

Supplementary Materials Content

for Efficacy and safety of postmenopausal osteoporosis treatments

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Table S1: Search Strategies

A	postmenopause osteoporosis OR post-menopause osteoporosis OR postmenopausal osteoporosis OR post-menopausal osteoporosis (<i>MeSHTerms</i>)
B	vitamin D OR calcium OR (bisphosphat* OR bis-phosphat* OR bisphosphonate* OR bis-phosphonate*) OR (Alendronate* OR alendronic acid* OR Fosamax OR Binosto OR Alendro* OR Marvil OR osmak) OR (Ibandronate* OR Ibandronic acid* OR Boniva OR Bondronat OR Bonviva) OR (Risedronate* OR Risedronic acid* OR Actonel OR Atelvia OR Benet OR Gusong OR Ribastamin OR Ribone OR Risofos) OR (Zoldronate* OR Zoldronic acid OR Zometa OR Reclast OR Aclasta) OR (Clodronate OR clodronic acid OR Bonefos) OR (Etidronate* OR etidronic acid* OR Didronel) OR (Pamidronate* OR pamidronic acid* OR Aredia) OR (Minodronate* OR minodronic acid*) OR (Tiludronate* OR tiludronic acid* OR Skelid) OR (Neridronate* OR neridronic acid*) OR (Olpadronate* OR olpadronic acid*) OR (Estrogen* OR Estradiol* OR norethisterone OR nor-ethisterone OR Medroxyprogesterone) OR (SERMs* OR Raloxifene OR Tamoxifen OR Toremifene OR Raloxifene OR Bazedoxifene) OR (parathyroid* OR PTH(1-34) OR Teriparatide OR PTH(1-84)) OR (Calcitonin OR Fortical) OR (RANK* OR monoantibod* or mono-antibod* or Denosumab) OR (Isoflavone OR Genistein) OR sodium fluoride OR (ranelic* OR Strontium ranelate) OR (steroid OR Tibilone) OR (diuretic* OR Hydrochlorothiazide OR Hydrochlorothiazide) OR (statin* OR Atrovastatin OR Fluvastatin OR lovastatin OR Pravastatin OR Rosuvastatin) OR (nitrate* OR Nitric oxide) OR (beta-blocker* or betablocker*) (<i>All fields</i>)
A AND B	Filters activated: Clinical Trial , Publication date to 2020/10/31 , Humans , Female .

