Supplement files

1. Tables (eTable 1- eTable 9)

2. Figures (eFigure 1- eFigure 60)

eTable 1. Search strategy.

#1	((zoledronic acid[MeSH Terms]) OR (zoledronate)) OR (2-(imidazol-1-yl)-1-hydroxyethylidene-1)
#2	((Alendronate[MeSH Terms]) OR (Aminohydroxybutane Bisphosphonate)) OR (Bisphosphonate)
#3	((Risedronic Acid[MeSH Terms]) OR (Risedronate Sodium)) OR (Risedronate)
#4	((Ibandronic Acid[MeSH Terms]) OR (Ibandronate)) OR (ibandronic)
#5	(((((Teriparatide[MeSH Terms]) OR (hPTH (1-34))) OR (Human Parathyroid Hormone (1-34))) OR (hPTH)) OR (1-34)) OR (parathyroid hormone)
#6	((abaloparatide[MeSH Terms])) OR (Parathyroid Hormone-Related Protein)
#7	((romosozumab[MeSH Terms]) OR (AMG 785)) OR (amg 785)
#8	(((((Parathyroid Hormone[MeSH Terms]) OR (Parathyroid Hormone (1-84))) OR (PTH (1- 84))) OR (PTH)) OR (Parathormone)) OR (Parathyroid Hormone Peptide (1-84))
#9	(((Denosumab[MeSH Terms]) OR (Xgeva)) OR (AMG 162)) OR (Prolia)
#10	((((Raloxifene[MeSH Terms]) OR (Raloxifene Hydrochloride)) OR (Keoxifene Hydrochloride)) OR (Raloxifene HCl)) OR (raloxifene hydrochloride)
#11	(bazedoxifene[MeSH Terms]) OR (bazedoxifene acetate)
#12	(strontium ranelate[MeSH Terms]) OR (protelos)
#13	(((Calcitonin[MeSH Terms]) OR (Calcitonin)) OR (Salmon calcitonin)) OR (Eel calcitonin)
#14	(((Estradiol[MeSH Terms]) OR (estrogen)) OR (medroxyprogesterone)) OR (tibolone)
#15	(randomized controlled trial[Publication Type]) OR (RCT[Publication Type])
#16	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #10 OR #11 OR #12 OR #13 OR #14
#17	osteoporosis, post-menopausal[MeSH Terms]
#18	#15 AND #16 AND #17

eTable 2. Inclusion/exclusion criteria of literature

PICOS	Inclusion	Exclusion
P	Postmenopausal women with primary osteoporosis.	1) Trials that also enrolled men or women who were not in menopause or with osteopenia; 2) Trials that also enrolled participants with low bone mineral density but without established osteoporosis
I	Trials that compared one or more of the interventions of interest to each other or to placebo, and the interventions were abaloparatide, alendronate, bazedoxifene, calcitonin, denosumab etidronate, hormone replacement therapy, ibandronate, lasofoxifene, Recombinant human parathyroid hormone (1-84), raloxifene, risedronate, romosozumab, strontium ranelate, teriparatide, zoledronate.	Calcium and/or vitamin D.
C	Placebo or abaloparatide, alendronate, bazedoxifene, calcitonin, denosumab etidronate, hormone replacement therapy, ibandronate, lasofoxifene, Recombinant human parathyroid hormone (1-84), raloxifene, risedronate, romosozumab, strontium ranelate, teriparatide, zoledronate.	Calcium and/or vitamin D.
O	Trials that measured at least one of the outcomes of interest, which were efficacy (new vertebral fractures) and safety (adverse events and serious adverse events).	Relevant outcomes were missing.
S	RCT irrespective of blinding or arm.	1) Articles without peer-reviewed or unpublished; 2) Studies that were repeatedly published or had qualitative outcomes; 3) Quasi-experimental studies, crossover, and observational studies.

eTable 3. Randomized Trials Included In Systematic Reviews or Meta-Analyses Evaluating Drugs for prevention of osteoporotic vertebral fractures in postmenopausal women.

	2011 [1]	2011 [2]	2011 [3]	2011 [4]	2012 [5]	2012 [6]	2012 [7]	2012 [8]	2013 [9]	2014 [10]	2015 [11]	2015 [12]	2015 [13]	2017 [14]	2017 [15]	2017 [16]	2017 [17]	2018 [18]	2020 [19]	2019 [20]	2019 [21]	2019 [22]	2019 [23]	2019 [24]	2019 [25]	2020 [26]	2020[27]
Hadji P 2012[28]															Y				Y			Y			Y	Y	Y
Hadji 2008[29]			Y																								
Saag 2007[30]	Y																										
Lewiecki 2009[31]			Y	Y																							
Reginster 2006[32]			Y																								
Ellis 2008[33]				Y							Y																
Black 2012[34]					Y				Y																		
Boonen 2011[35]					Y																						
Sambrook 2012[36]					Y																						
Boonen 2010[37]					Y									Y													
Hwang 2011[38]					Y									Y				Y									
Bubbear 2011[39]					Y																						
Saag 2007[40]					Y																						
Chesnut 1995[41]									Y																		
Kanis 1996[42]									Y																		
Shiraki 1998[43]									Y																		
McClung 1998[44]									Y																		
Greenspan 1998[45]									Y																		
Lau 2000[46]									Y									Y									
Bell 2002[47]									Y																		
Chailurkit 2003[48]									Y																		
Lyles 2007[49]									Y																		
Bekker 2004[50]											Y																
Kumagai 2011[51]											Y																
Smith 2009[52]											Y																
Orwoll 2012[53]											Y																
Brown 2009[54]											Y									Y							
Beck 2008[55]											Y																
Zebaze 2014[56]											Y																
Roux 2014[57]											Y									Y							
Brown 2014[58]											Y																
Anastasilakis 2013[59]											Y																
Seeman 2010[60]											Y																
Chesnut 2004[61]												Y												Y	Y		

Anastasilakis AD, 2008[62]															Y				Y			Y	Y			Y	
Miyauchi 2010[63]	Y																										
Kendler, 2018[64]/ Geusens 2018[65]																			Y					Y		Y	
Glüer CC, 2013[66]															Y				Y							Y	
Simon 2013[67]												Y															
Nakamura 2014[68]											Y	Y	Y							Y					Y		
Malouf-Sierra J, 2016[69]																			Y							Y	
Walker MD, 2012[70]																			Y							Y	
Aspenberg P, 2016[71]																			Y							Y	
Neer, 2001[72]	Y						Y	Y		Y		Y									Y		Y	Y	Y		Y
Greenspan, 2007[73]							Y																		Y		Y
Langdahl, 2017[74]																					Y		Y				Y
Saag, 2017[75]															Y						Y		Y	Y	Y		Y
Cosman, 2016[76]																					Y		Y	Y	Y		Y
Miller, 2016a[77]																					Y		Y	Y	Y		Y
Cosman, 2017[78]																					Y						
Bone 2018[79]																					Y						
Liberman 1995[80]		Y							Y			Y									Y			Y	Y		Y
Black, 2006[81]																		Y			Y						Y
Harris 1999[82]		Y										Y						Y			Y			Y	Y		Y
McClung 2001[83]												Y									Y			Y	Y		Y
Body 2002[84]																	Y				Y	Y	Y		Y		
Cummings 2009[85]/ Bone 2017[86]				Y							Y	Y	Y								Y			Y	Y		Y
Watts 1990[87]		Y										Y									Y						
Cummings 2010[88]								Y										Y			Y				Y		Y
Ettinger 1999[89]																					Y				Y		
Meunier 2004[90]																		Y			Y			Y	Y		Y
Roux 2008[91]																					Y						Y
Black 2007[92]		Y			Y				Y					Y				Y			Y			Y	Y		Y
Arlot 2005[93]																	Y					Y					
Cosman 2011[94]														Y	Y							Y	Y		Y		Y
Finkelstein 2010[95]								Y		Y					Y		Y					Y	Y				
Keaveny 2007[96]																	Y					Y					
McClung 2005[97]															Y		Y					Y			Y		Y

Panico 2011[98]																Y					Y			Y		Y
Reginster 2005[99]/2008[100]/ Adami 2006[101]																	Y						Y	Y		Y
Reginster 2000[102]		Y										Y					Y						Y	Y		Y
Fogelman 2000[103]												Y											Y	Y		Y
Black 1996[104]																							Y	Y		Y
Cummings 1998[105]		Y							Y			Y												Y		Y
Reid 2018[106]																										Y
Bone 2008[107]/Bone 2011[108]				Y							Y		Y											Y		Y
McClung 2006[109]											Y								Y					Y		Y
Miller 2016b[110]																			Y					Y		Y
Greenspan 2015[111]														Y										Y		Y
Recknor 2013[112]											Y								Y					Y		Y
Miller 2008a[113]																								Y		Y
McClung 2009a[114]			Y																					Y		Y
Miller 2008b[115]/ Emkey 2009[116]			Y																							
Bock 2012[117]																								Y		Y
Fogelman 2008[118]																								Y		Y
Ensrud 2008[119]																								Y		Y
Sambrook 2004[120]/ Maricic 2002[121]																		Y								Y
Recker 2007[122]																							Y	Y		Y
Lufkin 1998[123]																		Y						Y		Y
Silverman 2008[124]/2012[125]/ Villiers 2011[126]/ Palacios 2015[127]																Y		Y					Y	Y		Y
Luckey 2004[128]																								Y		Y
Greenspan 2002[129]									Y														Y	Y		Y
Eastell 2009[130]																										Y
Kendler 2010[131]/ Freemantle 2012[132]											Y								Y			Y				Y
Black 2003[133]		Y																								Y
Tucci 1996[134]									Y														Y			Y
Pols 1999[135]									Y			Y											Y	Y		Y
Meunier 2002[136]																							Y			Y
Bone 1997[137]									Y			Y											Y	Y		Y

McClung 2009b[138]													Y													Y
McClung 2006[139]																										Y
Meunier 2009[140]																								Y		Y
Rosen 2005[141]																										Y
Valimaki 2007[142]																										Y
Sethi 2008[143]								Y		Y													Y			
Miyauchi 2008[144]								Y		Y													Y			
Cosman 2010[145]										Y																
Cosman 2001[146]								Y		Y																
Ste-Marie 2006[147]								Y		Y																
Cosman 2005[148]								Y		Y																
Tsai 2013[149]/Leder 2014[150]										Y	Y															
Anastasilakis 2008b[151]																							Y			
Ishibashi 2017[152]																							Y			
Leder 2015[153]																							Y			
McClung 2014[154]																							Y			
Alexandersen1999[155]																								Y		
Bai 2013[156]													Y											Y		
Blair 2009[157]																								Y		
Bush 1996[158]																								Y		
Cauley 2003[159]																								Y		
Chesnut 2000[160]		Y																						Y		
Clemmesen 1997[161]																								Y		
Cosman 2009[162]																								Y		
Cummings 2008[163]																								Y		
Dursun, 2001[164]																								Y		
Gallagher, 2001[165]																								Y		
Gennari, 1985[166]																								Y		
Greenspan, 1998[167]																								Y		
Grey 2009 [168]													Y											Y		
Grey 2014[169]																								Y		
Gruber 1984[170]																								Y		
Henriksen 2016[171]																	Y							Y		
Hizmetli 1998[172]																								Y		
Hooper 2005[173]																								Y		

Hulley 1998[174]																								Y		
Ishida 2004[175]																								Y		
Itabashi 2011[176]																								Y		
Iwamoto 2008[177]																								Y		
Iwamoto 2011[178]																								Y		
Jacobsen 2012[179]																								Y		
Koh 2016[180]																								Y		
Komulainen 1998[181]																								Y		
Lees 2001[182]																								Y		
Lindsay 1990[183]																								Y		
Lufkin 1992[184]																								Y		
McClung 2004[185]																								Y		
Morii 2003[186]																		Y						Y		
Mortensen 1998[187]																								Y		
Mosekilde 2000[188]																								Y		
Muscoso 2004[189]																								Y		
Nachtigall 1979[190]																								Y		
Nakamura 2012a[191]											Y		Y											Y		
Nakamura 2012b[192]																								Y		
Overgaard 1992[193]																								Y		
Recker 1999[194]																								Y		
Recker 2004[195]																								Y		
Reid 2002[196]					Y																			Y		
Reid 2004[197]																								Y		
Rico 1995[198]																								Y		
Rogers 2009[199]																								Y		
Tanko 2004[200]																								Y		
Tierney 2009[201]																								Y		
Ushiroyama 2001[202]																								Y		
Vickers 2007[203]																								Y		
Weiss 1999[204]																								Y		
Wimalawansa 1998[205]																								Y		
Yan 2009[206]																		Y						Y		
Emkey 2005[207]			Y																					Y		
Cooper 2006[208]			Y																					Y		
Yang 2015[209]																		Y								

Eastell 2014[210]																		Y								
Abboskhujaeva 2014[211]																		Y								
Hwang 2008[212]																		Y								
Ilter 2006[213]																		Y								
Epstein 2006[214]																		Y								
Leung 2005[215]																		Y								
Hosking 2003[216]																		Y								
Kung 2000[217]																		Y								
Stepan 1999[218]																		Y								
Felsenberg 1998[219]																		Y								
Anastasilakis 2015[220]																				Y						
Kendler 2011[221]																				Y						
Niimi 2018[222]																				Y						

eTable 4. Excluded Trials and Reasons for Exclusion

1	Saag 2007	The participants had osteoporosis caused by glucocorticoid.
2	Hadji 2008	This was a crossover study.
3	Reginster 2006	Intervention and control are the same drug.
4	Ellis 2008	Women with nonmetastatic breast cancer under aromatase inhibitors.
5	Black 2012	Patients included men.
6	Boonen 2011	Patients included men.
7	Sambrook 2012	Patients included osteoporosis caused by glucocorticoid.
8	Bubbear 2011	Patients included men.
9	Saag 2007	Patients included men.
10	Chesnut 1995	Postmenopausal women with osteopenia.
11	Kanis 1996	This study did not reported vertebral fractures and adverse data.
12	Shiraki 1998	Patients were with osteopenia and osteoporosis.
13	McClung 1998	Patients were with osteopenia.
14	Greenspan 1998	Entry criteria were not based on BMD.
15	Lau 2000	This study did not reported vertebral fractures and adverse data.
16	Lyles 2007	Patients included men.
17	Bekker 2004	This study did not reported vertebral fractures and adverse data.
18	Kumagai 2011	This study did not reported vertebral fractures and adverse data.
19	Smith 2009	Patients included men men under anti-androgen for prostate cancer.
20	Orwoll 2012	Patients included men.
21	Beck 2008	Menopausal women with low BMD.
22	Zebaze 2014	Patients were with osteopenia.
23	Brown 2014	This was a post-hoc analysis
24	Emkey 2005	This was a crossover study.
25	Anastasilakis 2013	This study did not reported vertebral fractures and adverse data.
26	Miyauchi 2010	Patients included men.
27	Glüer CC 2013	Men with glucocorticoid-induced osteoporosis .
28	Simon 2013	This study did not reported vertebral fractures and adverse data.
29	Nakamura 2014	Patients included men.
30	Malouf-Sierra J 2016	Patients included men.
31	Walker MD 2012	Patients were men with low bone mineral density.
32	Aspenberg P 2016	Patients included men.
33	Body 2002	This study did not reported vertebral fractures and adverse data.
34	Arlot 2005	This study did not reported vertebral fractures and adverse data.
35	Keaveny 2007	This study did not reported vertebral fractures and adverse data.
36	Panico 2011	Patients with previous treatment without restrictions.
37	Greenspan 2002	This study did not reported vertebral fractures and adverse data.
38	Eastell 2009	The intervention was a combination therapy.
39	Black 2003	This study did not reported vertebral fractures and adverse data.
40	Sethi 2008	This study did not reported vertebral fractures and adverse data.
41	Cosman 2010	This study did not reported vertebral fractures and adverse data.

42	Cosman 2001	The intervention was a combination therapy.
43	Ste-Marie 2006	The intervention was a combination therapy.
44	Cosman 2005	The intervention was a combination therapy.
45	Tsai 2013	The intervention was a combination therapy.
46	Alexandersen 1999	Fractures reported as AEs but confirmed by radiography.
47	Blair 2009	The full text cannot be obtained.
48	Bush 1996	This study did not reported vertebral fractures and adverse data.
49	Dursun 2001	Patients were with osteopenia and osteoporosis.
50	Cosman 2009	This study did not reported vertebral fractures and adverse data.
51	Gallagher 2001	Patients were with normal BMD.
52	Gennari, 1985	The full text cannot be obtained.
53	Greenspan 1998	This study did not reported vertebral fractures and adverse data.
54	Grey 2009	Patients were with osteopenia.
55	Grey 2014	Patients were with osteopenia.
56	Gruber 1984	This study did not reported vertebral fractures and adverse data.
57	Hizmetli 1998	The full text cannot be obtained.
58	Hulley 1998	It was not clarified whether the patient had osteoporosis.
59	Iwamoto 2008	This was a retracted article.
60	Jacobsen 2012	It was not clarified whether the patient had osteoporosis.
61	Komulainen 1998	This study did not reported vertebral fractures and adverse data.
62	Lees 2001	Patients were with normal BMD.
63	Lindsay 1990	The full text cannot be obtained.
64	McClung 2004	Patients were with normal BMD, osteopenia and osteoporosis.
65	Mortensen 1998	Patients were with normal BMD.
66	Mosekilde 2000	Patients were with normal BMD.
67	Muscoso 2004	This study did not reported vertebral fractures and adverse data.
68	Nachtigall 1979	It was not clarified whether the patient had osteoporosis.
69	Nakamura 2014	Patients included men.
70	Recker 1999	Patients were with osteopenia and osteoporosis.
71	Reid 2002	Patients were with osteopenia and osteoporosis.
72	Reid 2004	Patients were with normal BMD or osteopenia.
73	Rogers 2009	Patients were with osteopenia.
74	Tanko 2004	Patients were with normal BMD.
75	Tierney 2009	It was not clarified whether the patient had osteoporosis.
76	Ushiroyama 2001	Patients were with osteopenia and osteoporosis.
77	Vickers 2007	It was not clarified whether the patient had osteoporosis.
78	Weiss 1999	It was not clarified whether the patient had osteoporosis.
79	Yan 2009	Fractures reported as AEs but confirmed by radiography.
80	Yang 2015	This study did not reported vertebral fractures and adverse data.
81	Abboskhujaeva 2014	The intervention was a combination therapy.
82	Ilter 2006	The two interventions were the same drug.
83	Epstein 2006	This was a review.
84	Stepan 1999	This study did not reported vertebral fractures and adverse data.

85	Eastell 2014	Patients were with osteopenia and osteoporosis.
86	Anastasilakis 2015	Postmenopausal women previously treated with zoledronic acid for 1 year.
87	Kendler 2011	This was a crossover study.
88	Niimi 2018	Patients previously treated with teriparatide for 2 year.

eTable 5. Risk of Bias Assessment.

