F | postmenopausal osteoporosis | 76 | Teriparatide | 9 |
|  |  | 544 |  |  |  |  | Placebo | 12 |
| Claus Christiansen, 2010 | NCT00205777 | 5607 | 66.4 | F | postmenopausal osteoporosis | 156 | Bazedoxifene/Raloxifene | 318 |
|  |  | 1885 |  |  |  |  | Placebo | 92 |
| Roberto Civitelli, 2002 |  | 68 | 59 | F | postmenopausal | 156 | Estrogen+Progesterone | 2 |
|  |  | 67 |  |  |  |  | Placebo | 2 |
| Steven R Cummings, 2008 (LIFT) | NCT00519857 | 2267 | 68.3 | F | postmenopausal osteoporosis | 260 | Tibolone | 60 |
|  |  | 2267 |  |  |  |  | Placebo | 42 |
| Steven R Cummings, 2011 (GENERATIONS) | NCT00088010 | 4676 | 67.5 | F | postmenopausal osteoporosis | 156 | Arzoxifene | 179 |
|  |  | 4678 |  |  |  |  | Placebo | 140 |
| Steven R Cummings, 2010 (PEARL) | NCT00141323 | 5704 | 67.5 | F | postmenopausal osteoporosis | 260 | Lasofoxifene | 326 |
|  |  | 2852 |  |  |  |  | Placebo | 170 |
| Joy N Tsai, 2013 (DATA) | NCT00926380 | 31 | 66 | F | postmenopausal osteoporosis | 52 | Teriparatide | 1 |
|  |  | 33 |  |  |  |  | Denosumab | 0 |
| Toshitaka Nakamura, 2012 (TOWER) |  | 290 | 75.3 | M/F (95%) | osteoporosis | 72 | Teriparatide | 2 |
|  |  | 288 |  |  |  |  | Placebo | 3 |
| Eric Orwoll, 2012 | NCT00980174 | 121 | 65 | M | osteoporosis | 52 | Denosumab | 5 |
|  |  | 121 |  |  |  |  | Placebo | 4 |
| Jacques P Brown, 2009 | NCT00330460 | 594 | 64.4 | F | postmenopausal osteoporosis | 52 | Denosumab | 7 |
|  |  | 595 |  |  |  |  | Alendronate | 9 |
| Kenneth G Saag, 2018 | NCT01575873 | 398 | 63.1 | M/F (70%) | Glucocorticoid-Induced Osteoporosis | 104 | Denosumab | 22 |
|  |  | 397 |  |  |  |  | Risedronate | 14 |
| D L Kendler, 2011 |  | 126 | 65.2 | F | postmenopausal osteoporosis | 52 | Denosumab | 0 |
|  |  | 124 |  |  |  |  | Alendronate | 2 |
| Michael R McClung, 2006 | NCT00043186 | 314 | 62.5 | F | postmenopausal osteoporosis | 52 | Denosumab | 19 |
|  |  | 46 |  |  |  |  | Placebo | 2 |
| Mohit Bhandari, 2016 | NCT01473589 | 78 | 70 | M/F (74%) | postmenopause with history of fracture | 52 | Teriparatide | 3 |
|  |  | 81 |  |  |  |  | Placebo | 0 |
| Akimitsu Miyauchi, 2010 | NCT00433160 | 137 | 69.6 | M/F (93.1%) | postmenopausal osteoporosis | 52 | Teriparatide | 0 |
|  |  | 70 |  |  |  |  | Placebo | 0 |
| Dennis M Black, 2007 (HORIZON) | NCT00145327 | 3875 | 73 | F | postmenopausal osteoporosis | 156 | Zoledronic acid | 219 |
|  |  | 3861 |  |  |  |  | Placebo | 206 |
| Steven Boonen, 2012 | NCT00439647 | 588 | 65.8 | M | primary or hypogonadism-associated osteoporosis | 104 | Zoledronic acid | 57 |
|  |  | 611 |  |  |  |  | Placebo | 48 |
| E Orwoll, 2000 |  | 146 | 63 | M | osteoporosis | 104 | Alendronate | 23 |
|  |  | 95 |  |  |  |  | Placebo | 16 |
| Paul D Miller, 2008 |  | 1273 | 57.5 | F | postmenopausal osteoporosis | 104 | Bazedoxifene/Raloxifene | 10 |
|  |  | 310 |  |  |  |  | Placebo | 2 |
| Stuart L Silverman, 2008 |  | 5607 | 66.4 | F | postmenopausal osteoporosis | 156 | Bazedoxifene/Raloxifene | 116 |
|  |  | 1885 |  |  |  |  | Placebo | 36 |
| Ian R Reid, 2018 |  | 1000 | 71 | F | postmenopausal osteoporosis | 312 | Zoledronic acid | 118 |
|  |  | 1000 |  |  |  |  | Placebo | 128 |
| Kenneth W Lyles, 2007 | NCT00046254 | 1065 | 74.5 | M/F (76%) | repair of a hip fracture | 99 | Zoledronic acid | 88 |
|  |  | 1062 |  |  |  |  | Placebo | 82 |
| Susan L Greenspan, 2015 (ZEST) | NCT00558012 | 89 | 85.4 | F | postmenopausal osteoporosis | 104 | Zoledronic acid | 20 |
|  |  | 92 |  |  |  |  | Placebo | 17 |
| H N Hodis, 2001 (EPAT) | NCT00115024 | 111 | 61.1 | F | postmenopausal | 104 | Estrogen | 3 |
|  |  | 111 |  |  |  |  | Placebo | 4 |
| S Mirkin, 2013 (SMART-4) |  | 889 | 54.4 | F | postmenopausal | 52 | Bazedoxifene+conjugated estrogens/Estrogen+Progesterone | 6 |