Table S2: The Excluded Studies at Full-text Stage with Reasons of Exclusion

Study	Reasons
(Bonnick, S. et al. 2007 ¹ , Chen, M. et al. 2001 ² , Iseri, K. et al. 2018 ³ , Rubinacci, A. et al. 2003 ⁴ , Braga, de Castro Machado A. et al. 1999 ⁵ , Castelo-Branco, C. et al. 2000 ⁶ , Cooper, L. et al. 2003 ⁷ , Dawson-Hughes, B. et al. 1990 ⁸ , Grados, F. et al. 2003 ⁹ , Haines, C. J. 1995 ¹⁰ , Harris, S. T. et al. 1991 ¹¹ , Hillard, T. C. et al. 1994 ¹² , Jirapinyo, M. et al. 2003 ¹³)	Non-aging-related postmenopausal osteoporosis
(Fitzpatrick, L. A. et al. 2011 ¹⁴ , You, L. et al. 2010 ¹⁵ , Bhattoa, H. P. et al. 2004 ¹⁶ , Watts, N. B. et al. 2003 ¹⁷ , Bell, N. H. et al. 2002 ¹⁸ , Greenspan, S. L. et al. 2002 ¹⁹ , Greenspan, S. L. et al. 2003 ²⁰)	Patients with osteopenia included
(Grbic, J. T. et al. 2008 ²¹)	Previous treatment for postmenopausal osteoporosis and continuous medication
(Chung, Ys. et al. 2009 ²² , Devogelaer, Jp. et al. 2007 ²³ , Gallagher, J. C. et al. 2006 ²⁴ , Cryer, B. et al. 2005 ²⁵ , Iwamoto, J. et al. 2004 ²⁶ , Iwamoto, J. et al. 2004 ²⁷ , Keaveny, M. et al, 2007 ²⁸ , Kung, A. W. et al, 2009 ²⁹ , Ljunghall, S. et al, 1991 ³⁰ , Lufkin, E. G. et al, 1994 ³¹ , Majima, T. et al. 2008 ³² , Gruber, H. E. et al. 1984 ³³ , Miller, P. D. et al. 2000 ³⁴ , Reid, I. R. et al. 2010 ³⁵ , Riggs, B. L. et al. 1982 ³⁶ , Stepan, J. J. et al. 2007 ³⁷ , Van Der Poest Clement, E. et al. 2000 ³⁸)	BMD was not reported as percentage increase or no concerned adverse effects (death, cancer, CVD, hip fracture, ONJ)
(Engelke, K. et al. 2014 ³⁹ , Yang, L. et al. 2013 ⁴⁰)	BMD was measured as volumetric BMD (vBMD)
(Arcoraci, V. et al. 2017 ⁴¹ , Agnusdei, D. et al. 1992 ⁴² , Gonnelli, S. et al. 1997 ⁴³ , Moscarini, M. et al. 1994 ⁴⁴ , Nakamura, T. et al. 2014 ⁴⁵ , Saaf, M. et al. 1999 ⁴⁶ , Zhang, X. et al. 2010 ⁴⁷ , Zhao, G. et al. 2003 ⁴⁸ , Eastell, R. et al. 2011 ⁴⁹ , Eastell, R. et al. 2014 ⁵⁰ , Cecchetti, M. et al. 1995 ⁵¹ , Chee, W. S. S. et al. 2003 ⁵² , Choi, Y. K. et al. 1997 ⁵³ , Douglas, A. S. et al. 1995 ⁵⁴ , Greendale, G. A. et al. 2002 ⁵⁵ , Hampson, G. et al. 2003 ⁵⁶ , Kovács, A. B. et al. 1994 ⁵⁷)	Non-pharmaceutical Interventions

(Hagino, H. et al. 2009 ⁵⁸ , Iwamoto, J. et al. 2005 ⁵⁹ , Kushida, K. et al. 2004 ⁶⁰ , Li, M. et al. 2010 ⁶¹ , Miller, P. D. et al. 2008 ⁶² , Reid, D. M. et al. 2008 ⁶³ , Sarioglu, M. et al. 2006 ⁶⁴ , Tanko, L. B. et al. 2003 ⁶⁵ , Balena, R. et al. 1998 ⁶⁶)	Comparison with drugs of the same class
(Suzuki, T. et al. 2018 ⁶⁷ , Gurlek, A. et al. 1997 ⁶⁸ , Lindsay, R. et al. 1997 ⁶⁹ , Orimo, H. et al. 2011 ⁷⁰ , Reid, I. R. et al. 2007 ⁷¹ , Ringe, J. D. et al. 2002 ⁷² , Deal, C. et al. 2005 ⁷³ , Gutteridge, D. H. et al. 2002 ⁷⁴ , Harris, S. T. et al. 2001 ⁷⁵ , Hodsman, A. B. et al. 1997 ⁷⁶ , Lindsay, R. et al. 1999 ⁷⁷)	Comparison with combination drug therapy
(Sakhaee, K. et al. 1993 ⁷⁸)	The BMD measurement was not by DXA
(Sone, T. et al. 2014 ⁷⁹)	Measurements of LS, TH and RU was not included in the reported sites
(Duvernoy, et al. 2005 ⁸⁰ , Itabash, A. et al. 2015 ⁸¹ , Marcus, R. et al. 2003 ⁸²)	Post-hoc study of previously data
(Dempster, D. W. et al. 2018 ⁸³ , Reginster, J. Y. et al. 2009 ⁸⁴ , Reginster, J. Y. et al. 2012 ⁸⁵ , Zanchetta, J. R. et al. 2010 ⁸⁶ , Kanis, J. A. et al. 2005 ⁸⁷ , Harrington, J. T. et al. 2004 ⁸⁸ , Sorensen O. H. et al. 2003 ⁸⁹ , Watts, N. B. et al. 2003 ⁹⁰ , Goldstein, S. R. et al. 2002 ⁹¹ , Maricic, M. et al. 2002 ⁹² , Liao E. Y. et al. 2018 ⁹³)	Extension study and lack of related long-term BMD change or concerned adverse effects