First author, year	Number	Study design	Baseline imbalance	Allocation concealment	Blinding					Funding	Fracture assessment	Overall RoB	Follow up (months)
					CG	OA	DC	DA	P				
Saag 2017[223]	1	Both	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit ource	Documented by medical personnel	Low	12
Cosman 2016[76]	2	Both	No	Probably Yes	Yes	No	NR	NR	Yes	Includes for-profit ource	Documented by medical personnel	Low	12
Ishibashi 2017[152]	3	RCT	No	Yes	Yes	Yes	Yes	Yes	Yes	Includes for-profit ource	Documented by medical personnel	Low	12
Cosman 2017[78]	4	Open-label	No	Probably Yes	NR	NR	NR	NR	Yes	Includes for-profit ource	Medical records or radiologic reports	High	18
Miller 2016a[224]	5	Double-blind	No	Probably Yes	No	Yes	Yes	NR	No	Includes for-profit ource	Documented by medical personnel	High	18
Langdahl 2017[225]	6	Open-label	No	Probably No	No	No	No	Yes	No	Includes for-profit ource	Documented by medical personnel	High	12
Kendler 2018[226]	7	Double-blind	No	Yes	Yes	Yes	Yes	Yes	Yes	Includes for-profit ource	Medical records or radiologic reports	Low	24
Cummings 2010[88]	8	Double-blind	No	Probably No	NR	NR	NR	NR	NR	Not reported or unclear	Vertebral fractures by medical personnel, non-vertebral by self-report	High	60
Meunier 2004[227]	9	Double-blind	No	Probably No	Yes	NR	NR	NR	Yes	Only not or-profit source/Not reported or unclear	Documented by medical personnel/ Vertebr al fractures by radiographs. Non vertebral fractures by radiographs and medical reports	High	36
Reginster 2008[228]	10	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Not reported or unclear	Vertebral fractures by medical personnel, non-vertebral not specified	High	60
Hadji 2012[229]	11	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source.	Documented by medical personnel	High	18
Reginster 2000[230]	12	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral not specified	High	36
Fogelman 2000[231]	13	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	24
Anastasilakis 2008[232]	14	Open-label	No	Probably No	NR	NR	NR	NR	NR	Not reported or unclear	NR	High	12
Cosman 2011[233]	15	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for- profit source	Documented by medical personnel	Low	12
Neer 2001[234]	16	RCT	No	NR or unclear	NR	NR	NR	Yes	NR	Includes for-profit source	Documented by medical personnel	High	21
McClung 2005[97]	17	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	18

Liberman 1995[80]	18	Double-blind	No	NR or unclear	Yes	Yes	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral not specified	High	36
Black 2006[235]	19	Double-blind	No	Yes	Yes	Yes	Yes	No	Yes	Includes for-profit source	Medical records or radiologic reports	Low	60
Black 1996[104]	20	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Not reported or unclear	Medical records or radiologic reports	Low	36
Cummings 1998[105]	21	Double-blind	No	Probably Yes	Yes	Yes	Yes	Yes	Yes	Includes for-profit source	Documented by medical personnel	Low	48
McClung 2006a[236]	22	Both	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	NR	Low	12
Harris 1999[237]	23	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	36
McClung 2001[83]	24	RCT	No	NR or unclear	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	High	36
Black 2007[238]	25	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	36
Reid 2018[106]	26	Double-blind	No	Yes	Yes	Yes	Yes	Yes	Yes	Includes for-profit source	Medical records or radiologic reports	Low	72
Bone 2008[107]	27	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	24
Bone 2018[79]	28	Open-label	No	Probably No	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	High	24
Cummings 2009[85]	29	Double-blind	No	NR or unclear	NR	NR	NR	NR	NR	Includes for-profit source	Medical records or radiologic reports	High	36
Miller 2016b[110]	30	Double-blind	No	NR or unclear	Yes	Yes	Yes	Yes	Yes	Includes for-profit source	Documented by medical personnel	Unclear	12
Brown 2009[239]	31	Double-blind	No	NR or unclear	Yes	Yes	Yes	Yes	Yes	Only not for-profit source	Documented by medical personnel	High	12
Roux 2014[57]	32	Open-label	No	NR or unclear	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	12
Greenspan 2015[240]	33	Double-blind	No	NR or unclear	Yes	Yes	Yes	Yes	Yes	Only not for-profit source	Documented by medical personnel	High	24
McClung 2009b[138]	34	Double-blind	No	NR or unclear	NR	NR	NR	NR	NR	Only not for-profit source/Not reported or unclear	Medical records or radiologic reports	Unclear	24
Boonen 2010[241]	35	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Medical records or radiologic reports	Unclear	36
Hwang 2011[242]	36	Double-blind	No	NR or unclear	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	36
Recknor 2013[243]	37	Open-label	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	NR	Unclear	12
Miller 2008a[244]	38	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	NR	Low	12
McClung 2009a[114]	39	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral by self-report	High	12

Bock 2012[245]	40	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Only not for-profit source.	Documented by medical personnel	Low	12
Cooper 2006[208]	41	Open-label	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	NR	Unclear	6
Greenspan 2007[73]	42	Double-blind	No	Probably Yes	Yes	Yes	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	18
Fogelman 2008[246]	43	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral by self-report	High	24
Ensrud 2008[119]	44	Double-blind	No	Probably Yes	Yes	Yes	Yes	Yes	Yes	Includes for-profit source	Documented by medical personnel	Low	5.6yr
Ettinger 1999[89]	45	Double-blind	No	Probably Yes	Yes	Yes	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral not specified	Low	36
Sambrook 2004[247]	46	Double-blind	No	Yse	Yes	Yes	Yes	NR	Yes	Includes for-profit source	NR	Low	12
Bone 1997[137]	47	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	24
Recker 2007[122]	48	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	5yr
Lufkin 1998[248]	49	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral not specified	Low	12
Luckey 2004[249]	50	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	NR	Low	12
Kendler 2010a[250]	51	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	12
Tucci 1996[251]	52	Double-blind	No	Probably Yes	NR	NR	NR	NR	Yes	NR	Medical records or radiologic reports	Unclear	36
Silverman 2008[252]	53	Double-blind	No	Probably Yes	Yes	Yes	NR	Yes	Yes	Includes for-profit source	Documented by medical personnel	Low	36
Pols 1999[135]	54	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	12
Bell 2002[253]	55	Double-blind	No	Probably Yes	Yes	NR	NR	NR	NR	NR	Medical records or radiologic reports	Unclear	24
Chailurkit 2003[254]	56	NR	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	NR	Unclear	12
Rosen 2005[255]	57	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Unclear	12
Seeman 2010[256]	58	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	12
Finkelstein 2010[257]	59	RCT	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	6
Kung 2000[258]	60	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	12
Meunier 2002[259]	61	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	24

Roux 2008[91]	62	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	NR	Medical records or radiologic reports	Unclear	48
McClung 2006b[139]	63	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Documented by medical personnel	Unclear	24
Meunier 2009[260]	64	Double-blind	No	Probably No	Yes	NR	NR	NR	Yes	Only not for-profit source/Not reported or unclear	Documented by medical personnel/Vertebral fractures by radiographs. Non-vertebral fractures by radiographs and medical reports	High	48
Hwang 2008[212]	65	Double-blind	No	Probably No	NR	NR	NR	NR	NR	Includes for-profit source	Medical records or radiologic reports	Unclear	12
Miller 2008b[261]	66	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	24
Välimäki 2007[262]	67	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	24
Chesnut 2004[263]	68	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	36
Watts 1990[87]	69	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	NR	Medical records or radiologic reports	Low	24
Leder 2015[153]	70	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	NR	Low	6
McClung 2014[154]	71	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	12
Chesnut 2000[160]	72	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Medical records or radiologic reports	Low	36
Chesnut 2000[160]	72	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Medical records or radiologic reports	Low	36
Clemmesen 1997[264]	73	Double-blind	No	Probably No	Yes	Yes	NR	NR	Yes	Not reported or unclear	Documented by medical personnel	High	24
Cummings 2008[163]	74	Double-blind	No	Probably No	Yes	NR	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	High	34
Henriksen 2016[171]	75	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	36
Hooper 2005[173]	76	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	24
Ishida 2004[175]	77	RCT	No	NR or unclear	NR	NR	NR	NR	NR	Not reported or unclear	Documented by medical personnel	High	24
Itabashi 2011[265]	78	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral by self-report	High	26
Iwamoto 2011[#266]	79	RCT	Yes	NR or unclear	Yes	NR	NR	NR	NR	Only not for profit source	Documented by medical personnel	High	6
Koh 2016[180]	80	Double-blind	No	NR or unclear	Yes	Yes	Yes	NR	Yes	Includes for-profit source	Documented by medical personnel	Unclear	6
Lufkin 1992[184]	81	Double-blind	No	NR or unclear	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	High	12
Morii 2003[^186]	82	Double-blind	Yes	Probably Yes	Yes	Yes	NR	NR	Yes	Includes for-profit source	Vertebral fractures by medical personnel, non-vertebral not specified	Low	12

Nakamura 2012a[267]	83	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	12
Nakamura 2012b[268]	84	Double-blind	No	NR or unclear	Yes	Yes	NR	NR	Yes	Includes for-profit source	Medical records or radiologic reports	High	18
Overgaard 1992[193]	85	Double-blind	No	Probably Yes	Yes	NR	NR	NR	Yes	Only not for-profit source	Documented by medical personnel	Low	24
Zhang 2009[269]	86	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	NR	NR	Unclear	6
Sugimoto 2019[270]	87	Double-blind	No	Probably Yes	NR	NR	NR	NR	NR	Includes for-profit source	Medical records or radiologic reports	Unclear	36
Recker 2004[271]	88	Double-blind	No	Probably Yes	Yes	Yes	NR	NR	Yes	Includes for-profit source	Documented by medical personnel	Low	36
Rico 1995[198]	89	RCT	No	NR or unclear	NR	NR	NR	NR	NR	Not reported or unclear	Documented by medical personnel	High	24
Wimalawansa 1998[205]	90	RCT	No	Probably Yes	NR	Yes	NR	NR	NR	Not reported or unclear	Documented by medical personnel	Unclear	48
Miyauchi 2008[272]	91	Double-blind	No	Probably Yes	Yes	Yes	Yes	NR	Yes	Includes for-profit source	NR	Low	6
Bai 2013[156]	92	RCT	No	NR or unclear	NR	NR	NR	NR	NR	Only not for profit source	Documented by medical personnel	High	24

CG (care giver), OA (outcome assessor), DC (data collector), DA (data analyst), P (patient), NR (not reported)

[#] Women in the Calcitonin group were significantly older and thinner; [^] Placebo had lower lumbar spine BMD; P = 0.004.

eTable 6. Characteristics of the Included Trials and Participants.

First author, year		Region	Trial phase	Study design		Age (yr)	White (%)	Calcium (mg/d)	Vitamin D (IU/d)	Arm	Sample size	Intervention	Follow up (months)
Saag 2017[223]	1	MN	III	Both		74.3	68.4	500 - 1,000	600 - 800	1	2046	Romosozumab 210 mg/ mo, sc	12
										2	2047	Alendronate 70 mg/ wk, oral	
Cosman 2016[76]	2	MN	III	Both		70.8	60.4	500 - 1,000	600 - 800	1	3589	Romosozumab 210 mg/mo,sc	12
										2	3591	Placebo	
Ishibashi 2017[152]	3	MN	III	RCT		67.7	0	≥500	≥600	1	189	Romosozumab 70, 140 or 210 mg/mo, sc	12
										2	63	Placebo	
Cosman 2017[78]	4	MN	III	Open-label		68.6	77.3	500 - 1,000	400 - 800	1	558	Abaloparatide 80 µg/ d, sc	18
										2	581	Placebo	
Miller 2016a[224]	5	MN	III	Double-blind		69.0	79.7	500-1,000	400 - 800	1	824	Abaloparatide 80 µg/ d, sc	18
										2	818	Teriparatide 20 µg/d, sc	
										3	821	Placebo	
Langdahl 2017[225]	6	MN	III	Open-label		71.5	89.0	500 - 1,000	600 - 800	1	218	Romosozumab 210 mg/mo, sc	12
										2	218	Teriparatide 20 mg/d, sc	
Kendler 2018[226]	7	MN	III	Double-blind		72.1	97.5	500 - 1,000	400 - 800	1	680	Teriparatide 20 mg/d, sc	24
										2	680	Risedronate 35 mg/wk, oral	
Cummings 2010[88]	8	MN	III	Double-blind		67.5	74.2	1,000	400 - 800	1	5704	Lasofoxifene 0.25 or 0.5 mg/d	60
										2	2852	Placebo	
Meunier 2004[227]	9	MN	III	Double-blind		69.3	NR	1,500	400 - 800	1	719	Strontium ranelate 2 g/d, oral	36
										2	723	Placebo	
Reginster 2008[228]	10	MN	III	Double-blind		76.7	NR	>1,000	400 - 800	1	2479	Strontium ranelate 2 g/d, oral	60
										2	2456	Placebo	
Hadji 2012[229]	11	MN	III	Double-blind		71.0	80.4	1,000	800	1	360	Teriparatide 20 µg/d, sc	18
										2	350	Risedronate 35 mg/wk, oral	
Reginster 2000[230]	12	MN	III	Double-blind		71.0	96.0	1000	500	1	815	Risedronate 2.5 or 5 mg/d, oral	36
										2	707	Placebo	
Fogelman 2000[231]	13	MN	III	Double-blind		64.5	100.0	1000	NR	1	364	Risedronate 2.5 or 5 mg/d, oral	24
										2	180	Placebo	
Anastasilakis 2008[232]	14	Greece	II	Open-label		65.1	100	500	400	1	22	Risedronate 35 mg/wk, oral	12
										2	22	Teriparatide 20 µg/d, sc	
Cosman 2011[233]	15	MN	III	Double-blind		64.9	97.6	1000 - 1200	400 - 800	1	180	Zoledronate 5 mg/y, iv	12
										2	138	Teriparatide 20 µg/d, sc	
Neer 2001[234]	16	MN	III	RCT		69	99	1000	400 -1200	1	1085	Teriparatide 20 or 40 µg/d, sc	21
										2	552	Placebo	
McClung 2005[97]	17	MN	III	Double-blind		65.9	62.0	1000	400 - 800	1	102	Teriparatide 20 µg/d, sc	18
										2	101	Alendronate 10 mg/d, oral	
Liberman 1995[80]	18	MN	III	Double-blind		64.0	100.0	500	NR	1	597	Alendronate 5 or 10 mg/d, oral	36
										2	397	Placebo	
Black 2006[235]	19	MN	III	Double-blind		73.2	97.4	500	250	1	662	Alendronate 5 or 10 mg/d, oral	60

										2	437	Placebo	
Black 1996[104]	20	MN	III	Double-blind		70.8	97.0	500	250	1	1022	Alendronate 5 or 10 mg/d, oral	36
										2	1005	Placebo	
Cummings 1998[105]	21	MN	III	Double-blind		68.0	97.0	500	250	1	2214	Alendronate 5 or 10 mg/d, oral	48
										2	2218	Placebo	
McClung 2006a[236]	22	MN	III	Both		63.2	85.0	1000	400	1	47	Alendronate 70 mg/ wk, oral	12
										2	272	Denosumab 6, 14 or 30 mg/3 mo; 14, 60, 100 or 210 mg/6 mo, sc	
										3	46	Placebo	
Harris 1999[237]	23	MN	III	Double-blind		69.0	96.0	1000	500	1	821	Risedronate 5 mg/d, oral	36
										2	820	Placebo	
McClung 2001[83]	24	MN	III	RCT		77.7	98.0	1000	≤500	1	3104	Risedronate 5 mg/d, oral	36
										2	3134	Placebo	
Black 2007[238]	25	MN	III	Double-blind		73.1	86.0	1000 -1500	400 - 1200	1	3875	Zoledronate 5 mg/12 months, iv	36
										2	3861	Placebo	
Reid 2018[106]	26	New Zealand	III	Double-blind		71.0	94.5	1000	50000/mo	1	1000	Zoledronate 5 mg/18 months, iv	72
										2	1000	Placebo	
Bone 2008[107]	27	MN	III	Double-blind		59.4	83.0	1000	400 - 800	1	166	Denosumab 60 mg/6 mo, sc	24
										2	166	Placebo	
Bone 2018[79]	28	MN	III	Open-label		70.1	77.3	500 - 1000	400 - 800	1	558	Abaloparatide 80 mg/d, sc	24
										2	581	Placebo	
Cummings 2009[85]	29	MN	III	Double-blind		72.3	99.0	≥1000	≥800	1	3,902	Denosumab 60 mg/6 mo, sc	36
										2	3,906	Placebo	
Miller 2016b[110]	30	MN	III	Double-blind		69.0	96.9	≥1000	≥800	1	320	Denosumab 60 mg/6 mo, sc	12
										2	320	Zoledronate 5 mg/12 mo, iv	
Brown 2009[239]	31	MN	III	Double-blind		64.4	84.4	≥500	≥400	1	594	Denosumab 60 mg/6 mo, sc	12
										2	595	Alendronate 70 mg/ wk, oral	
Roux 2014[57]	32	MN	III	Open-label		67.7	97.6	≥1000	≥800	1	435	Denosumab 60 mg/6 mo, sc	12
										2	435	Risedronate 150 mo, oral	
Greenspan 2015[240]	33	MN	III	Double-blind		85.5	NR	1200	800	1	89	Zoledronate 5 mg/24 mo, iv	24
										2	92	Placebo	
McClung 2009b[138]	34	MN	III	Double-blind		60	92.7	500 - 1200	400 - 800	1	198	Zoledronate 5 mg/y, iv	24
										2	181	Zoledronate 5 mg/24 mo, iv	
										3	202	Placebo	
Boonen 2010[241]	35	MN	III	Double-blind		>75	NR	1000 -1500	400 - 1200	1	1,961	Zoledronate 5 mg/y, iv	36
										2	1,927	Placebo	
Hwang 2011[242]	36	MN	III	Double-blind		72.5	Asian	1000 -1500	400 - 1200	1	163	Zoledronate 5 mg/y, iv	36
										2	160	Placebo	
Recknor 2013[243]	37	MN	III	Open-label		66.7	85.1	≥500	≥800	1	417	Denosumab 60 mg/6 mo, sc	12
										2	416	Ibandronate 150 mg/mo, oral	
Miller 2008a[244]	38	MN	III	Double-blind		65.6	82.1	500	400	1	874	Ibandronate 150 mg/mo, oral	12
										2	859	Alendronate 70 mg/ wk, oral	
McClung 2009a[114]	39	MN	III	Double-blind		53.5	100.0	500	400	1	77	Ibandronate 150 mg/mo, oral	12
										2	83	Placebo	
Bock 2012[245]	40	Germany	III	Double-blind		69.0	100.0	500	400	1	35	Ibandronate 150 mg/mo, oral	12
										2	33	Placebo	

Cooper 2006[208]	41	MN	II	Open-label		67.8	96.7	NR	NR	1	547	Ibandronate 150 mg/mo, oral	6
										2	529	Alendronate 70 mg/ wk, oral	
Greenspan 2007[73]	42	MN	III	Double-blind		64.4	84.8	700	400	1	1286	PTH 100 µg/d, sc	18
										2	1246	Placebo	
Fogelman 2008[246]	43	MN	III	Double-blind		58.8	100.0	1050	800	1	90	PTH 100 µg/d, sc	24
										2	90	Placebo	
Ensrud 2008[119]	44	MN	III	Double-blind		67.5	84.0	NR	NR	1	5044	Raloxifene 60 mg/d oral	5.6yr
										2	5057	Placebo	
Ettinger 1999[89]	45	MN	III	Double-blind		65.0	95.7	500	400 - 600	1	5129	Raloxifene 60 or 120 mg/d oral	36
										2	2576	Placebo	
Sambrook 2004[247]	46	MN	III	Double-blind		61.6	79.1	NR	NR	1	241	Raloxifene 60 mg/d oral	12
										2	246	Alendronate 70 mg/ wk, oral	
Bone 1997[137]	47	MN	III	Double-blind		70.9	97.3	500	NR	1	268	Alendronate 1.0, 2.5 or 5 mg/d, oral	24
										4	91	Placebo	
Recker 2007[122]	48	MN	III	Double-blind		65.6	86.8	500	400	1	707	Raloxifene 60 mg/d oral	5yr
										2	716	Alendronate 10 mg/d, oral	
Lufkin 1998[248]	49	MN	III	Double-blind		69.1	100.0	750	800	1	95	Raloxifene 60 or 120 mg/d oral	12
										2	45	Placebo	
Luckey 2004[249]	50	MN	III	Double-blind		64	92	500	200	1	233	Alendronate 70 mg/ wk, oral	12
										2	223	Raloxifene 60 mg/d oral	
Kendler 2010[#250]	51	MN	III	Double-blind		67.6	NR	1000	400	1	253	Denosumab 60 mg/6 mo, sc	12
										2	249	Alendronate 70 mg/ wk, oral	
Tucci 1996[251]	52	MN	III	Double-blind		64.7	91	500	NR	1	192	Alendronate 5/10 mg/d, oral	36
										2	192	Placebo	
Silverman 2008[252]	53	MN	III	Double-blind		66.4	87	≤1,200	400 – 800	1	1886	Bazedoxifene 20 mg/d oral	36
										2	1872	Bazedoxifene 40 mg/d oral	
										3	1849	Raloxifene 60 mg/d oral	
										4	1885	Placebo	
Pols 1999[135]	54	MN	III	Double-blind		62.8	94	500	NR	1	950	Alendronate 10 mg/d, oral	12
										2	958	Placebo	
Bell 2002[253]	55	MN	III	Double-blind			African	500	500	1	50	Alendronate 10 mg/d, oral	24
										2	50	Placebo	
Chailurkit 2003[254]	56	Thai	III	NR		62	Asian	500	NR	1	32	Alendronate 10 mg/d, oral	12
										2	38	Placebo	
Rosen 2005[255]	57	MN	III	Double-blind		64.5	95.3	1000	400	1	520	Alendronate 70 mg/ wk, oral	12
										2	533	Risedronate 35 mg/d, oral	
Seeman 2010[256]	58	MN	II	Double-blind		60.6	96	≥500	≥400	1	82	Alendronate 70 mg/ wk, oral	12
										2	83	Denosumab 60 mg/6 mo, sc	
										3	82	Placebo	
Finkelstein 2010[257]	59	USA	II	RCT		64.4	NR	1000–1200	400	1	29	Alendronate 10 mg/d, oral	6
										2	20	Teriparatide 40 µg/d, sc	
Kung 2000[258]	60	China	III	Double-blind		64.5	Asian	500	NR	1	35	Alendronate 10 mg/d, oral	12
										2	35	Placebo	
Meunier 2002[259]	61	MN	III	Double-blind		66.2	100	500	800	1	262	Strontium ranelate 0.5, 1.0 or 2.0 g/d, oral	24
										2	91	Placebo	
Roux 2008[91]	62	MN	III	Double-blind		60	NR	NR	NR	1	168	Strontium ranelate 2 g/d, oral	48