|  |  | 172 |  |  |  |  | Placebo | 0 |
| Joann V Pinkerton, 2014 (SMART-5) | NCT00808132 | 1369 | 54.1 | F | postmenopausal | 52 | Bazedoxifene+conjugated estrogens/Estrogen+Progesterone | 4 |
|  |  | 474 |  |  |  |  | Placebo | 2 |
| L Xu, 2011 |  | 248 | 57.2 | F | postmenopausal | 26 | Bazedoxifene | 0 |
|  |  | 239 |  |  |  |  | Placebo | 2 |
| W F Lems, 2006 |  | 94 | 61.6 | M/F (56%) | rheumatoid arthritis on chronic low-dose prednisone | 52 | Alendronate | 4 |
|  |  | 69 |  |  |  |  | Placebo | 6 |
| L E Nachtigall, 1979 |  | 84 | 55.1 | F | postmenopausal | 520 | Estrogen+Progesterone | 1 |
|  |  | 84 |  |  |  |  | Placebo | 4 |
| A DeCensi, 2013 (HOT) | NCT01579734 | 938 | 53.3 | F | postmenopausal | 260 | Tamoxifen | 13 |
|  |  | 946 |  |  |  |  | Placebo | 10 |
| J C Gallagher, 2001 (STOP IT) |  | 121 | 71.5 | F | postmenopausal | 156 | Estrogen+Progesterone/Estrogen | 9 |
|  |  | 123 |  |  |  |  | Placebo | 7 |
| M Komulainen, 1999 |  | 115 | 52.8 | F | postmenopausal | 260 | Estrogen+Progesterone | 2 |
|  |  | 115 |  |  |  |  | Placebo | 0 |
| L Mosekilde, 2000 |  | 502 | 50 | F | postmenopausal | 260 | Estrogen+Progesterone | 2 |
|  |  | 504 |  |  |  |  | Placebo | 5 |
| P Ravn, 1999 |  | 663 | 55 | F | postmenopausal | 208 | Alendronate | 123 |
|  |  | 502 |  |  |  |  | Placebo | 88 |
| R R Recker, 1999 |  | 64 | 73.2 | F | postmenopausal osteoporosis | 182 | Estrogen+Progesterone | 1 |
|  |  | 64 |  |  |  |  | Placebo | 1 |
| M G Modena, 1999 |  | 100 | 56.5 | F | hypertensive postmenopausal | 78 | Estrogen+Progesterone | 0 |
|  |  | 100 |  |  |  |  | Placebo | 0 |
| P Alexandersen, 2000 |  | 150 | 59 | F | postmenopausal | 104 | Estrogen+Progesterone | 1 |
|  |  | 50 |  |  |  |  | Placebo | 0 |
| A E Hak, 2001 |  | 86 | 47.2 | F | perimenopausal | 26 | Estrogen+Progesterone | 0 |
|  |  | 35 |  |  |  |  | Placebo | 1 |
| Cesar E Fernandes, 2008 |  | 53 | 52.1 | F | postmenopausal | 26 | Estrogen+Progesterone/Estrogen | 0 |
|  |  | 24 |  |  |  |  | Placebo | 1 |
| Michiel L Bots, 2006 (OPAL) |  | 502 | 58.8 | F | postmenopausal | 156 | Tibolone/CEE+MPA | 14 |
|  |  | 257 |  |  |  |  | Placebo | 4 |
| S Mitchell Harman, 2014 (KEEPS) | NCT00154180 | 452 | 52.7 | F | postmenopausal | 208 | Estrogen+Progesterone | 2 |
|  |  | 275 |  |  |  |  | Placebo | 1 |
| P Angerer, 2001 (PHOREA) |  | 215 | NA | F | postmenopausal with increased intima-media thickness in >/=1 segment of the carotid arteries | 48 | Estrogen+Progesterone | 3 |
|  |  | 106 |  |  |  |  | Placebo | 2 |
| Sheila Ronkin, 2005a |  | 249 | 53 | F | postmenopausal | 26 | Bazedoxifene/Estrogen+Progesterone | 0 |
|  |  | 53 |  |  |  |  | Placebo | 0 |
| Sheila Ronkin, 2005b |  | 143 | 52.5 | F | postmenopausal | 26 | Bazedoxifene | 1 |
|  |  | 52 |  |  |  |  | Placebo | 0 |
| S Y Ran, 2017 |  | 78 | 49.4 | F | postmenopausal | 260 | Estrogen+Progesterone | 2 |
|  |  | 75 |  |  |  |  | Placebo | 1 |
| C C Johnston Jr, 2000 |  | 859 | 54.6 | F | postmenopausal | 156 | Raloxifene | 1 |
|  |  | 286 |  |  |  |  | Placebo | 0 |
| Howard N Hodis, 2016 (ELITE) | NCT00114517 | 297 | 60.1 | F | postmenopausal | 260 | Estrogen+Progesterone/Estrogen | 7 |
|  |  | 299 |  |  |  |  | Placebo | 7 |
| R A Mulnard, 2000 |  | 81 | 75 | F | mild to moderate Alzheimer disease | 52 | Estrogen | 4 |
|  |  | 39 |  |  |  |  | Placebo | 0 |
| Louise Lind Schierbeck, 2012 (DOPS) | NCT00252408 | 502 | 49.8 | F | postmenopausal | 520 | Estrogen+Progesterone/Estrogen | 2 |
|  |  | 504 |  |  |  |  | Placebo | 5 |
| Rogerio A Lobo, 2018 (REPLENISH) | NCT01942668 | 1684 | 54.6 | F | postmenopausal | 52 | Estrogen+Progesterone | 9 |
|  |  | 151 |  |  |  |  | Placebo | 0 |
| L Warming, 2004 |  | 180 | 58.5 | F | postmenopausal | 104 | Estrogen+Progesterone | 2 |
|  |  | 60 |  |  |  |  | Placebo | 0 |