Abbreviation: BMD, bone mineral density; CVD, cardiovascular diseases; ONJ, osteonecrosis of the jaw; DXA, dual-energy x-ray absorptiometry; LS, lumber spine; TH, total hip; RU, radius

Table S3: Characteristics of the Included Studies

Name	Country	Race (%)	Yrs since menopause	Group	Subject	Mean age	BMI
(Watts, N. B. et al. 2019) ⁹⁴	International	N/A	26.7±7.3	SC 60mg Denosumab Q6M for 7yrs	2343	74.9±5.0	N/A
			26.7±7.4	Placebo for 3yrs and Denosumab for 7 yrs	2207	74.8±5.1	
(Sugimoto, T. et al. 2019) ⁹⁵	Japan	Japanese (100)	N/A	IM 20U Elactonin weekly for 36M	316	75.5±5.7	23.3±3.4
				Placebo	309	75.5±5.7	23.2±3.3
(Kendler, D. L. et. Al. 2018) ⁹⁶	International	White (99)	N/A	SC 20ug Teriparatide daily for 24M	498	72.6±8.77	26.9±4.61
		Black (1)		Oral 35mg Risedronate weekly for 24M	515	71.6±8.58	27.1±4.64
		Asian (1)					
(Tsai, J. N. et al. 2017) ⁹⁷	USA.	White (100)	N/A	SC 20mcg Teriparatide daily for 48M	27	66.1±7.9	25.5±3.7
				SC 60mg Denosumab Q6M for 48M	27	65.1±6.2	23.8±4.1
(Saag, K. G. et al. 2017) ⁹⁸	USA.	Hispanic (32.3)	N/A	SC 210mg Romosozumab QM for 12M	1750	74.4±7.5	25.46±4.41
		Non-hispanic (67.7)		PO 70mg Alendronate QW for 12M	1757	74.2±7.5	25.36±4.42
(Liang, B. C. et al. 2017) ⁹⁹	China	Chinese (100)	9.78±1.45	IV 5mg Zoldronic acid Q12M for 24M	155	57.11±2.75	21.82±1.08
			9.98±1.55	Placebo	95	57.12±3.16	21.58±0.96
(Koh, J. M. et al. 2016) ¹⁰⁰	Korea	Korean (100)	19±7.02	SC 60mg Denosumab Q6M for 6M	68	67.0±4.86	23.5±2.83
			17.5±6.20	Placebo	66	66.0±4.77	23.7±2.29
(Kim, H. et al. 2016) ¹⁰¹	International	White (66.3)	N/A	PO 0.8mg Calcitonin (SMC021) daily for 3yrs	2064	66.5±6.12	26.1±4.17
		Asian (12.9)		Placebo	2125	67.0±6.16	26.0±4.15