										2	185	Placebo	
McClung 2006b[139]	63	MN	III	Double-blind		58.5	NR	1000	250	1	164	Lasofoxifene 0.25 or 1.0 mg/d	24
										2	163	Raloxifene 60 mg/d oral	
										3	83	Placebo	
Meunier 2009^[260]	64	MN	III	Double-blind		69.3	100	NR	NR	1	719	Strontium ranelate 2.0 g/d, oral	48
										2	726	Placebo	
Hwang 2008[212]	65	MN	III	Double-blind		65	Asian	500	800	1	64	Strontium ranelate 2.0 g/d, oral	12
										2	61	Placebo	
Miller 2008b[261]	66	MN	III	Double-blind		57.8	94	600	NR	1	962	Bazedoxifene 10, 20 or 40 mg/d oral	24
										2	311	Raloxifene 60 mg/d oral	
										3	310	Placebo	
Välimäki 2007[262]	67	MN	III	Double-blind		65.9	100	1000	400	1	114	Risedronate 5 mg/d, oral	24
										2	57	Placebo	
Chesnut 2004[263]	68	MN	III	Double-blind		69	NR	500	400	1	975	Ibandronate 2.5 mg/d, oral	36
										2	977	Ibandronate 20 mg every other day for 12 doses every 3 months	
										3	977	Placebo	
Watts 1990[87]	69	MN	III	Double-blind		65	NR	≥1000	≥1000	1	195	Etidronate 400 mg/d, oral	24
										2	183	Placebo	
Leder 2015[153]	70	MN	III	Double-blind		65.0	61.3	400 - 800	500 - 1000	1	131	Abaloparatide 20, 40 or 80 mg/d, sc	6
										2	45	Teriparatide 20 µg/d, sc	
										5	45	Placebo	
McClung 2014[154]	71	MN	III	Double-blind		66.5	86	1000	800	1	51	Romosozumab 70, 140, 210 mg/mo or 140, 210 mg/ 3mo, sc	12
										2	55	Teriparatide 20 µg/d, sc	
										3	51	Alendronate 70 mg/ wk, oral	
										4	52	Placebo	
Chesnut 2000[160]	72	MN	III	Double-blind		68.3	NR	1000	400	1	944	Salmon calcitonin intranasal 100, 200, or 400 IU/day	36
										2	311	Placebo	
Clemmesen 1997[264]	73	MN	II	Double-blind		68	NR	1000	NR	1	44	Risedronate 2.5 mg/d (continuous), oral	24
										2	44	Risedronate 2.5 mg/d ((2.5 mg daily risedronate for 2 weeks followed by 10 weeks on placebo), oral	
										3	44	Placebo	
Cummings 2008[163]	74	MN	III	Double-blind		68.3	NR	315	200	1	2267	Hormone replacement therapy (tibolone 1.25 mg/d)	34
										2	2267	Placebo	
Henriksen 2016[171]	75	MN	III	Double-blind		66.8	66.5	800 - 1000	400 - 800	1	2334	Salmon calcitonin 0.8 mg/d, oral	36
										2	2331	Placebo	
Hooper 2005[173]	76	MN	III	Double-blind		53	98	1000	NR	1	257	Risedronate 2.5 or 5 mg/d, oral	24
										2	126	Placebo	
Ishida 2004[175]	77	Japan	III	RCT		69.5	NR	NR	NR	1	66	Hormone replacement therapy (conjugated estrogen 0.625 mg/d plus medroxyprogesterone 2.5 mg/d)	24
										2	66	Etidronate	
										3	66	Eel calcitonin 20 IU/wk	
										4	66	Placebo	
Itabashi 2011[265]	78	MN	III	Double-blind		63	Asian	610	400	1	283	Bazedoxifene 20 or 40 mg/d oral	26
										2	142	Placebo	
Iwamoto 2011[266]	79	MN	III	RCT		79.8	NR	NR	NR	1	97	Alendronate 35 mg/wk, oral	6
										2	97	Calcitonin im 20 IU/week	
Koh 2016[180]	80	MN	III	Double-blind		66.5	100	≥1000	≥400	1	69	Denosumab 60 mg/6 mo, sc	6

										2	66	Placebo	
Lufkin 1992[184]	81	MN	III	Double-blind		64.7	NR	NR	NR	1	36	Hormone replacement therapy (Estradiol 0.1 mg/day +MPA 10 mg/day)	12
										2	39	Placebo	
Morii 2003[186]	82	MN	III	Double-blind		64.7	Asian	500	200	1	183	Raloxifene 60 or 120 mg/d oral	12
										2	97	Placebo	
Nakamura 2012a[267]	83	MN	III	Double-blind		65.1	Asian	600	400	1	157	Denosumab 14, 60 or 100 mg/6 mo, sc	12
										2	55	Placebo	
Nakamura 2012b[268]	84	MN	III	Double-blind		75.3	Asian	610	400	1	276	Teriparatide 56.5 μg/wk, sc	18
										2	273	Placebo	
Overgaard 1992[193]	85	MN	III	Double-blind		68-72	NR	500	No	1	156	Salmon calcitonin 50, 100 or 200 IU/day, intranasal	24
										2	52	Placebo	
Zhang 2009[269]	86	MN	III	Double-blind		65.25	Asian	600	125	1	100	PTH 20 μg/d, sc	6
										2	105	Elcatonin 20 IU/wk	
Sugimoto 2019[270]	87	MN	III	Double-blind		75.5	Asian	400	400	1	433	Elcatonin 20 IU/wk	36
										2	436	Placebo	
Recker 2004[271]	88	MN	III	Double-blind		67	NR	500	400	1	1912	Ibandronate 0.5 or 1 mg/3 mo, iv	36
										2	950	Placebo	
Rico 1995[198]	89	Spain	III	RCT		69.2	NR	500	No	1	36	Salmon calcitonin im 100 IU/day for 10 days each month, intranasal	24
										2	36	Placebo	
Wimalawansa 1998[205]	90	England	III	RCT		64.9	100	1000	400	1	18	Hormone replacement therapy (premarin 0.625 mg/day + norgestrel 150 μg for 12 days each month	48
										2	18	Placebo	
Miyauchi 2008[272]	91	MN	III	Double-blind		71.1	Asian	610	400	1	120	Teriparatide 10 μg, 20 μg or 40 μg daily, sc	6
										2	39	Placebo	
Bai 2013[156]	92	China	III	RCT		56.8	Asian	600	400	1	138	Zoledronate 5 mg/y, iv	24
										2	242	Placebo	

Subjects received open-label branded alendronate 70 mg once weekly for 1 month and then were randomly assigned to either continued weekly alendronate therapy or subcutaneous denosumab 60 mg every 6 months and were followed for 12 months.
^ patients in the strontium ranelate group were randomized either to switch to placebo (50%, SR/placebo group) or to continue on strontium ranelate 2 g/ day (50%, SR/SR group), while all patients in the placebo group were switched to strontium ranelate 2 g/day. We did not extract the data of the fourth year. Patients were supplemented in vitamin D and calcium according to their need.

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eTable 7. Node Splitting Analyses on Vertebral Fracture.

Side	Direct		Indirect		Difference		
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P>z
Abaloparatide VS Ibandronate	-0.0174119	0.7482911	1.621273	0.6427079	-1.638685	0.9864143	0.097
Abaloparatide VS Placebo	1.998909	0.5182419	0.6501423	0.7056628	1.348767	0.8277521	0.103
Abaloparatide VS Teriparatide	0.3506919	0.770868	0.165618	0.6192236	0.185074	0.9718293	0.849
Alendronate VS Calcitonin	1.05E-11	2.049434	-0.2422759	0.3553771	0.2422759	2.080018	0.907
Alendronate VS Denosumab	-0.691081	1.645544	-0.6167593	0.4307527	-0.0743217	1.708623	0.965
Alendronate VS Placebo	0.5294609	0.2245798	0.7912885	0.4000535	-0.2618277	0.4588501	0.568
Alendronate VS Raloxifene	-0.4542774	0.7060514	0.3498596	0.306024	-0.8041371	0.7695188	0.296
Alendronate VS Romosozumab	-0.4684899	0.4528431	-0.748037	0.5534775	0.279547	0.7151253	0.696
Alendronate VS Teriparatide	0.1177827	0.6534047	-0.932947	0.323879	1.05073	0.7292704	0.15
Bazedoxifene VS Placebo	0.551421	0.4513419	0.0068044	0.9677628	0.5446167	1.069854	0.611
Bazedoxifene VS Raloxifene	-0.0300775	0.4625784	0.51456	0.9517115	-0.5446375	1.069853	0.611
Calcitonin VS Placebo	0.8318741	0.2992612	0.5913	2.057919	0.2405741	2.07932	0.908
Denosumab VS Ibandronate	0.0024125	1.086103	0.7185958	0.551687	-0.7161833	1.218186	0.557
Denosumab VS Placebo	1.151271	0.4143862	1.503542	0.8986016	-0.3522711	0.9961439	0.724
Denosumab VS Zoledronate	2.209776	1.549074	0.1723293	0.4418225	2.037447	1.610849	0.206
Etidronate VS Placebo	0.8728926	0.6073128	3.24372	254.519	-2.370827	254.5195	0.993
HRT VS Placebo	0.7626169	0.3923283	3.195547	118.4075	-2.43293	118.4079	0.984
Ibandronate VS Placebo	0.255382	0.4080425	1.726673	0.7101416	-1.471291	0.8189596	0.072
Lasofoxifene VS Placebo	0.4522047	0.425378	2.997899	241.8469	-2.545694	241.8473	0.992
PTH VS Placebo	1.14611	0.569711	3.402681	407.0736	-2.25657	407.0737	0.996
Placebo VS Raloxifene	-0.2950316	0.2344493	-1.099263	0.7334685	0.8042318	0.7695034	0.296
Placebo VS Risedronate	-0.4063351	0.2563069	-0.5133924	0.4650762	0.1070573	0.531023	0.84
Placebo VS Romosozumab	-1.317416	0.5138934	-1.037882	0.4973105	-0.2795348	0.7151253	0.696
Placebo VS Strontium Ranelate	-0.4700006	0.2011888	-3.088405	61.71641	2.618404	61.71675	0.966
Placebo VS Teriparatide	-1.513859	0.3348998	-1.110403	0.3453045	-0.4034561	0.4778397	0.398
Placebo VS Zoledronate	-0.9864656	0.2307168	0.764235	0.9512932	-1.750701	0.9786987	0.074
Risedronate VS Teriparatide	-0.8385412	0.360327	-0.9454883	0.390057	0.1069471	0.5310286	0.84
Teriparatide VS Zoledronate	1.829209	1.162675	0.3140701	0.3357844	1.515139	1.210192	0.211

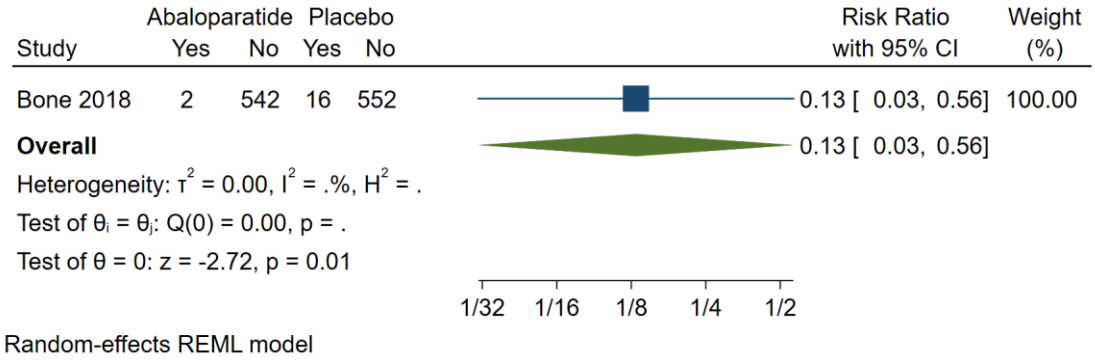
eTable 8. Node Splitting Analyses on All Adverse Event.

	Direct		Indirect		Difference		
Side	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P>z
Abaloparatide VS Ibandronate	0.0961461	0.1435711	-0.08033	0.138199	0.176473	0.199278	0.376
Abaloparatide VS Placebo	-0.1440292	0.1186361	0.132279	0.147516	-0.27631	0.189653	0.145
Abaloparatide VSTeriparatide	-0.0914849	0.1667188	-0.18278	0.167037	0.091294	0.235892	0.699
Alendronate VS Denosumab	-0.0796717	0.1339278	0.008281	0.095609	-0.08795	0.164956	0.594
Alendronate VS Ibandronate	-0.1250165	0.1128771	0.121231	0.095704	-0.24625	0.148048	0.096
Alendronate VS Placebo	0.0578067	0.0623145	-0.14016	0.076863	0.197965	0.099419	0.046*
Alendronate VS Raloxifene	0.010737	0.1064783	-0.12677	0.149586	0.137507	0.183785	0.454
Alendronate VS Romosozumab	-0.1255145	0.1189033	0.026958	0.118137	-0.15247	0.16509	0.356
Alendronate Teriparatide	-1.318177	0.4930268	-0.06572	0.10003	-1.25246	0.505562	0.013*
Bazedoxifene VS Placebo	0.1546776	0.1434724	-0.46927	0.358876	0.62395	0.404294	0.123
Bazedoxifene VS Raloxifene	-0.0976686	0.1472378	0.506678	0.290988	-0.60435	0.337329	0.073
Calcitonin VS PTH	0.3422511	0.3033611	0.958878	0.180622	-0.61663	0.353061	0.081
Calcitonin VS Placebo	-0.0344561	0.1317042	-0.65107	0.327574	0.616614	0.35306	0.081
Denosumab VS Ibandronate	-0.144148	0.1662153	0.109164	0.103344	-0.25331	0.195723	0.196
Denosumab VS Placebo	0.0342938	0.1126626	-0.02824	0.092707	0.062529	0.146226	0.669
Denosumab VS Risedronate	0.2479802	0.1698212	0.003991	0.109793	0.243989	0.202222	0.228
Denosumab VS Zoledronate	1.01E-10	0.1878482	0.197116	0.113974	-0.19712	0.219721	0.37
HRT VS Placebo	0.7437909	0.5631426	-0.01069	140.9509	0.754481	140.9517	0.996
Ibandronate VS Placebo	-0.2067133	0.1106639	0.066108	0.087534	-0.27282	0.141159	0.053
Lasofoxifene VS Placebo	-0.2129051	0.1398532	0.160541	1.038795	-0.37345	1.044926	0.721
Lasofoxifene VS Raloxifene	-0.4455519	0.6359006	-0.2036	0.168496	-0.24195	0.65615	0.712
PTH VS Placebo	-0.9933354	0.1236053	-0.3767	0.330715	-0.61663	0.353059	0.081
Placebo VS Raloxifene	-0.0458486	0.1415347	0.012285	0.11771	-0.05813	0.184349	0.753
Placebo VS Risedronate	0.1105782	0.0990613	0.025514	0.128126	0.085064	0.163054	0.602
Placebo VS Romosozumab	-0.0183048	0.1097419	-0.01903	0.128877	0.000729	0.163937	0.996
Placebo VS Strontium Ranelate	0.0230482	0.1136459	0.054798	100.5799	-0.03175	100.58	1
Placebo VS Teriparatide	-0.0623683	0.1518625	-0.12275	0.115146	0.060381	0.192048	0.753
Placebo VS Zoledronate	0.1627083	0.0889787	0.079084	0.183083	0.083624	0.203165	0.681
Risedronate VS Risedronate	-0.0429965	0.1223675	-0.36186	0.144365	0.318863	0.189791	0.093
Romosozumab VS Teriparatide	-0.5040923	0.1901978	0.115684	0.117321	-0.61978	0.222681	0.005*
Teriparatide VS Zoledronate	0.5684547	0.3977862	0.2161	0.121999	0.352355	0.416074	0.397

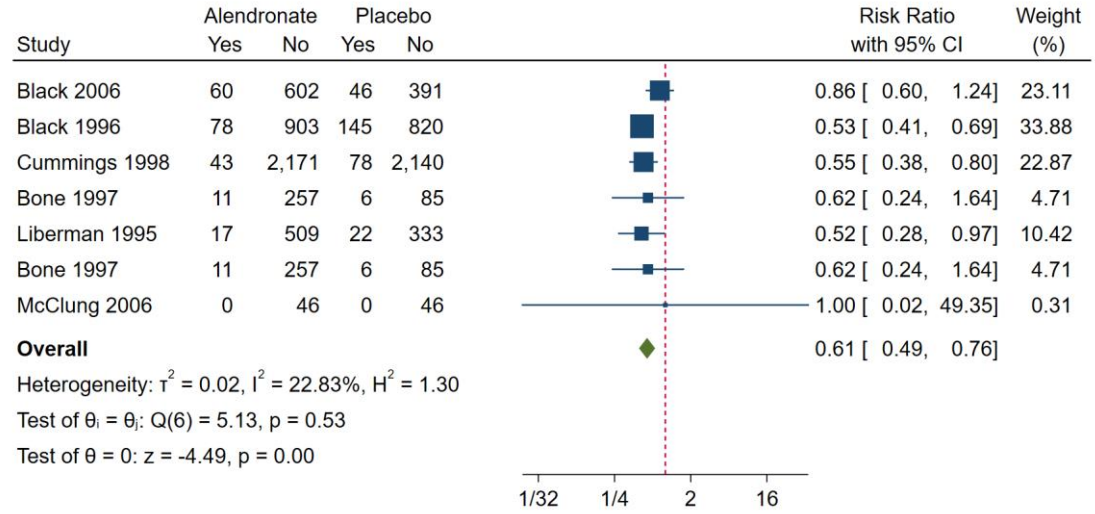
eTable 9. Node Splitting Analyses on Serious Adverse Event.