Supplemental Table 3. Bias Assessment



Supplemental Figure 1. Comparison-adjusted funnel plot of the publication bias

Supplemental Table 4. SIDE (direct-indirect evidence inconsistency with back-calculation (or SIDDE model)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| comparison | Number of studies with direct evidence | Direct evidence proportion | NMA OR+ | Direct OR++ | Indirect OR\* | Ratio of Ratios\*\* | Z value | p-value |
| Biphosphonate:anti-RANKL | 8 | 0.19 | 0.81 | 0.8 | 0.81 | 0.98 | -0.09 | 0.93 |
| HRT:anti-RANKL | 0 | 0 | 0.86 |  | 0.86 |  |  |  |
| Placebo:anti-RANKL | 5 | 0.86 | 0.8 | 0.8 | 0.8 | 1.01 | 0.03 | 0.98 |
| PTH:anti-RANKL | 2 | 0.02 | 0.75 | 1.08 | 0.75 | 1.45 | 0.31 | 0.75 |
| Romosozumab:anti-RANKL | 0 | 0 | 0.78 |  | 0.78 |  |  |  |
| Biphosphonate:HRT | 0 | 0 | 0.95 |  | 0.95 |  |  |  |
| Biphosphonate:Placebo | 8 | 0.87 | 1.01 | 1 | 1.11 | 0.9 | -0.71 | 0.48 |
| Biphosphonate:PTH | 3 | 0.51 | 1.08 | 0.87 | 1.35 | 0.65 | -1.45 | 0.15 |
| Biphosphonate:Romosozumab | 1 | 0.69 | 1.04 | 1.24 | 0.7 | 1.76 | 2.36 | 0.02 |
| HRT:Placebo | 33 | 1 | 1.07 | 1.07 |  |  |  |  |
| HRT:PTH | 0 | 0 | 1.14 |  | 1.14 |  |  |  |
| HRT:Romosozumab | 0 | 0 | 1.1 |  | 1.1 |  |  |  |
| Placebo:PTH | 5 | 0.47 | 1.07 | 1.2 | 0.96 | 1.25 | 0.74 | 0.46 |
| Placebo:Romosozumab | 2 | 0.34 | 1.02 | 0.77 | 1.18 | 0.65 | -1.76 | 0.08 |
| PTH:Romosozumab | 1 | 0.05 | 0.96 | 0.19 | 1.05 | 0.18 | -2.12 | 0.03 |

Note: + Estimated treatment effect (OR) in network meta-analysis; ++ Estimated treatment effect (OR) derived from direct evidence; \* Estimated treatment effect (OR) derived from indirect evidence; \*\* Direct versus indirect ratio of ratios.

Supplemental Table 5. Inconsistency (design inconsistency)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Tests of heterogeneity (within designs) and inconsistency (between designs) | | | | | |
|  | Q | df | p-value |  |  |
| Total | 57.31 | 63 | 0.679 |  |  |
| Within designs | 47.79 | 58 | 0.828 |  |  |
| Between designs | 9.52 | 5 | 0.09 |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Design-specific decomposition of within-designs Q statistic | | |  |
|  | Q | df | p-value |
| anti-RANKL:Biphosphonate | 6.59 | 7 | 0.473 |
| anti-RANKL:Placebo | 0.35 | 4 | 0.987 |
| anti-RANKL:PTH | 0.91 | 1 | 0.339 |
| Biphosphonate:Placebo | 6.16 | 7 | 0.521 |
| Biphosphonate:PTH | 0.93 | 2 | 0.628 |
| HRT:Placebo | 22.91 | 32 | 0.881 |
| Placebo:PTH | 8.84 | 4 | 0.065 |
| Placebo:Romosozumab | 1.09 | 1 | 0.297 |