(Cosman, F. et al. 2016) ¹⁰²	International	Hispanic (39.4)	N/A	Placebo	61	70.8±6.9	24.74±4.42
		Non-hispanic (60.6)		PO 210mg Romosozumab QM for 12M	65	70.9±7.0	24.66±4.30
(Miller, P. D. et al. 2016) ¹⁰³	International	White (79.8)	20.6±8.3	SC 80ug Abaloparatide daily for 1yr	652	68.9±6.5	25±3.5
		Asian (16.0)	19.9±8.1	SC 20ug Teriparatide daily for 1yr	704	68.8±6.6	25.2±3.6
		Black (2.8)	20.4±8.2	Placebo	694	68.7±6.5	25.1±3.6
(Zhang, Z. L. et al. 2015) ¹⁰⁴	China	Chinese (100)	N/A	PO 70mg Alendronate with 5600 IU D3 QW for 6M	95	65.6±8.0	23.0±3.5
				0.25µg Calcitonin daily for 6M	101	64.8±7.4	22.7±2.9
(Palacios, S. et al. 2015) ¹⁰⁵	International	White (85.2)		Oral 20mg Bazedoxifene daily for 7yrs	421	66.5±6.5	26.6±3.8
		Black (7.1)					
		Hispanic (5.2)		Placebo	441	66.5±6.8	26.3±3.8
		Other (2.5)					
(Leder, B. Z. et al. 2015) ¹⁰⁶	International	White (62.2)	N/A	SC 20ug Teriparatide daily for 24weeks	39	64.5±7.5	26±3.6
		Asian (24.4)		Placebo	42	65.0±7.1	26±3.4
		Other (13.3)					
(Leder, B. Z. et al. 2014) ¹⁰⁷	International	White (100)	27±20	SC 60mg Teriparatide Q6M for 2yrs	28	65.5±7.9	25.5±3.8
			36±23	SC 20ug Denosumab daily for 2yrs	31	66.3±8.3	24.1±3.9
(Abboskhujieva, L. S. et al. 2014) ¹⁰⁸	N/A	N/A	N/A	Strontium ranelate	16	63.3±1.5	30.4±1.06
				Placebo	16	62.9±1.52	31.2±1.14
(Kim, H. et al. 2013) ¹⁰⁹	Denmark	N/A	N/A	Placebo	29	65.8±6.2	25.23±3.4
	Estonia			SC 20ug Teriparatide daily for 24weeks	31	66.4±7.1	24.79±4.14

(Rizzoli, R. et al. 2012) ¹¹⁰	International	Caucasian (100)	N/A	2g Strontium ranelate daily for 24M	30	63.6±7.5	23.1±3.3
				70mg Alendronate weekly for 24M	27	63.8±7.6	22.6±2.7
(Zhang, L. et al. 2012) ¹¹¹	China	Chinese (100)	14.7±7	SC 20ug rhPTH daily for 12M	89	64.3±7.5	23.04±3.92
			13.5±7.2	IM 20 U Elactonin weekly for 12M	35	63.3±7.3	22.75±3
(Binkley, N. et al. 2012) ¹¹²	USA.	N/A	N/A	Oral 0.2mg Calcitonin daily for 48 weeks	189	66.5±7.6	25.63±4.44
				Placebo	82	66.5±8	25.67±3.79
(Cosman, F. et al. 2011) ¹¹³	USA.	White (97.8)	N/A	SC 20ug Teriparatide/IV placebo daily for 52 wks	138	63.8±9.1	25.3±4.15
		Other (2.2)		IV 5mg Zoledronic acid yearly for 52 wks	137	66.1±9	25.3±4.42
(Tuppurainen, M. et al. 2010) ¹¹⁴	Finland	N/A	11.5±5.5	Oral 2mg/1mg Estradiol/Norethisterone daily for 5yrs	45	60.9±2.8	25.6±3.6
			11.2±3.9	Placebo	51	60.9±2.5	25.9±4.1
(Finkelstein, J. S. et al. 2010) ¹¹⁵	USA.	N/A	N/A	Oral 10mg Alendronate daily	29	64±6	25.6±4.5
				SC 40ug Teriparatide daily	20	65±7	24.9±3.6
(Ensrud, K. et al. 2010) ¹¹⁶	International	White (74.3)	N/A	Oral 0.5mg Lasofoxifene daily for 5yrs	2852	67.3±5.2	25.4±3.7
		Asian (18.3)		Placebo	2852	67.5±5.2	25.4±3.8
		Other (7.5)					
(Cummings, S. R. et al. 2010) ¹¹⁷	International	White (74.3)	N/A	Oral 0.5mg Lasofoxifene daily for 5yrs	2852	67.3±5.2	25.4±3.7
		Asian (18.3)		Placebo	2852	67.5±5.2	25.4±3.8
		Other (7.5)					
(LaCroix, A. Z. et al. 2010) ¹¹⁸	International	White (74.3)	N/A	Oral 0.5mg Lasofoxifene daily for 5yrs	2852	67.3±5.2	25.4±3.7
		Black (0.9)		Placebo	2852	67.5±5.2	25.4±3.8
		Asian (18.3)					