	Direct		Indirect		Difference		
Side	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P>z
Abaloparatide VS Ibandronate	-0.3816	0.2211449	0.039768	0.1521001	-0.421372	0.2684017	0.116
Abaloparatide VS Placebo	0.007163	0.1283009	-0.3741635	0.2019412	0.3813264	0.2388212	0.11
Abaloparatide VS Teriparatide	0.079512	0.1809446	-0.1374274	0.2034582	0.2169394	0.2726158	0.426
Alendronate VS Denosumab	-0.15186	0.1767023	-0.0673127	0.1282412	-0.0845517	0.2178777	0.698
Alendronate VS Ibandronate	-0.12657	0.2389595	-0.1764886	0.1327064	0.0499222	0.2733361	0.855
Alendronate VS Placebo	-0.11688	0.1333196	-0.1866439	0.102383	0.0697611	0.1677085	0.677
Alendronate VS Raloxifene	-0.29978	0.1957281	-0.1293355	0.133539	-0.1704472	0.2361617	0.47
Alendronate VS Romosozumab	-0.10692	0.1250959	-0.1351378	0.153176	0.028219	0.1955987	0.885
Alendronate VS Teriparatide	0.173974	0.7022704	-0.0848551	0.1274393	0.2588287	0.7144777	0.717
Bazedoxifene VS Placebo	0.15444	0.1091297	0.4221753	0.399109	-0.2677352	0.4131605	0.517
Bazedoxifene VS Raloxifene	0.185624	0.1013131	-0.1934114	0.3344678	0.379035	0.347586	0.276
Calcitonin VS Etidronate	-1.58E-11	0.537597	-1.59035	0.812022	1.59035	0.9738533	0.102
Calcitonin VS HRT	-0.15063	0.5536925	-1.740976	0.8227664	1.59035	0.9738533	0.102
Calcitonin VS PTH	0.048553	2.006123	-0.0902049	0.2020437	0.1387582	2.016272	0.945
Calcitonin VS Placebo	0.165798	0.1089565	0.3043386	2.013057	-0.138541	2.016002	0.945
Denosumab VS Ibandronate	-0.61463	0.2800534	0.0303638	0.1031907	-0.6449945	0.2984598	0.031*
Denosumab VS Placebo	-0.05534	0.0897132	-0.0888574	0.1361742	0.0335127	0.1643841	0.838
Denosumab VS Risedronate	0.063904	0.2646515	-0.0806827	0.0993228	0.1445866	0.2826755	0.609
Denosumab VS Zoledronate	0.162072	0.2968116	-0.1769452	0.1106258	0.3390173	0.3167573	0.284
Etidronate VS Placebo	0.922395	0.4753954	-0.6679704	0.9210862	1.590365	0.9738487	0.102
HRT VS Placebo	1.07302	0.4935238	-0.5173446	0.9305722	1.590365	0.9738486	0.102
Ibandronate VS Placebo	-0.12987	0.0944288	0.2736514	0.1490818	-0.4035259	0.1766759	0.022*
Lasofoxifene VS Placebo	-0.01536	0.0960638	0.5151299	0.7893496	-0.530494	0.801622	0.508
Lasofoxifene VS Raloxifene	9.26E-02	0.4091308	-0.0382647	0.1345086	0.1308339	0.4306623	0.761
PTH VS Placebo	0.256002	0.1701464	0.1172191	2.009005	0.1387833	2.016197	0.945
Placebo VS Raloxifene	-0.00368	0.1030874	-0.089022	0.1997794	0.085342	0.2264529	0.706
Placebo VS Risedronate	-0.01472	0.0687975	0.0952697	0.1638334	-0.1099866	0.1790923	0.539
Placebo VS Romosozumab	0.045223	0.1201689	0.0354875	0.1470307	0.0097353	0.1860861	0.958
Placebo VS Strontium Ranelate	0.041111	0.0935681	0.2031932	136.6413	-0.1620821	136.6414	0.999
Placebo VS Teriparatide	-0.10497	0.1664363	0.1870875	0.1224568	-0.2920602	0.2059511	0.156
Placebo VS Zoledronate	-0.09056	0.065053	0.2484592	0.3076665	-0.3390164	0.3167535	0.284
Risedronate VS Teriparatide	0.052998	0.1317469	0.1293568	0.1612245	-0.0763588	0.2097215	0.716
Romosozumab VS Teriparatide	0.410096	0.2826434	-0.0504909	0.1338114	0.4605868	0.3114141	0.139

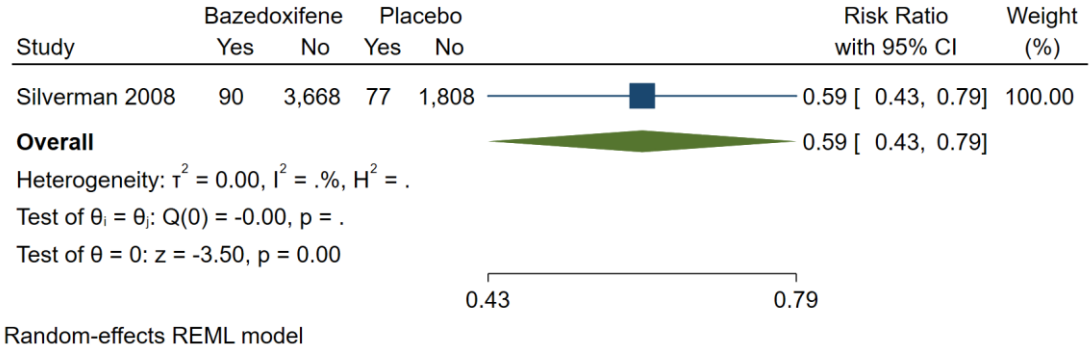
eFigure 1. Abaloparatide Compared with Placebo on Vertebral Fracture.



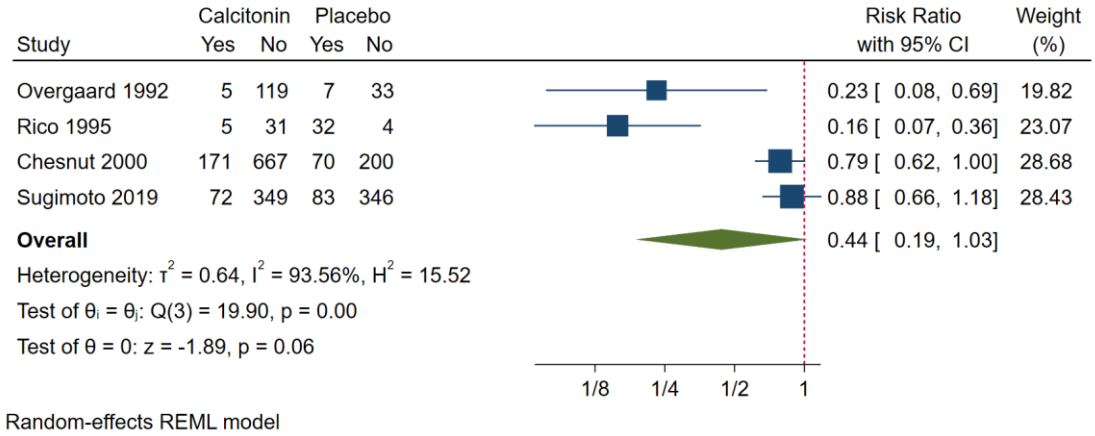
eFigure 2. Alendronate Compared with Placebo on Vertebral Fracture.



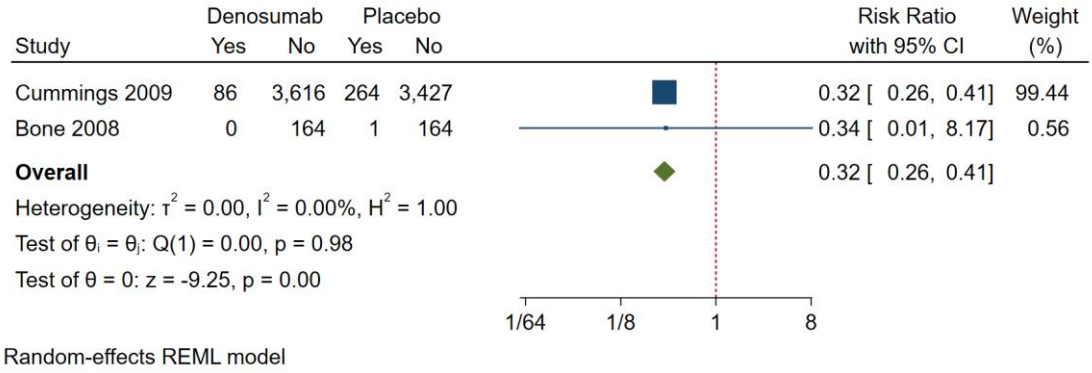
eFigure 3. Bazedoxifene Compared with Placebo on Vertebral Fracture.



eFigure 4. Calcitonin Compared with Placebo on Vertebral Fracture.

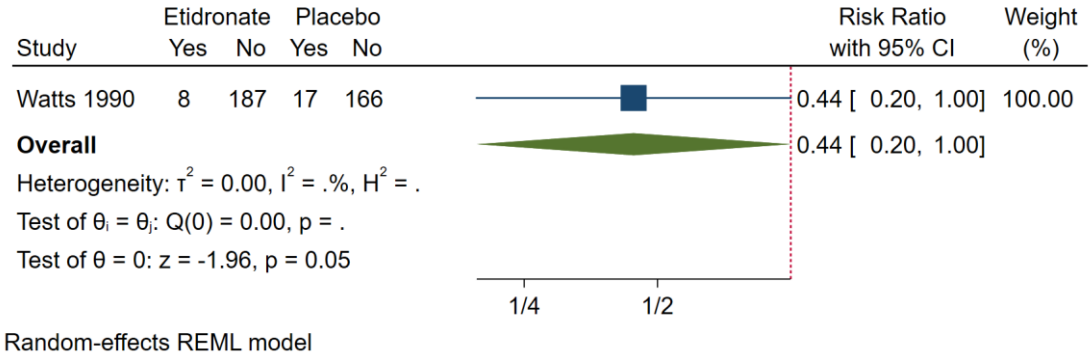


eFigure 5. Denosumab Compared with Placebo on Vertebral Fracture.



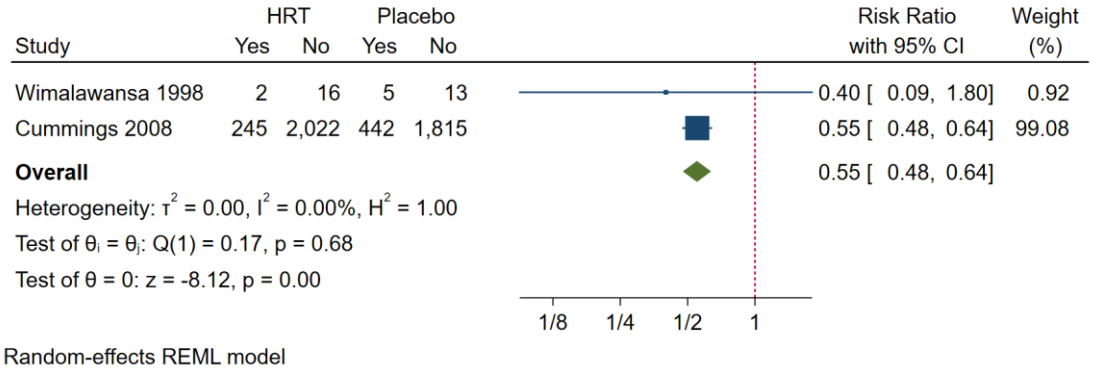
Random-effects REML model

eFigure 6. Etidronate Compared with Placebo on Vertebral Fracture.

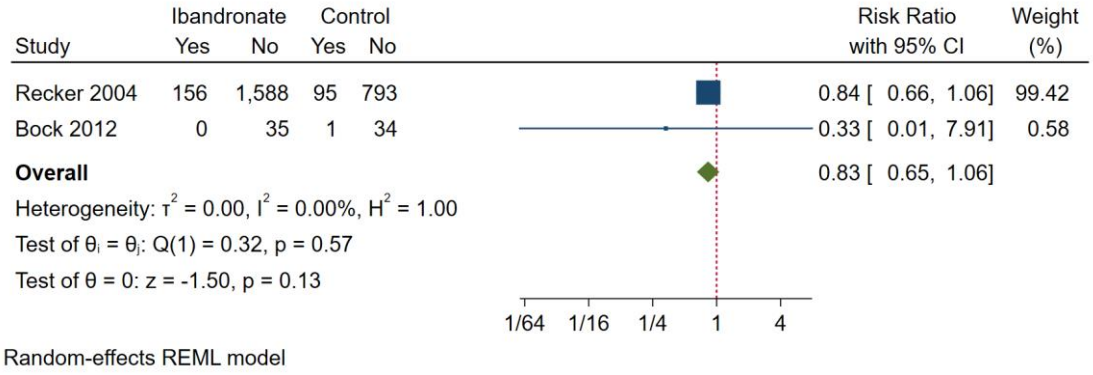


Random-effects REML model

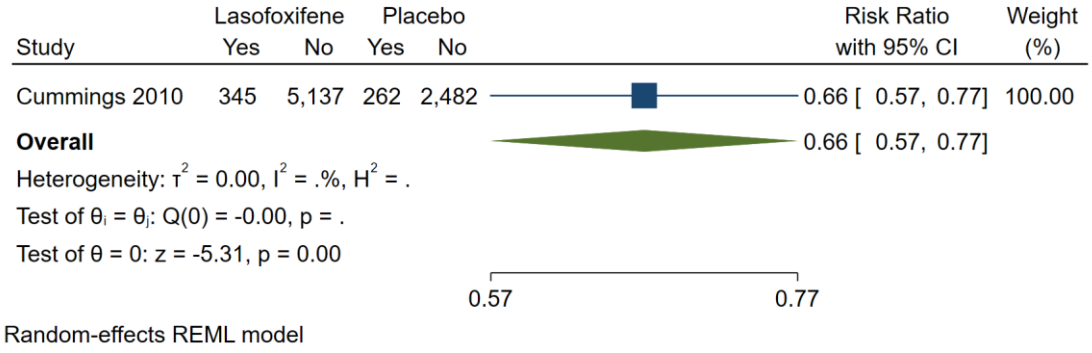
eFigure 7. HRT Compared with Placebo on Vertebral Fracture.



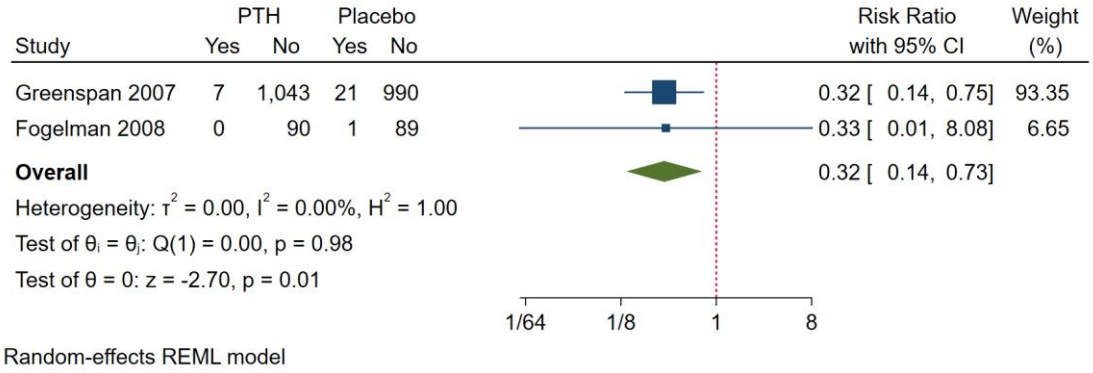
eFigure 8. Ibandronate Compared with Placebo on Vertebral Fracture.



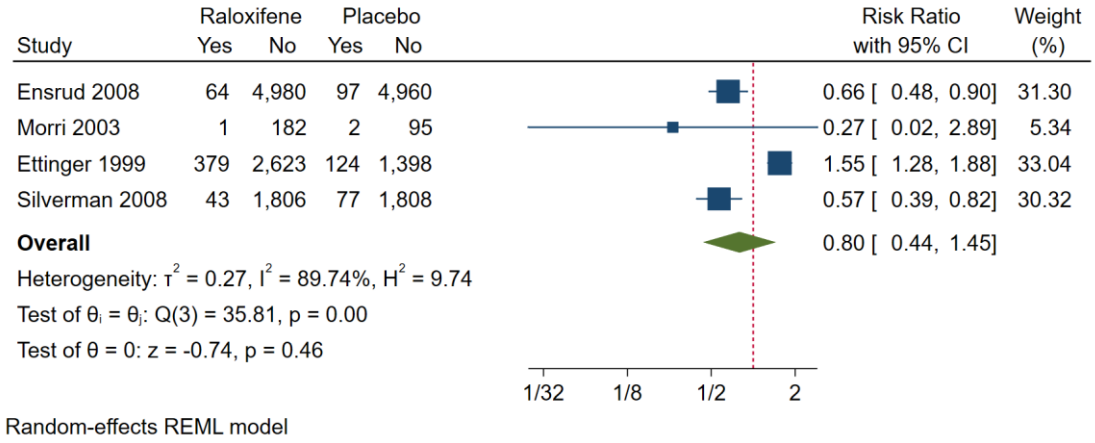
eFigure 9. Lasofoxifene Compared with Placebo on Vertebral Fracture.



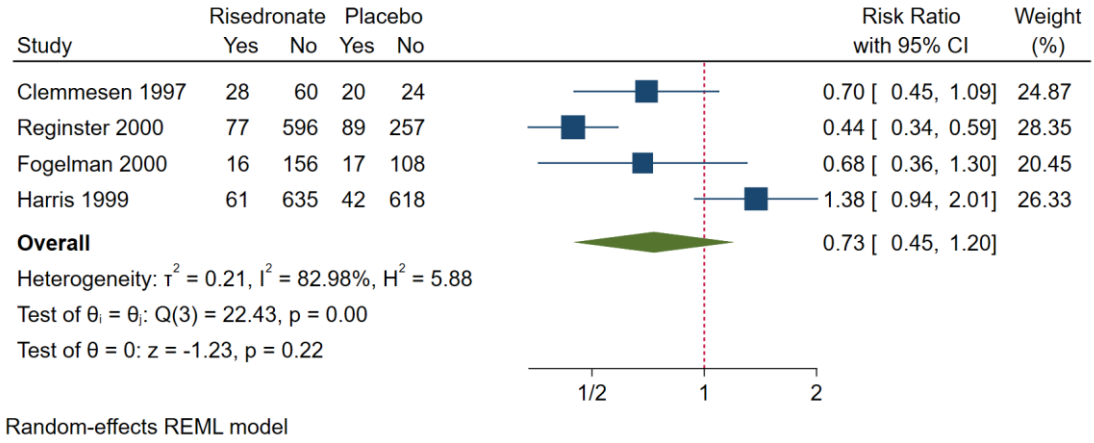
eFigure 10. PTH Compared with Placebo on Vertebral Fracture.



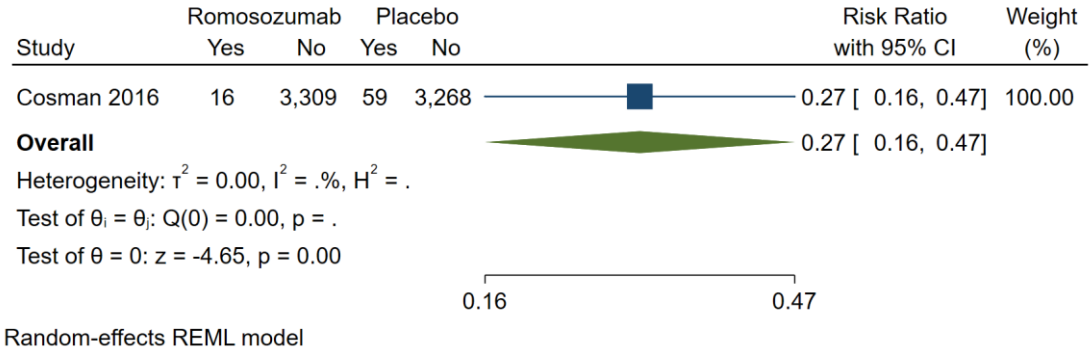
eFigure 11. Raloxifene Compared with Placebo on Vertebral Fracture.



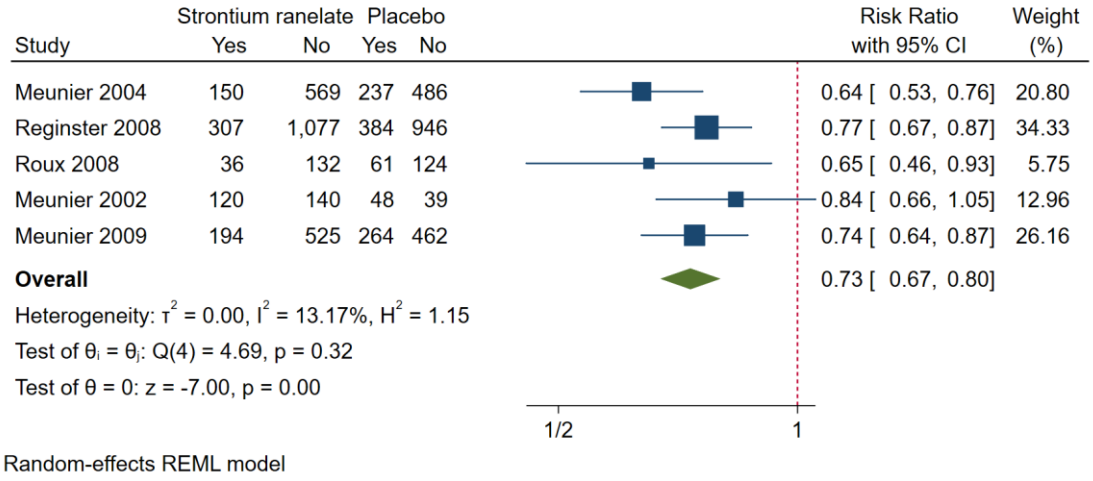
eFigure 12. Risedronate Compared with Placebo on Vertebral Fracture.



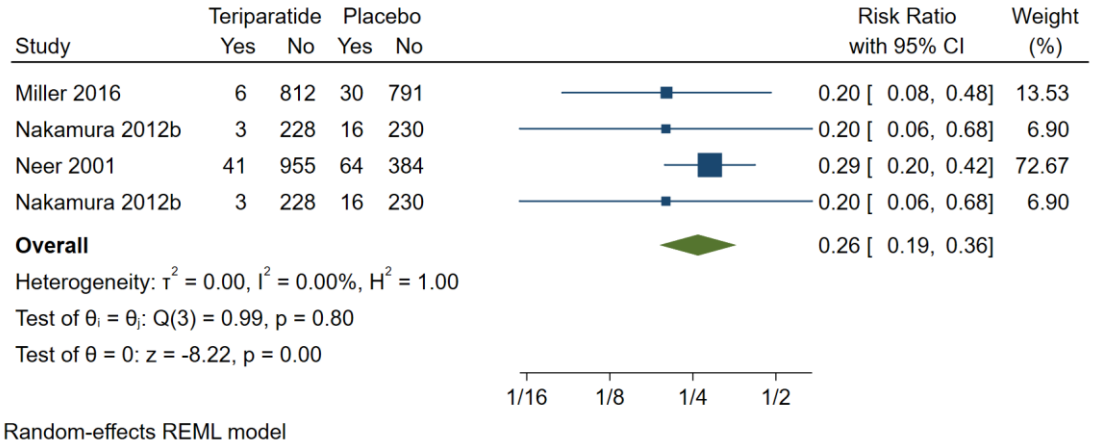
eFigure 13. Romosozumab Compared with Placebo on Vertebral Fracture.