		Hispanic 4.9)					
(Christiansen, C. et al. 2010) ¹¹⁹	International	White (87.1)					
		Black (6.4)	19.7±8.6	Oral 20mg Bazedoxifene daily for 3yrs	1254	66.5±6.5	26.6±3.8
		Hispanic (4.7)	19.5±8.8	Placebo	1256	66.5±6.8	26.3±3.8
		Other (1.9)					
(Yan, Y. et al. 2009) ¹²⁰	China	Chinese (100)	15.36±6.88	Oral 70mg Alendronate weekly for 12M	280	65.19±6.47	23.12±2.89
			15.14±6.66	Placebo	280	64.66±5.87	23.31±3.13
(Cummings, S. R. et al. 2009) ¹²¹	International	N/A	N/A	SC 60mg Denosumab Q6M for 36M	3902	72.3±5.2	26±4.1
				Placebo	3906	72.3±5.2	26±4.2
(Silverman, S. L. et al. 2008) ¹²²	International	White (87.1)	19.5±8.7	Oral 60mg Raloxifene daily for 36M	1252	66.4±6.7	26.4±3.8
			19.5±8.8	Placebo	1256	66.5±6.8	26.3±3.8
(Iwamoto, J. et al. 2008) ¹²³	Japan	Japanese (100)	N/A	Oral 5mg Alendronate daily for 12M	50	70.3±7.6	21.9±2.6
				Oral 60mg Raloxifene daily for 12M	52	68.5±7.2	21.7±2.5
(Miyauchi, A. et al. 2008) ¹²⁴	Japan	Japanese (100)	23.32±7.1	SC 40ug Teriparatide daily over 24weeks	27	72.5±6.1	21.59±3.68
			19.49±3.8	Placebo	34	69.9±3.6	21.36±2.61
(Hwang, J. S. et al. 2008) ¹²⁵	Taiwan	N/A	16.2±1.0	Oral 2g Stronium ranelate daily for 12M	64	64.3±0.8	23.5±0.4
			18.2±1.1	Placebo	61	65.8±1	26.2±4.1
(Sethi, B. K. et al. 2008) ¹²⁶	India	N/A	15.7±6.4	SC 20ug Teriparatide daily for 6M	38	61±6.3	26.2±4.1
			16.0±7.6	Placebo	35	63±6.3	25.3±3.9
(Greenspan, S. L. et al. 2007) ¹²⁷	International	White (83.8)	18.1±9.5	SC 100ug PTH(1-84) daily for 18M	824	64±7.4	25.6±1.34
		Hispanic (13.3)	18.2±9.5	Placebo	877	64.3±7.4)	25.7±4.27
		Black (1.4)					