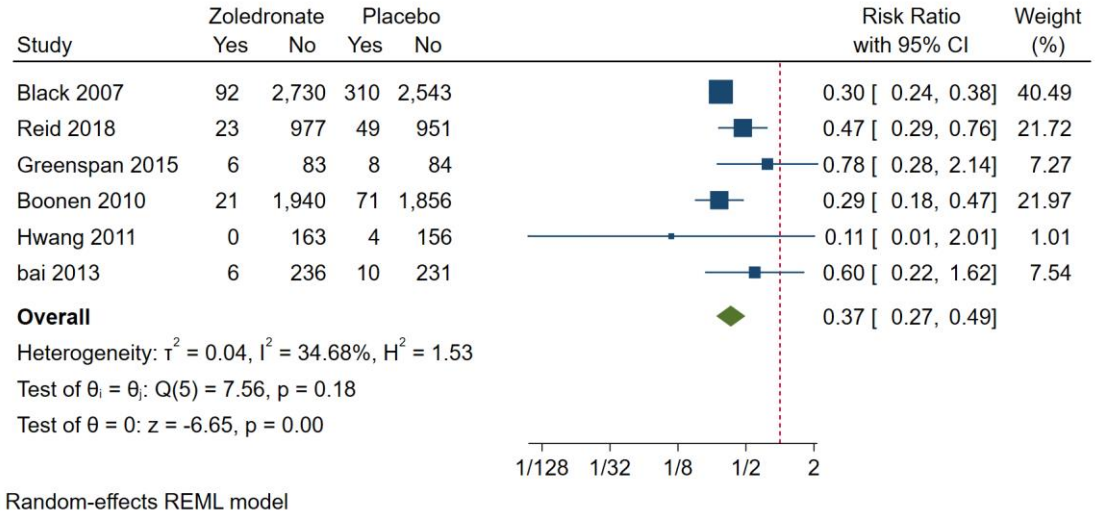
eFigure 14. Strontium ranelate Compared with Placebo on Vertebral Fracture.



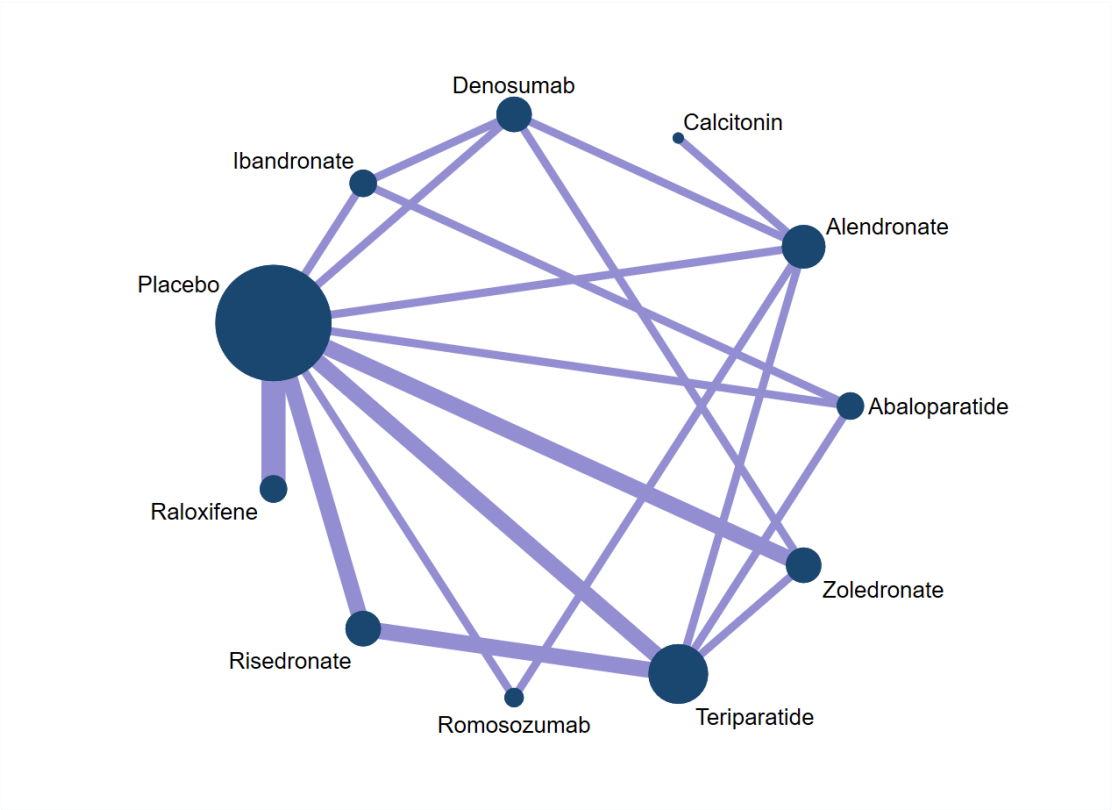
eFigure 15. Teriparatide Compared with Placebo on Vertebral Fracture.



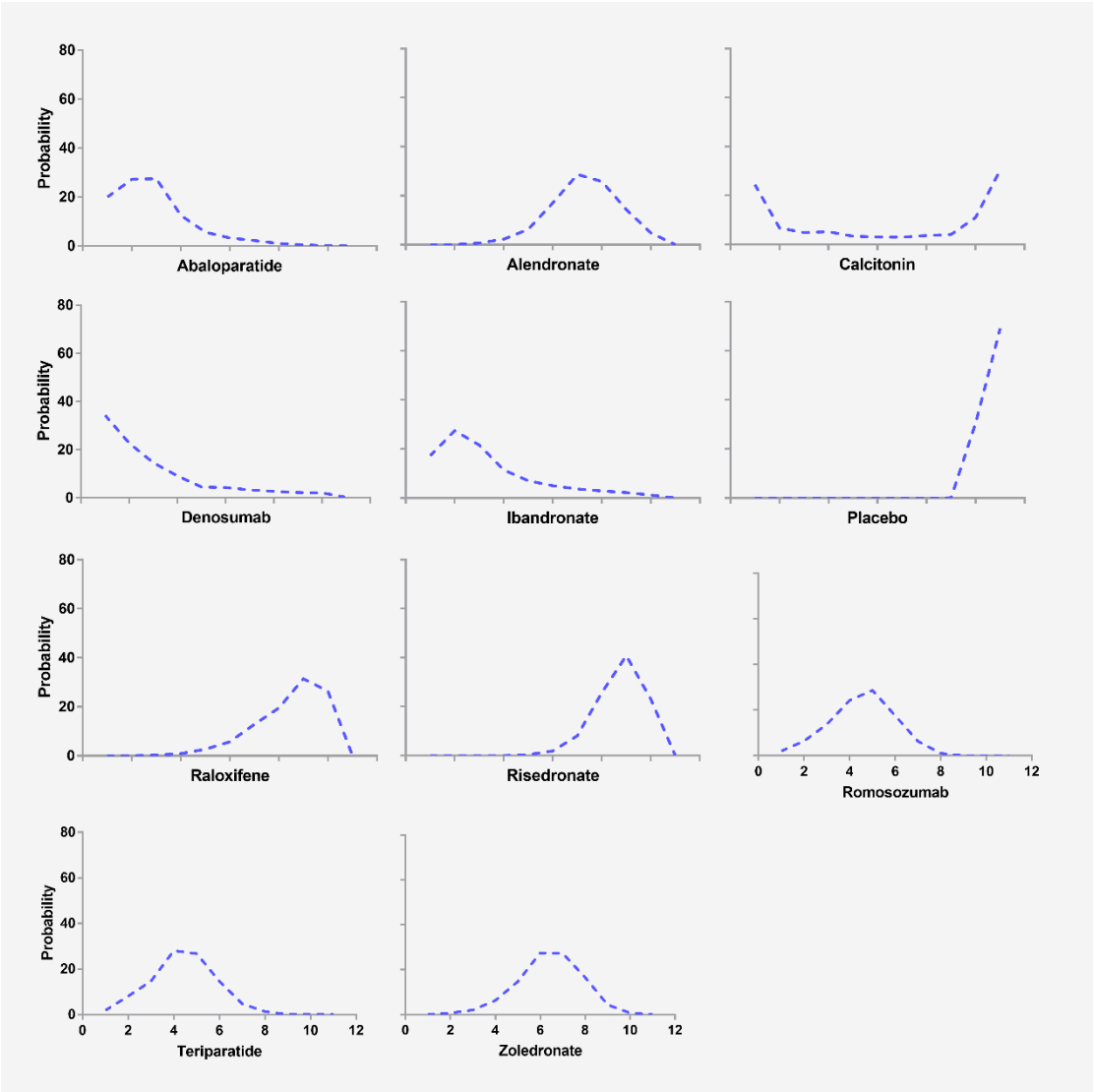
eFigure 16. Zoledronate Compared with Placebo on Vertebral Fracture.



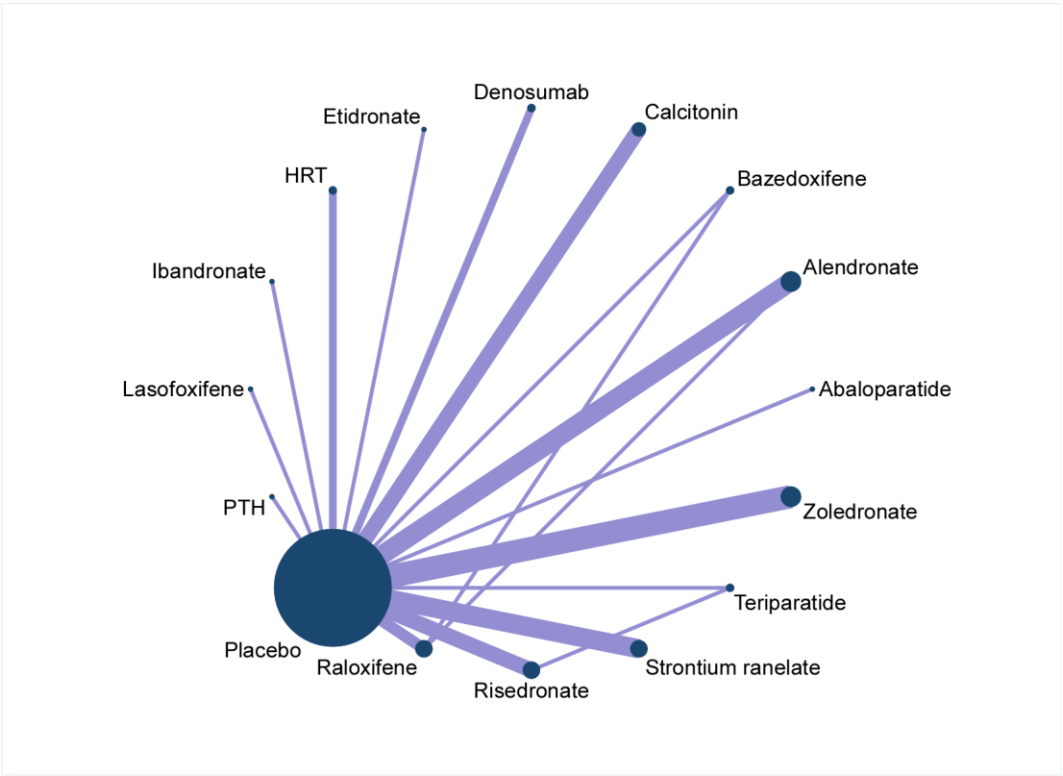
eFigure 17. Network Plots of Comparison-based Network Meta-analyses on Vertebral Fracture in Short-term (≤ 18 months) Follow-up.



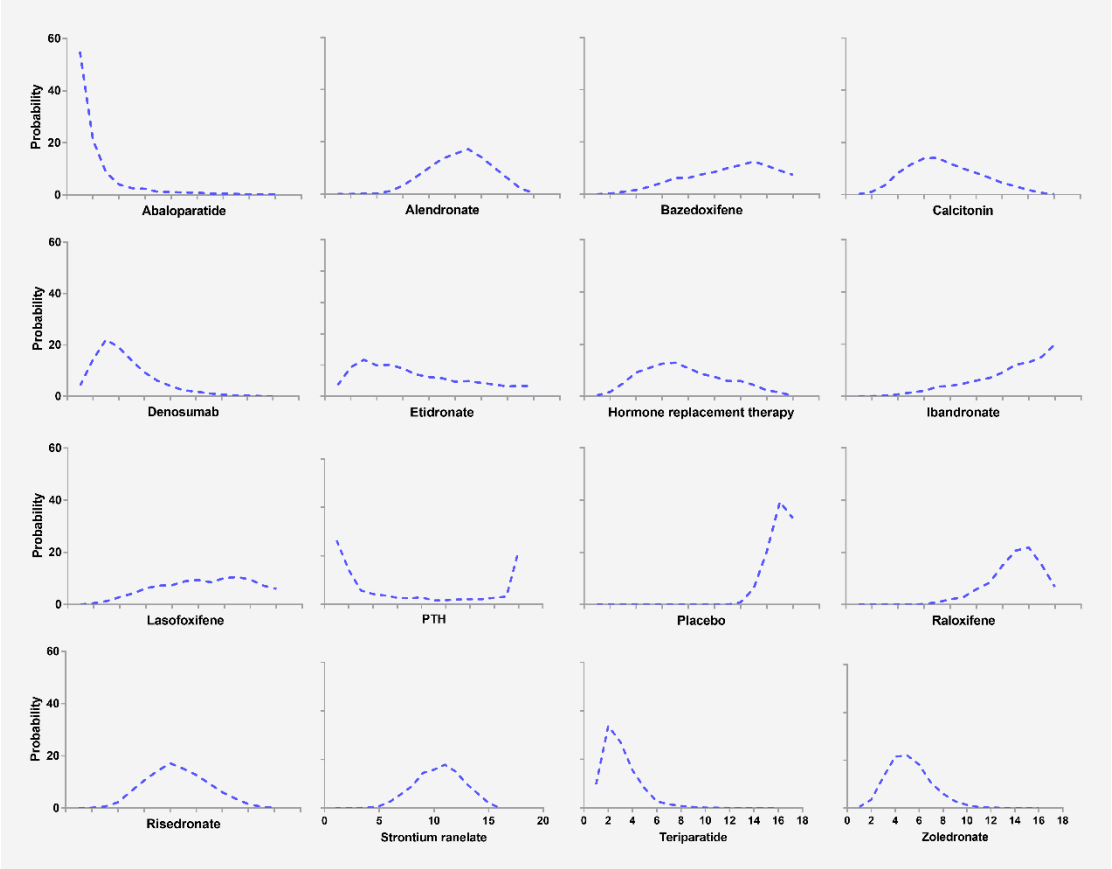
eFigure 18. Rank Probability of Vertebral Fracture in Short-term (≤ 18 months) Follow-up Based Network Meta-analysis in the Consistency Model.



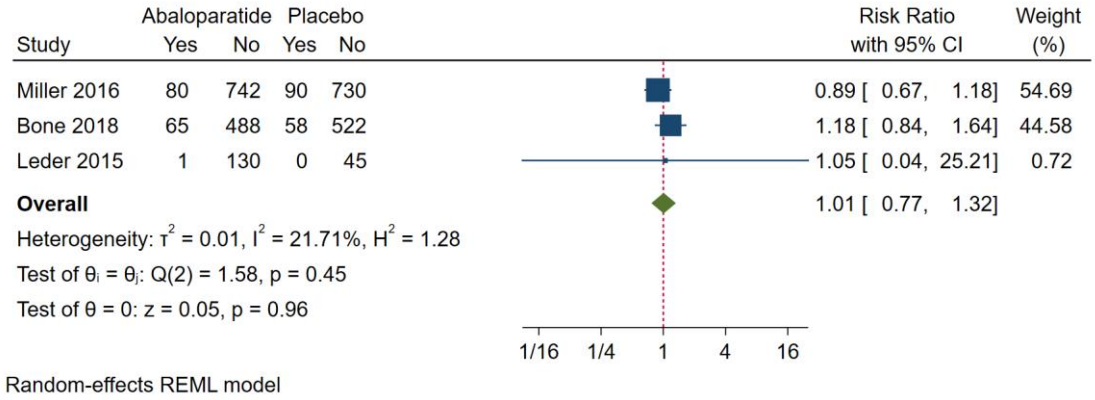
eFigure 19. Network Plots of Comparison-based Network Meta-analyses on Vertebral Fracture in Long-term (> 18 months) Follow-up.



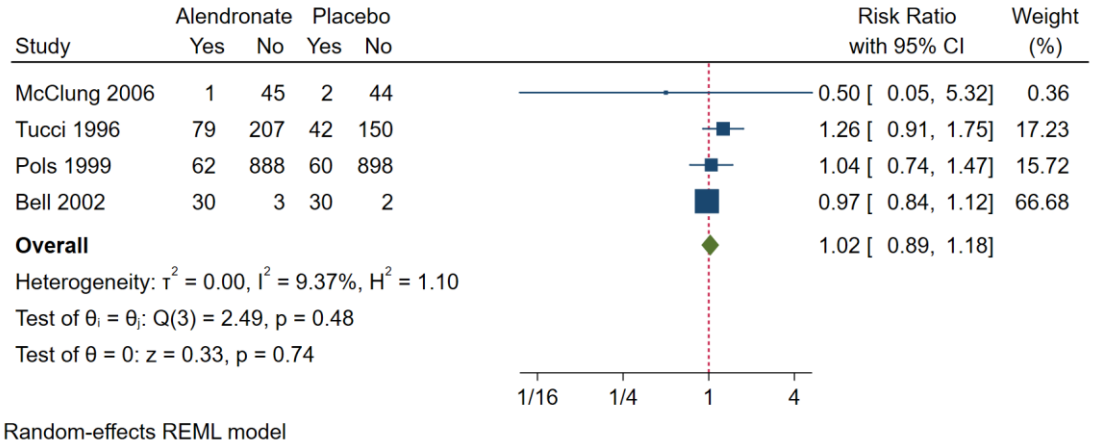
eFigure 20. Rank Probability of Vertebral Fracture in Long-term (> 18 months) Follow-up Based Network Meta-analysis in the Consistency Model.



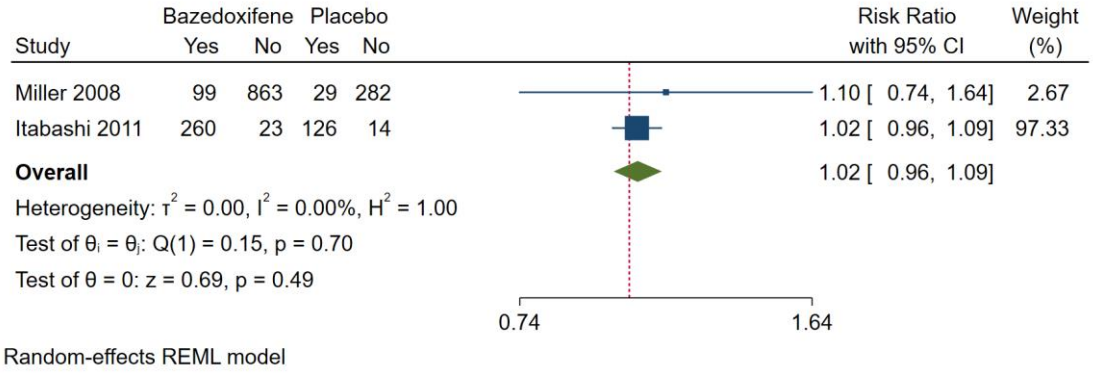
eFigure 21. Abaloparatide Compared with Placebo on Serious Adverse Event.



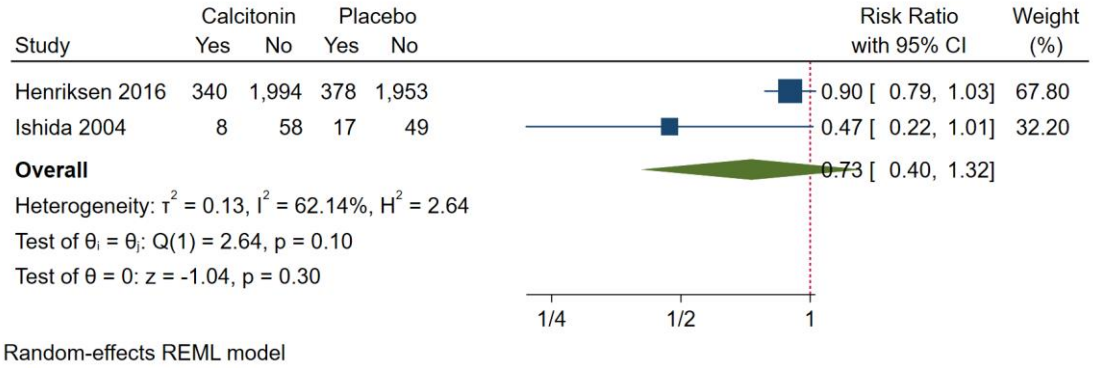
eFigure 22. Alendronate Compared with Placebo on Serious Adverse Event.



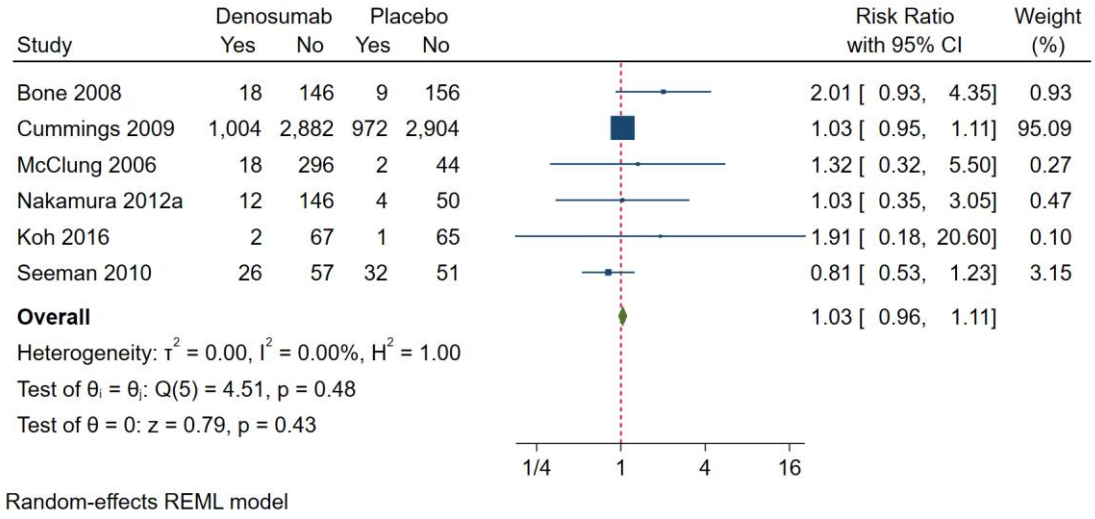
eFigure 23. Bazedoxifene Compared with Placebo on Serious Adverse Event.



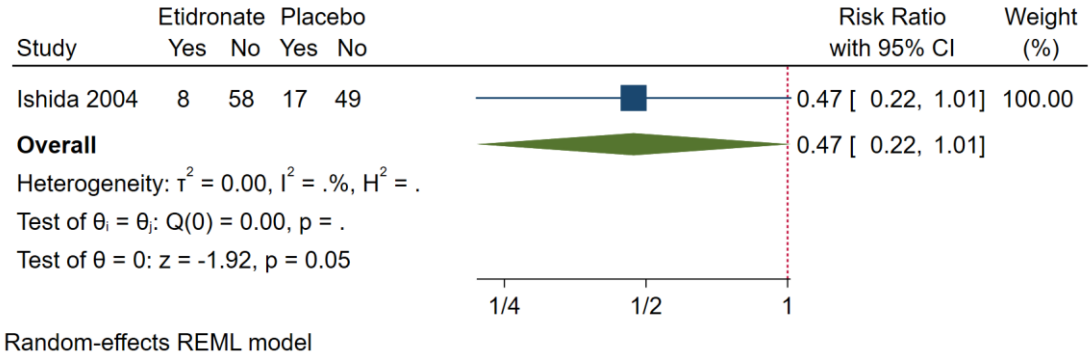
eFigure 24. Calcitonin Compared with Placebo on Serious Adverse Event.



eFigure 25. Denosumab Compared with Placebo on Serious Adverse Event.

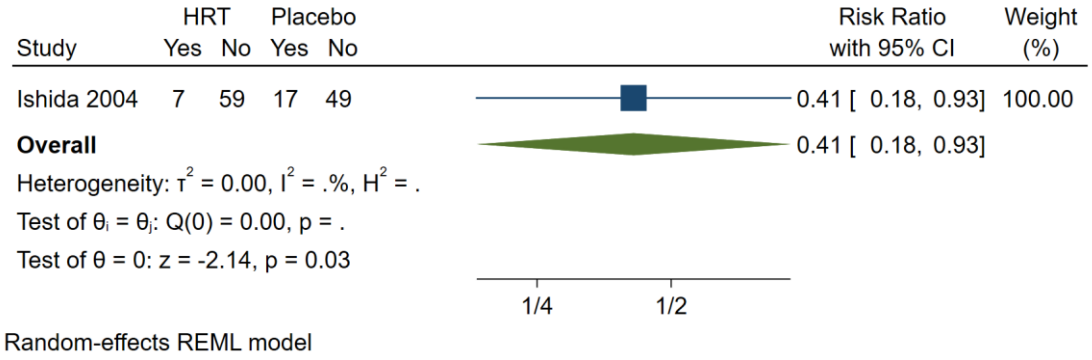


eFigure 26. Etidronate Compared with Placebo on Serious Adverse Event.



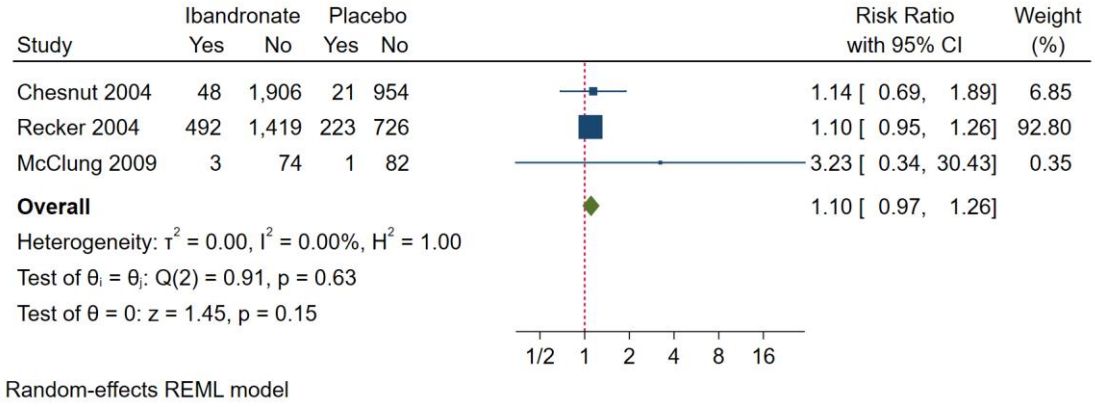
Random-effects REML model

eFigure 27. HRT Compared with Placebo on Serious Adverse Event.



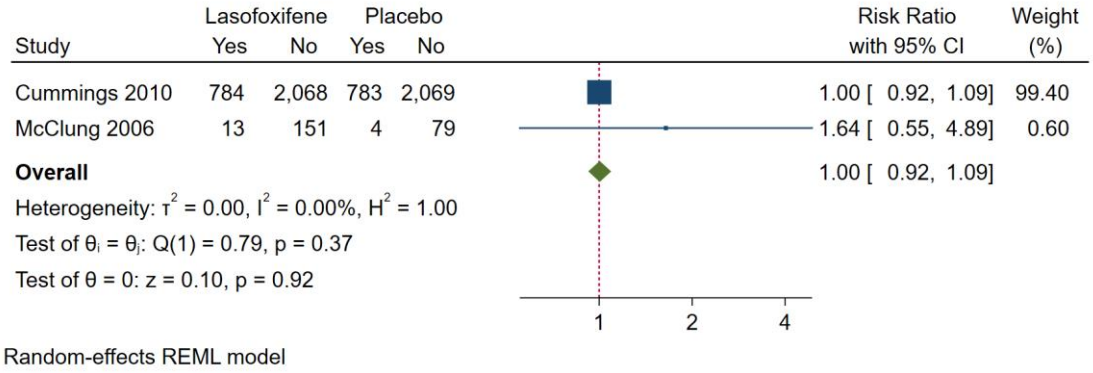
Random-effects REML model

eFigure 28. Ibandronate Compared with Placebo on Serious Adverse Event.



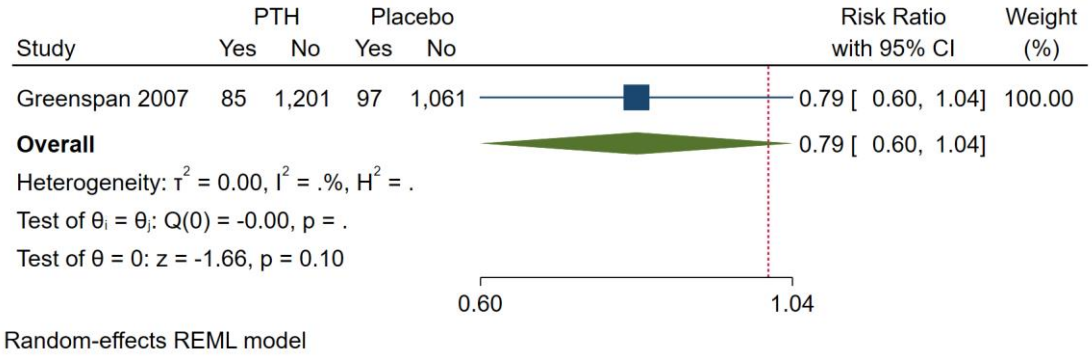
Random-effects REML model

eFigure 29. Lasofoxifene Compared with Placebo on Serious Adverse Event.

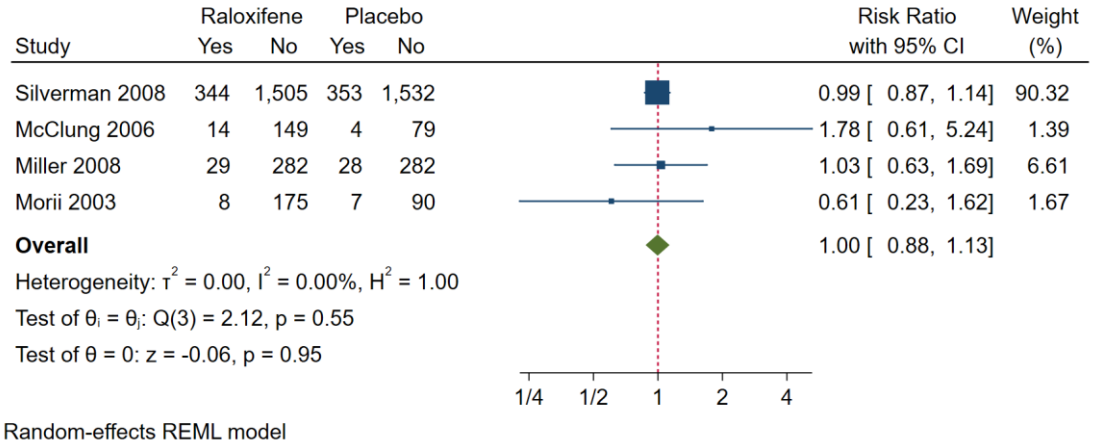


Random-effects REML model

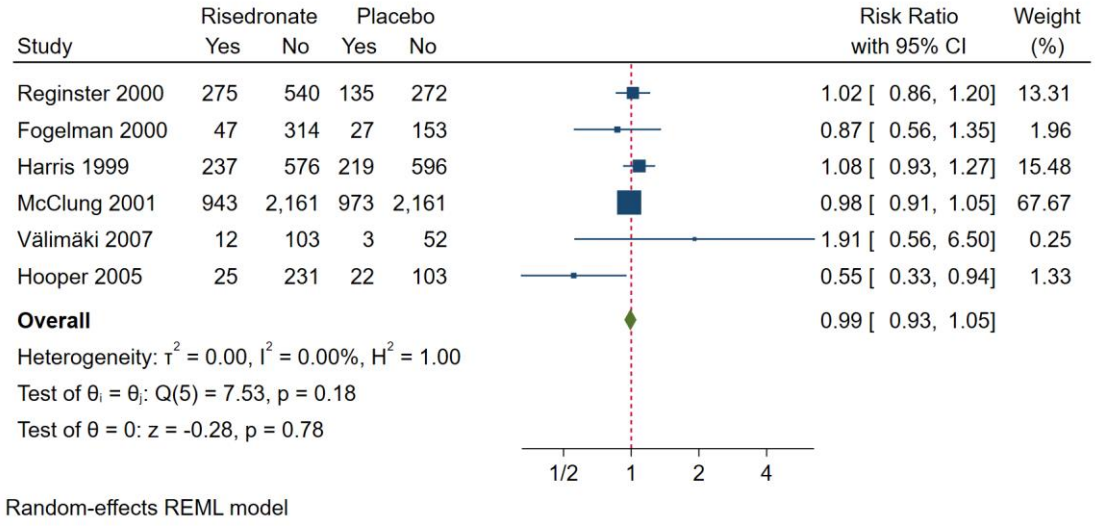
eFigure 30. PTH Compared with Placebo on Serious Adverse Event.



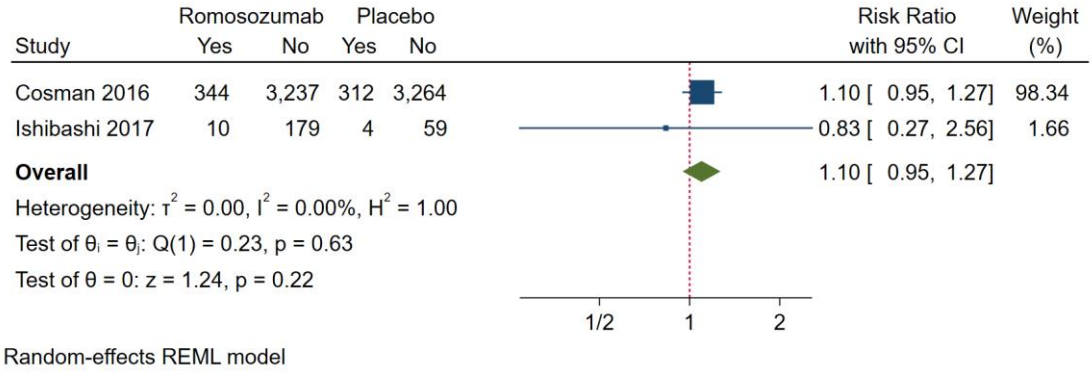
eFigure 31. Raloxifene Compared with Placebo on Serious Adverse Event.



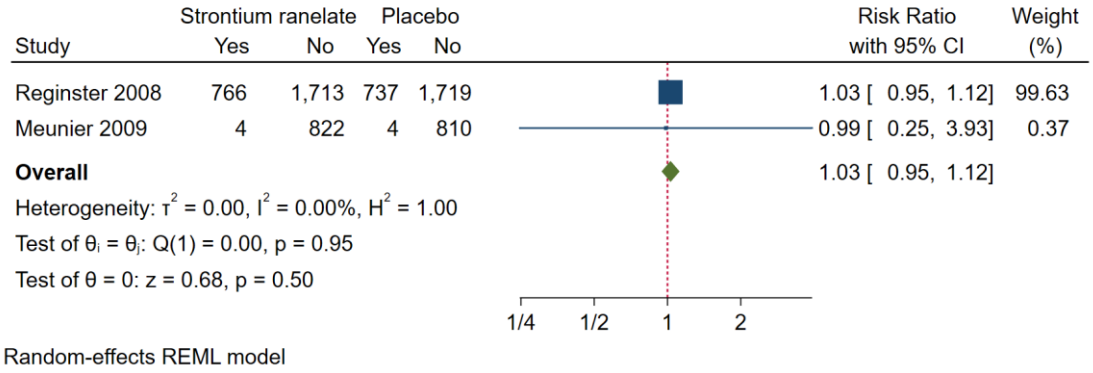
eFigure 32. Risedronate Compared with Placebo on Serious Adverse Event.



eFigure 33. Romosozumab Compared with Placebo on Serious Adverse Event.

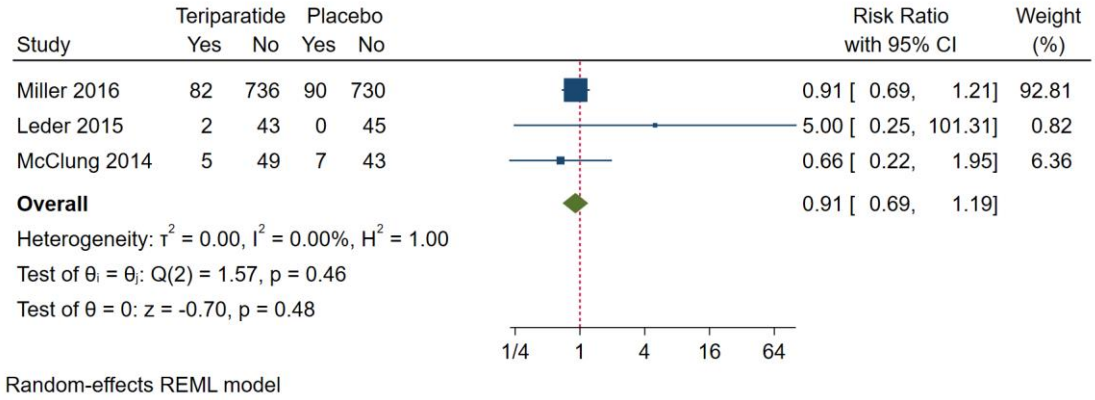


eFigure 34. Strontium ranelate Compared with Placebo on Serious Adverse Event.



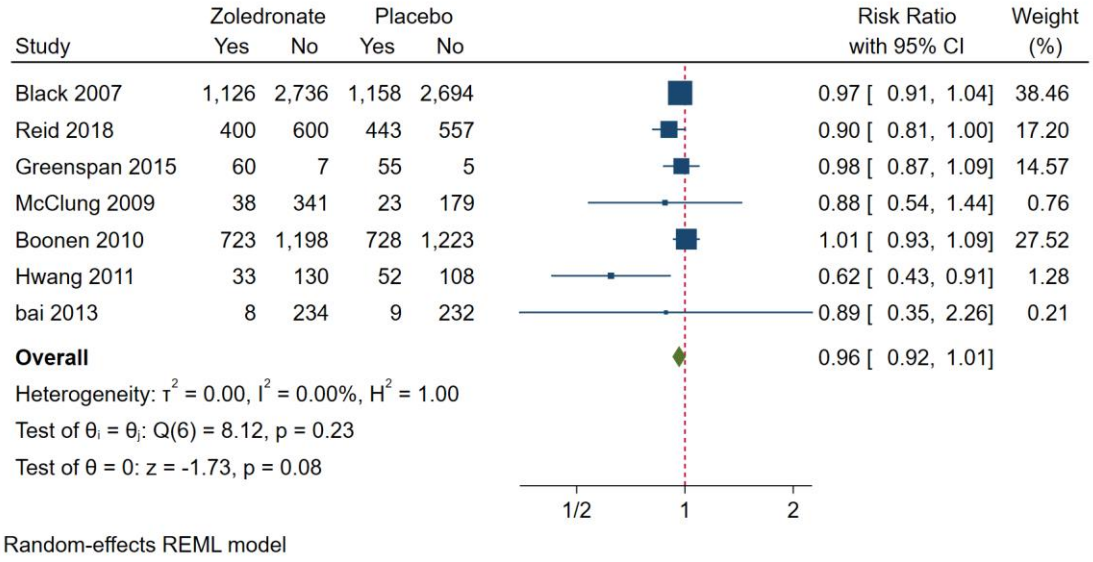
Random-effects REML model

eFigure 35. Teriparatide Compared with Placebo on Serious Adverse Event.

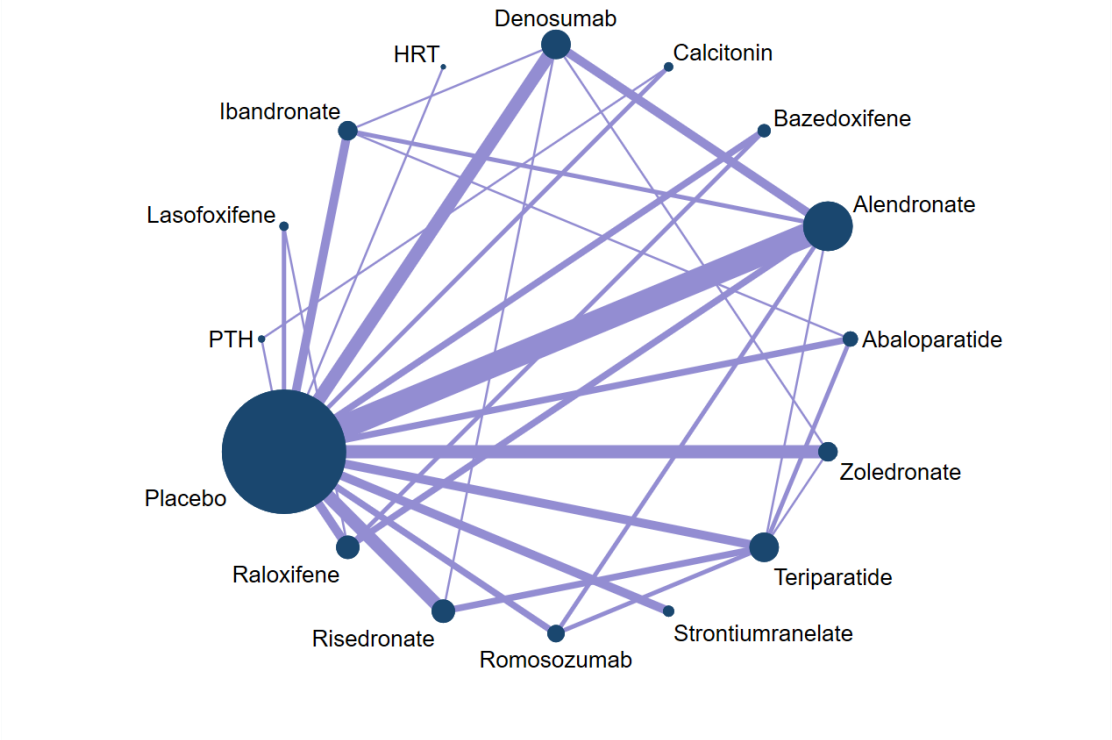


Random-effects REML model

eFigure 36. Zoledronate Compared with Placebo on Serious Adverse Event.

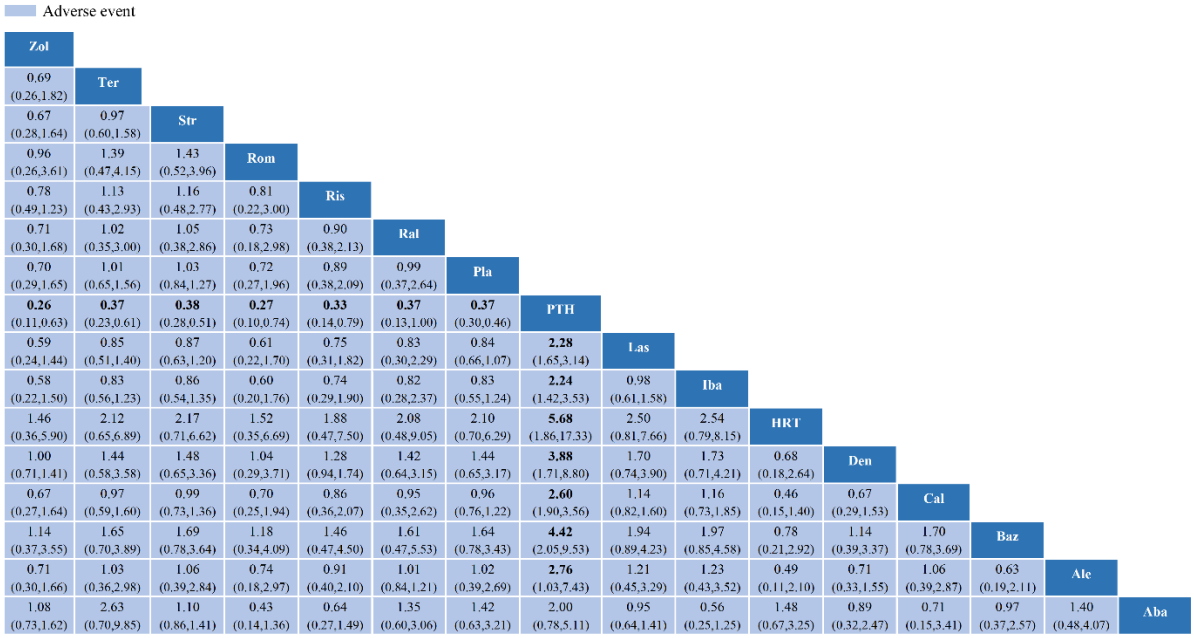


eFigure 37. Network Plots of Comparison-based Network Meta-analyses on All Adverse Event.



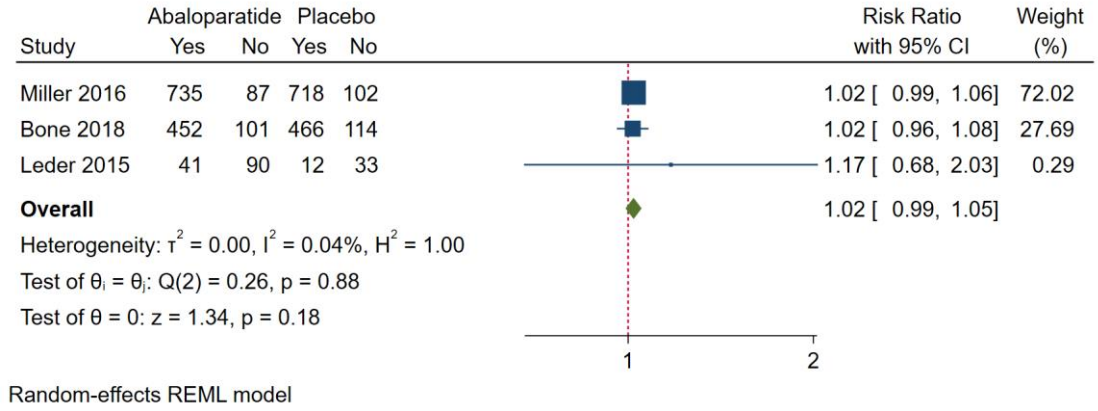
Each circular node represents a type of intervention. The circle size is proportional to the total number of patients. The width of the lines is proportional to the number of studies performing head-to-head comparisons in the same study. HRT: Hormone replacement therapy; PTH: parathyroid hormone.

eFigure 38. Adverse event based on network meta-analysis in the inconsistency model.

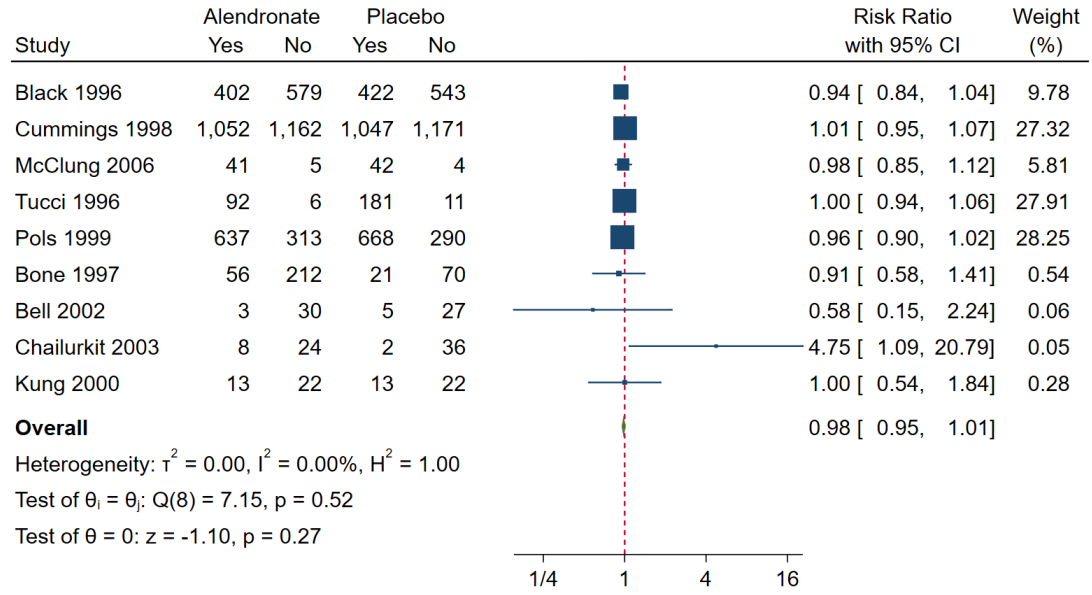


Each cell of the profile contains the pooled mean difference and 95% credibility intervals for disability change; significant results are in bold. Aba: Abaloparatide; Ale:Alendronate; Baz: Bazedoxifene; Cal: Calcitonin; Den: Denosumab; HRT: Hormone replacement therapy; Iba: Ibandronate; Las: Lasofoxifene; PTH: parathyroid hormone; Ral: Raloxifene; Ris: Risedronate; Rom: Romosozumab; Str: Strontiumranelate; Ter: Teriparatide; Zol: Zoledronate.

eFigure 39. Abaloparatide Compared with Placebo on All Adverse Event.

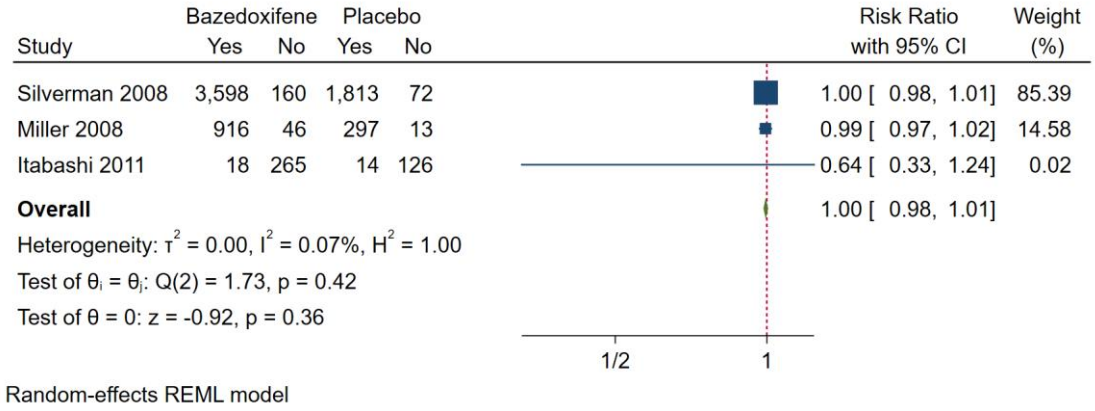


eFigure 40. Alendronate Compared with Placebo on All Adverse Event.

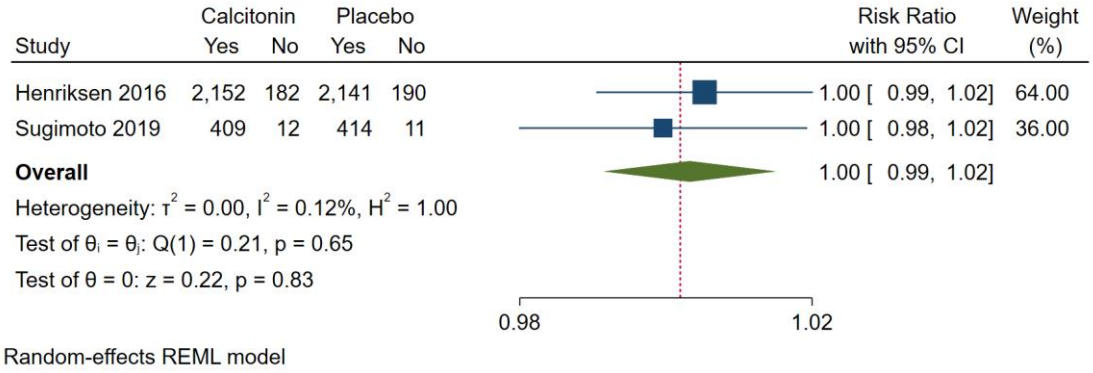


Random-effects REML model

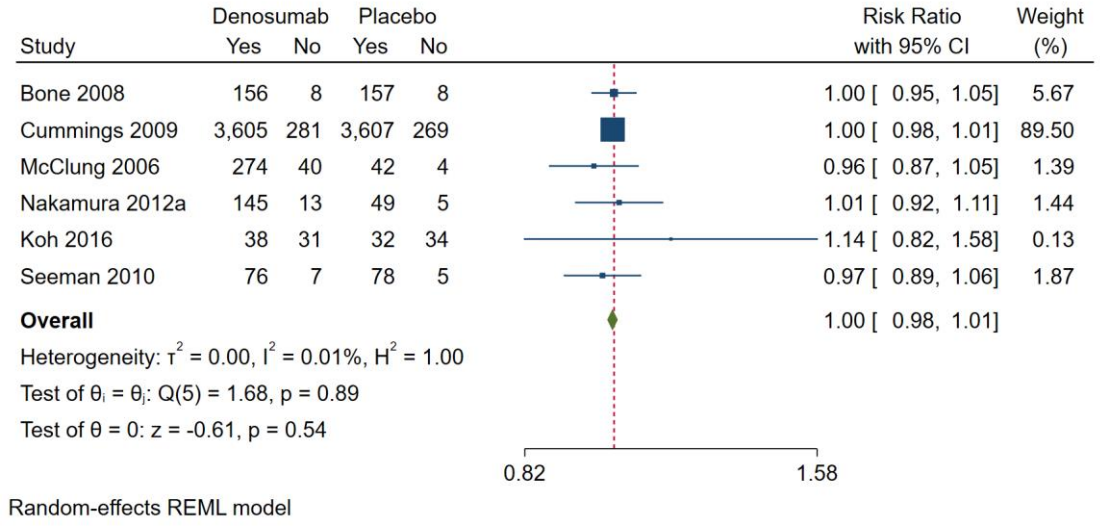
eFigure 41. Bazedoxifene Compared with Placebo on All Adverse Event.



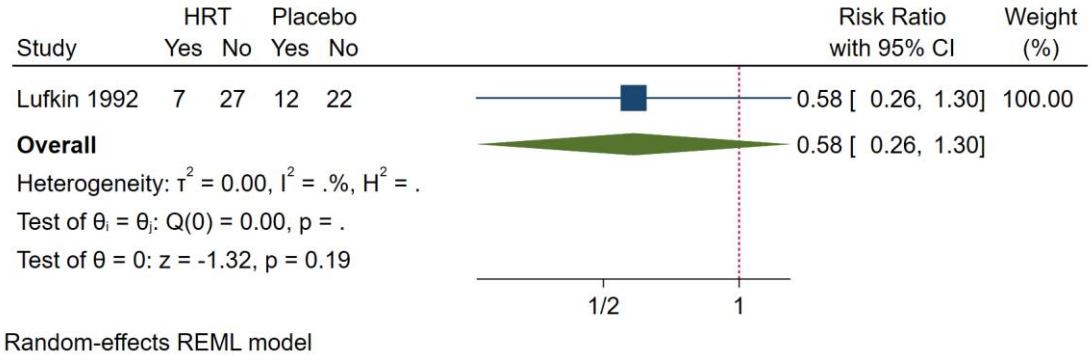
eFigure 42. Calcitonin Compared with Placebo on All Adverse Event.



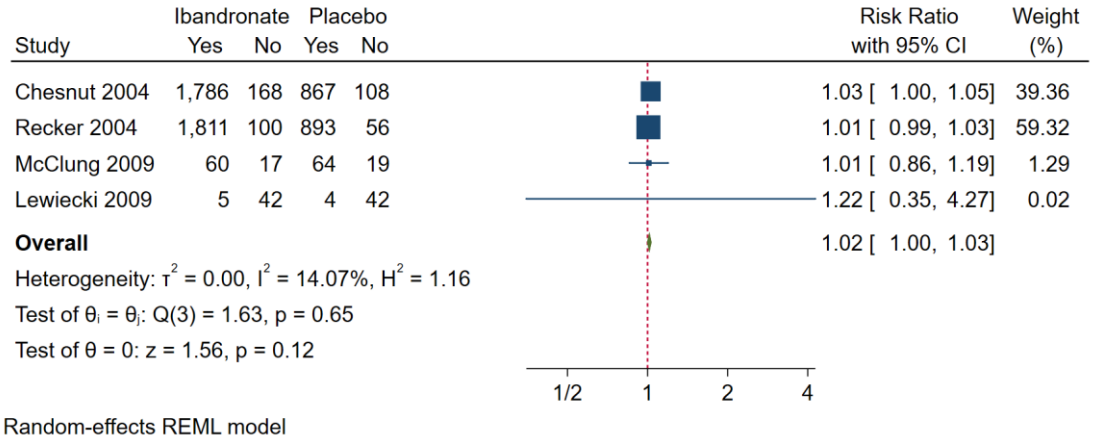
eFigure 43. Denosumab Compared with Placebo on All Adverse Event.



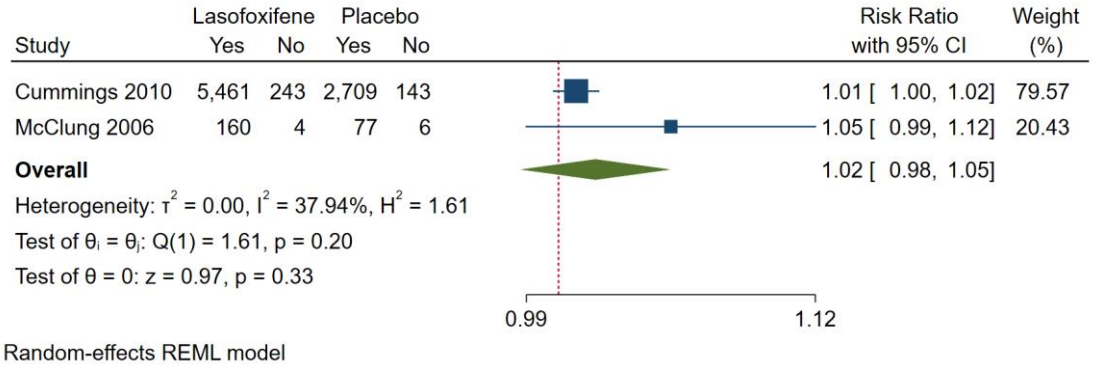
eFigure 44. HRT Compared with Placebo on All Adverse Event.



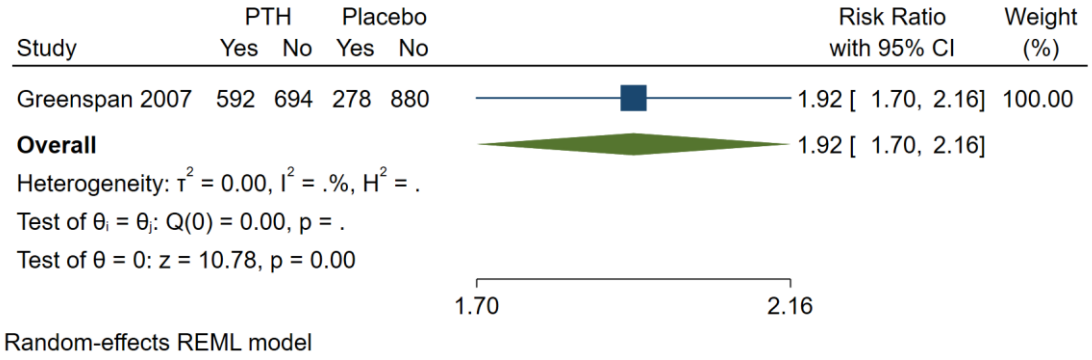
eFigure 45. Ibandronate Compared with Placebo on All Adverse Event.



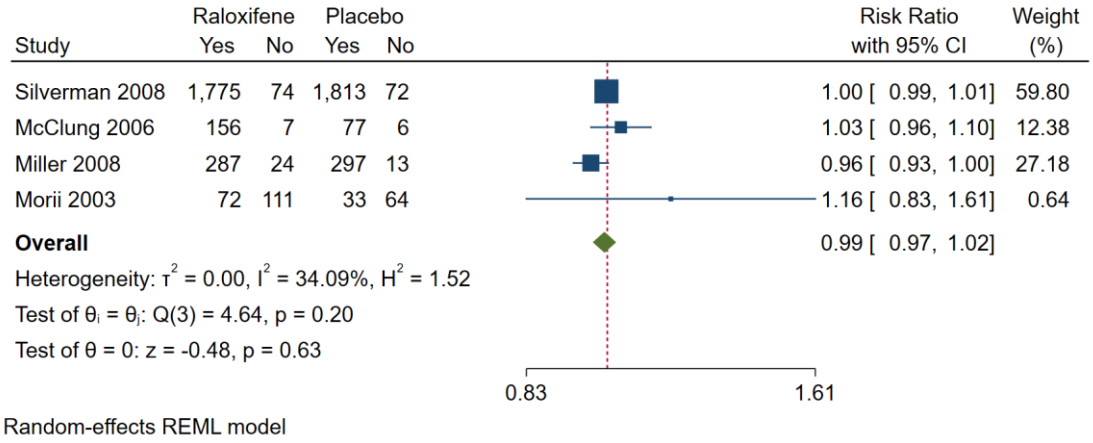
eFigure 46. Lasofoxifene Compared with Placebo on All Adverse Event.



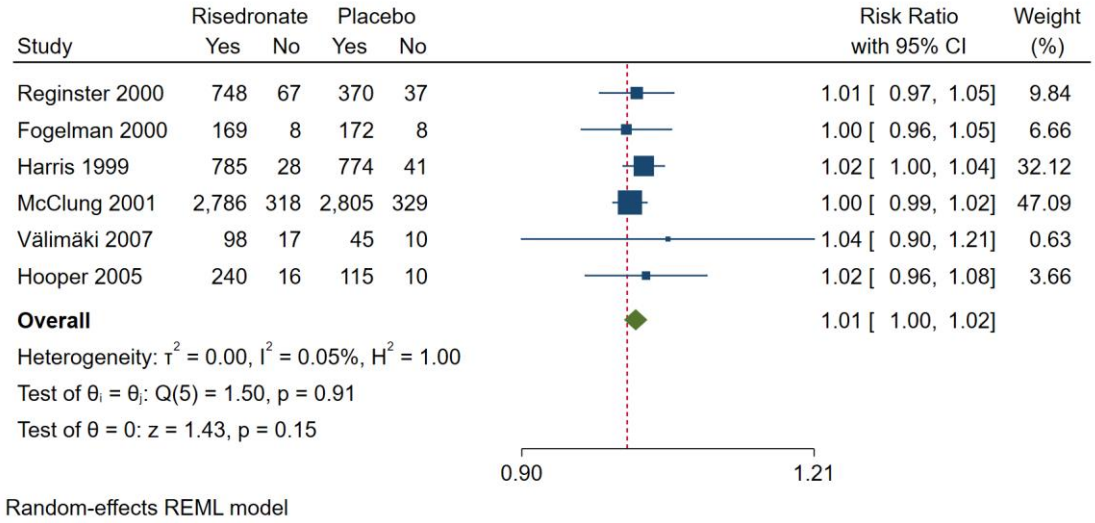
eFigure 47. PTH Compared with Placebo on All Adverse Event.



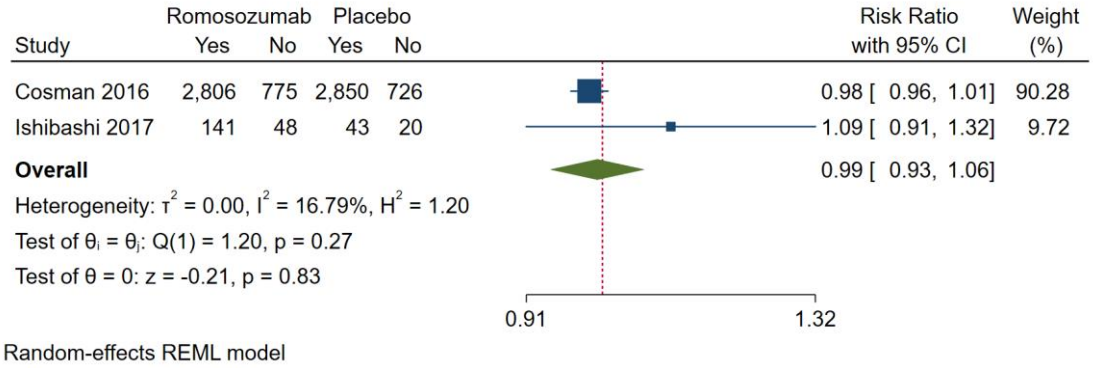
eFigure 48. Raloxifene Compared with Placebo on All Adverse Event.



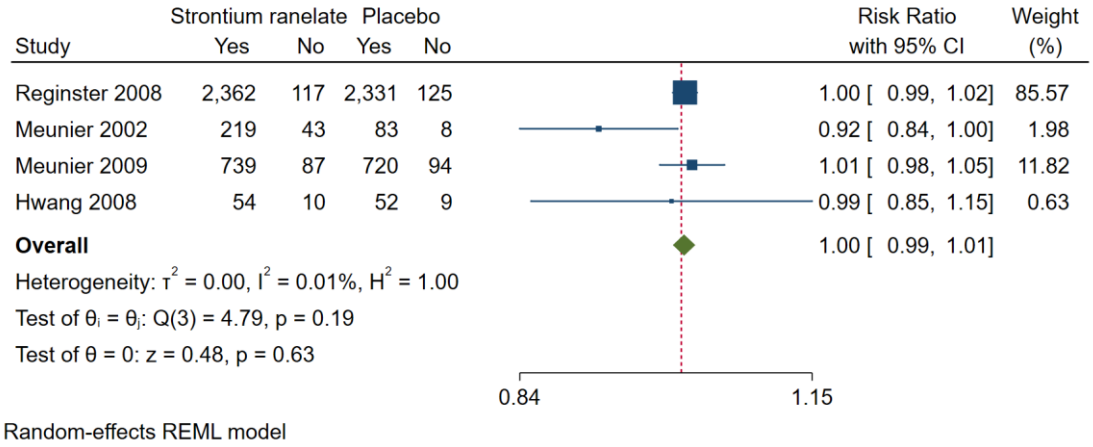
eFigure 49. Risedronate Compared with Placebo on All Adverse Event.



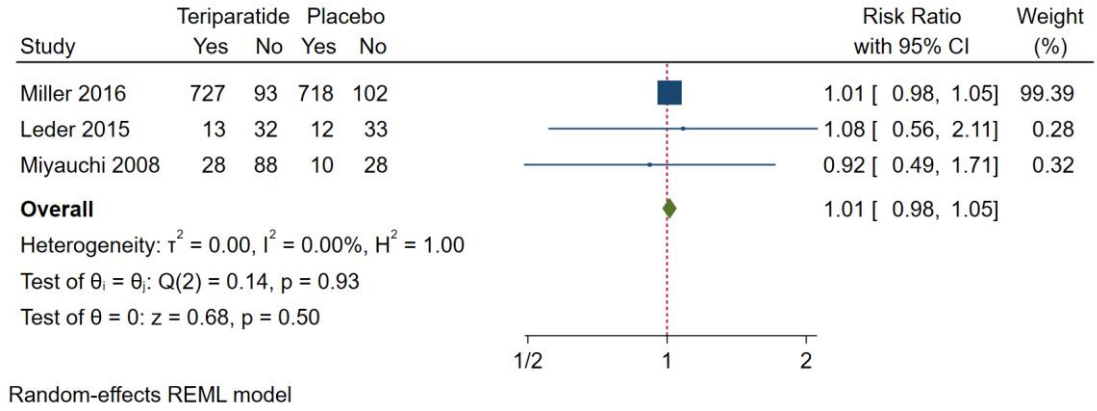
eFigure 50. Romosozumab Compared with Placebo on All Adverse Event.



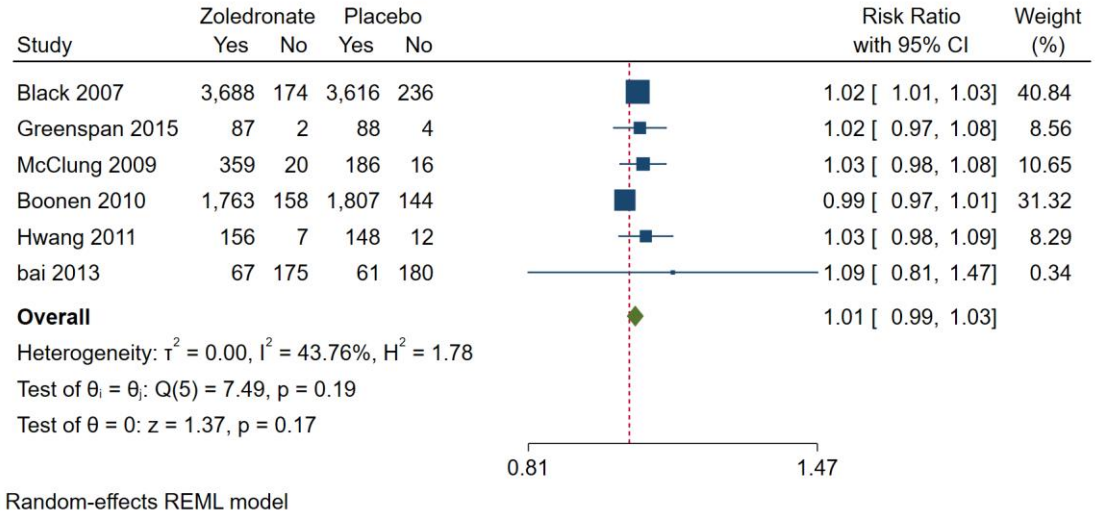
eFigure 51. Strontium Ranelate Compared with Placebo on All Adverse Event.



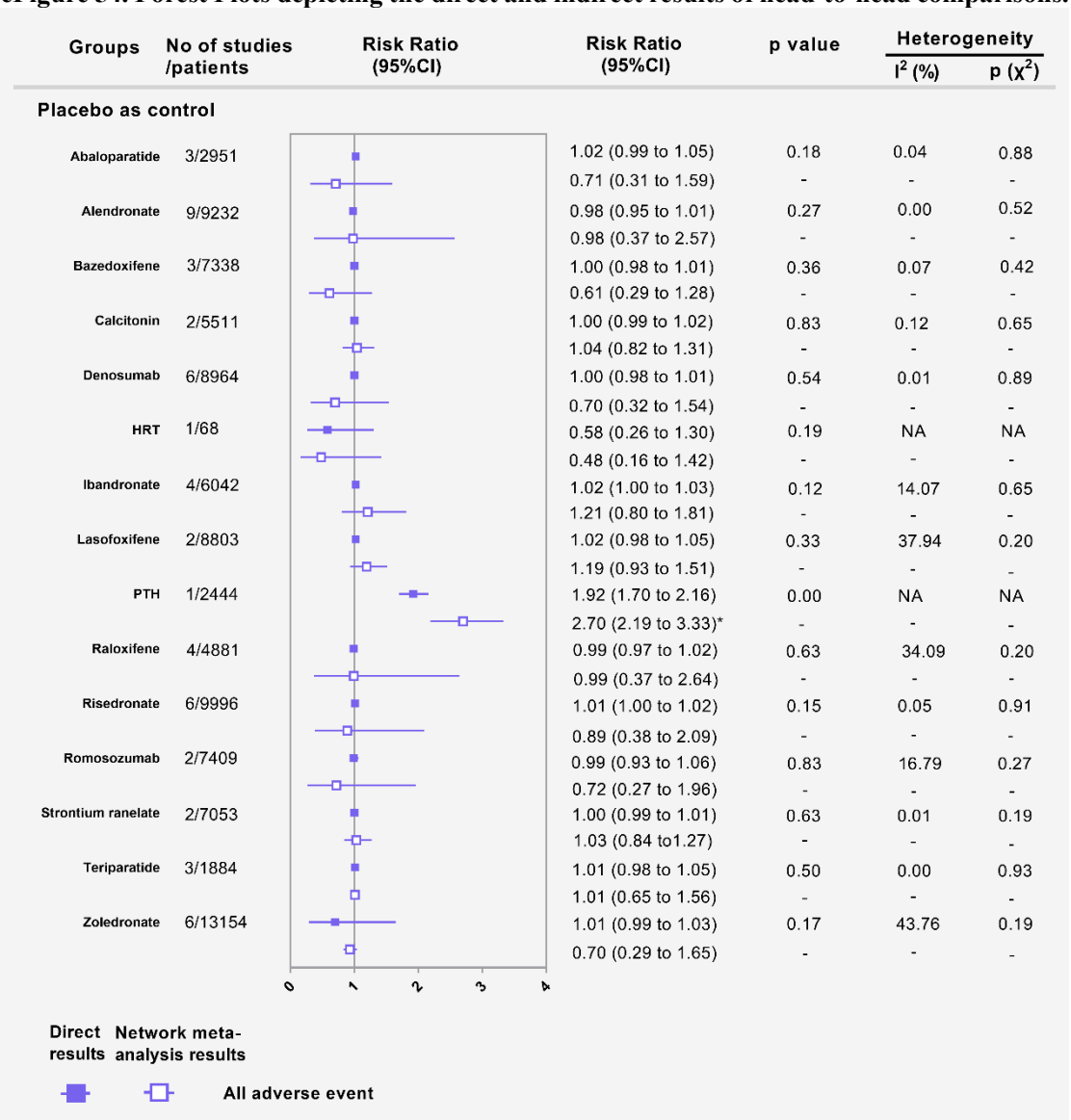
eFigure 52. Teriparatide Compared with Placebo on All Adverse Event.



eFigure 53. Zoledronate Compared with Placebo on All Adverse Event.

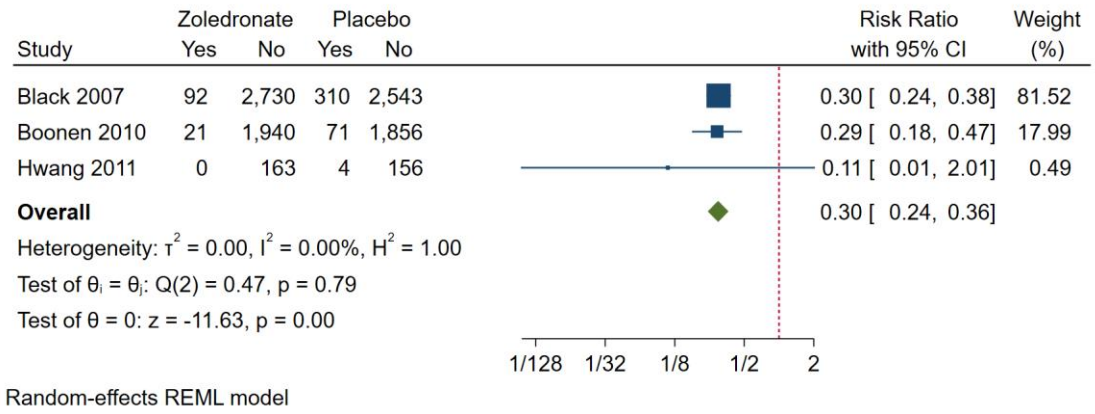


eFigure 54. Forest Plots depicting the direct and indirect results of head-to-head comparisons.

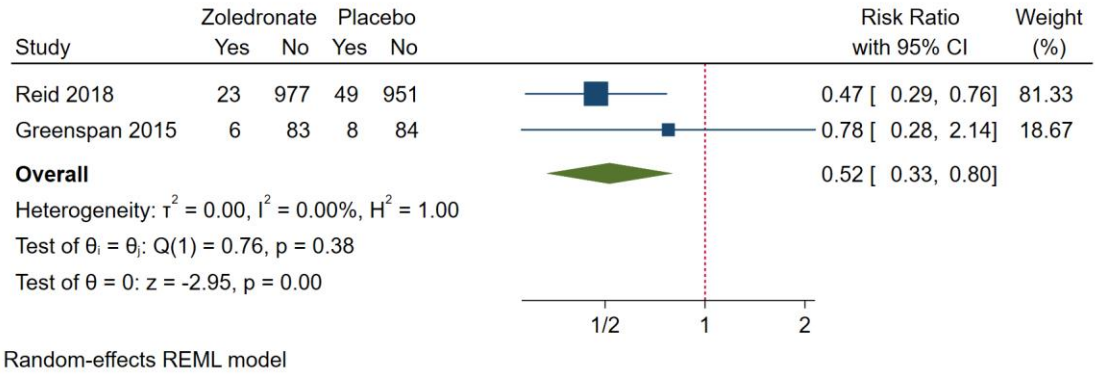


*Values in brackets are 95% CI.

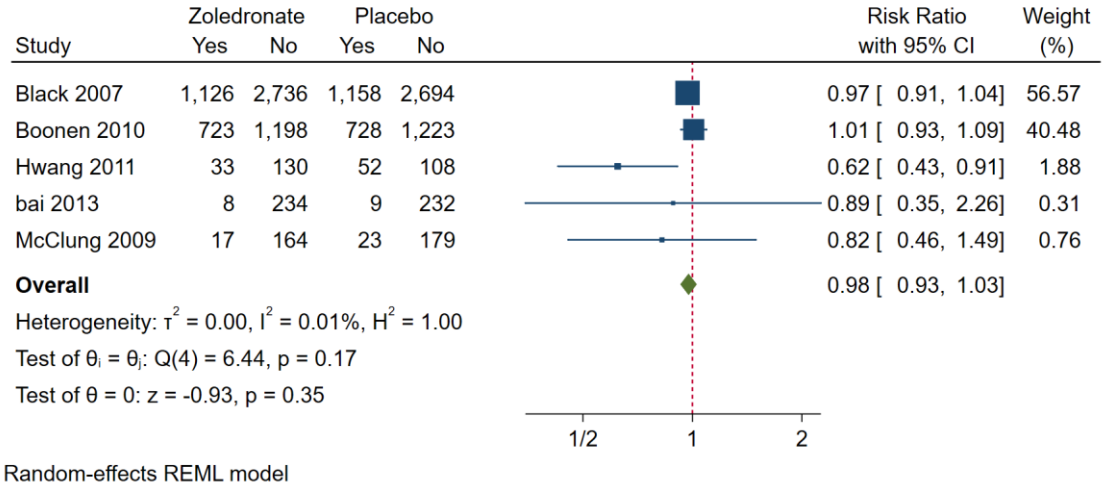
eFigure 55. Sensitivity analyses based on the frequency of administration (5 mg zoledronate once a year: vertebral fractures).



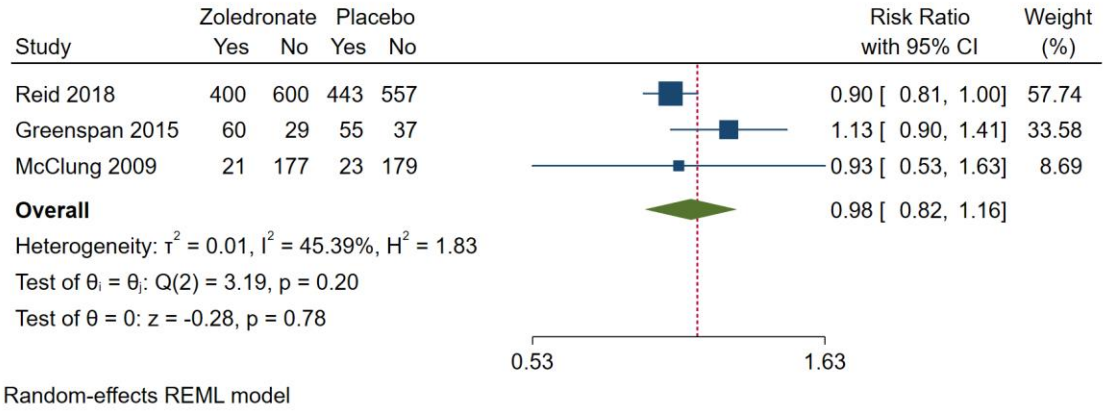
eFigure 56. Sensitivity analyses based on the frequency of administration (other frequency of 5 mg zoledronate: vertebral fractures).



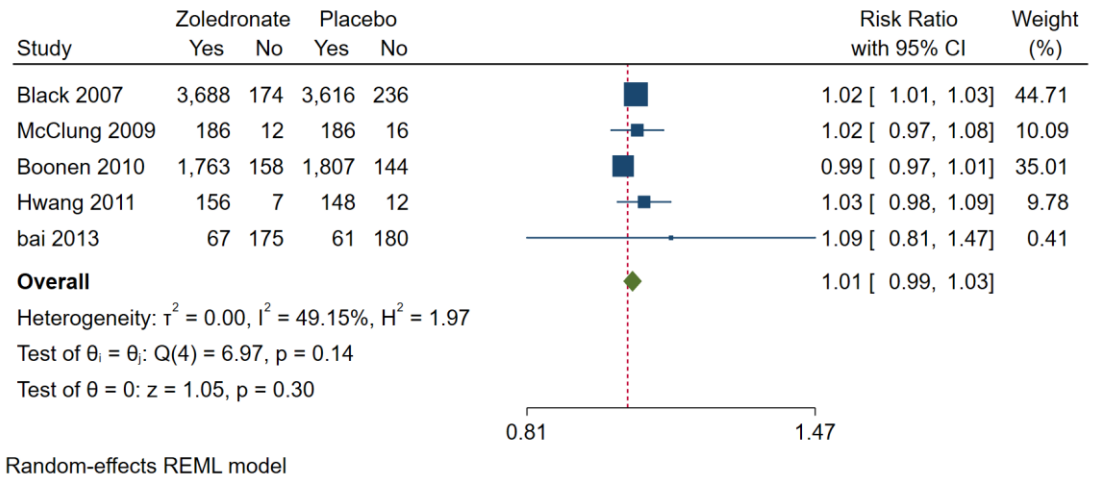
eFigure 57. Sensitivity analyses based on the frequency of administration (5 mg zoledronate once a year: serious adverse event).



eFigure 58. Sensitivity analyses based on the frequency of administration (other frequency of 5 mg zoledronate: serious adverse event).



eFigure 59. Sensitivity analyses based on the frequency of administration (5 mg zoledronate once a year: all adverse event).



eFigure 60. Sensitivity analyses based on the frequency of administration (other frequency of 5 mg zoledronate: all adverse event).