		Asian (0.7)					
(Black, D. M. et al. 2007) ¹²⁸		West Europe (30.1)					
		East Europe (20)					
	International	North America (19.8)	N/A	IV(15min) 5mg Zoldronic acid yearly for 3yrs	3248	73.1±5.34)	25.1±4.3
		Latin America (16.1)		Placebo	3269	73±5.4)	25.4±4.3
		Asian (14)					
(Tanakol, R. et al. 2007) ¹²⁹	Turkey	N/A	154±91(M)	Oral 400mg Clodronate daily for 36M	30	59.3±5.9	25.1±4.7
			109±93(M)	Placebo	49	55.4±9	26.9±5
(Kung, A. W. C. et al. 2006) ¹³⁰	International	Asian (100)	22.8±8.3	SC 20ug Teriparatide 1-34 daily for 6M	39	70.6±7.1	N/A
			22.9±8.7	SC 100IU Calcitonin daily for 6M	41	70.6±6.6	
(Hwang, J. S. et al. 2006) ¹³¹	Taiwan	N/A	20.06±1.38	SC 20ug Teriparatide daily for 6M	34	68.06±1.07	24.34±0.62
			19.72±1.38	Placebo	29	66.90±1.39	23.62±0.50
(Gonnelli, S. et al. 2006) ¹³²	Italy	N/A	N/A	SC 20ug Teriparatide 1-34 daily for 12M	27	71.3±7.0	24.7±3.3
				Placebo	28	71.0±6.8	24.8±3.1
(Ensrud, K. et al. 2006) ¹³³	International	White (96)	18±8	Oral 60mg or 120mg Raloxifene daily for 4yrs	2336	66±7	25.2±3.9
			18±8	Placebo	1106	66±7	25.2±3.9
(Martino, S. et al. 2005) ¹³⁴	International	White (96)	17.8±8	Oral 60mg or 120mg Raloxifene daily for 4yrs	2725	65.7±6.8	25.2±3.9
			18±8	Placebo	1286	65.9±6.7	25.2±3.9
(McClung, M. R. et al. 2005) ¹³⁵	N/A	White (59)	19.9±9.6	Oral 10mg Alendronate daily for 18M	101	66.6±8.5	25.3±4.5
			19.5±10.3	IV 20ug Teriparatide daily for 18M	102	65.3±8.4	25.7±4
(Leung, J. Y. Y. et al. 2005) ¹³⁶	China	N/A	15.5±1.6	Oral 5mg Risedronate daily for 18M	31	67±6	N/A
			15.5±2.2	Placebo	34	67±6	

(Ho, A. Y. Y. et al. 2005) ¹³⁷	China	N/A	11.6±5.8	Oral 70mg Alendronate weekly for 12M	29	60.6±5.5	22.4±3.2
			12±4.8	Placebo	29	62±4	23.1±2.8
(Dominguez, L. J. et al. 2005) ¹³⁸	N/A	N/A	N/A	IM 100mg Clodronate weekly for 12M	85	69.8±4.33	N/A
				Placebo	75	70.7±4.24	
(Li, Y. et al. 2005) ¹³⁹	China	N/A	N/A	Oral 5mg Risedronate daily for 12M	30	N/A	N/A
				Placebo	30		
(Kushida, K. et al. 2004) ¹⁴⁰	Japan	Japanese (100)	22±7.2	Oral 5mg Alendronate daily for 3yrs	90	71.2±5.3	N/A
			22.4±7.6	Oral 1ug Alfacalcidol daily for 3yrs	80	72.6±5.7	
(Ishida, Y. et al. 2004) ¹⁴¹	Japan	Japanese (100)	N/A	Oral 0.625mg Estrogen daily for 24M	62	70±15	N/A
				Oral 200mg Etidronate daily for 24M	62	70±15	
				Oral 20IU Calcitonin weekly for 24M	62	69±17	
				Oral 1ug Alfacalcidol daily for 24M	63	71±12	
				Oral 1ug Alfacalcidol daily for 24M	63	68±11	
				Placebo	60	68±8	
(Adami, S. et al. 2004) ¹⁴²	Italy	N/A	17.6±6.4	IV 2mg Ibandronate Q3M for 12M	221	65.5±4.5	N/A
			17.7±7.3	Placebo	118	65.5±4.7	
(Ste-Marie, L. G. et al. 2004) ¹⁴³	Canada	N/A	23.9±7.9	Oral 5mg Risedronate daily for 60M	44	69.5±6.8	N/A
			23.3±10.1	Placebo	42	69.2±9.15	
(Meunier, P. J. et al. 2004) ¹⁴⁴	International	N/A	22.1±8.8	Oral 2g Stronium ranelate daily for 3yrs	628	69.4±7.2	26.1±4.1
			21.6±8.7	Placebo	632	69.2±7.3	26.2±4.1
(Luckey, M. et al. 2004) ¹⁴⁵	USA.	White (92.3)	17.8	Oral 60mg Raloxifene daily for 12M	193	64.7±9.8	25.3±4.8
		Black (2.4)	17.3	Oral 70mg Alendronate weekly for 12M	179	63.8±9.9	25.3±5.2

		Asian (1.5)					
		Other (3.7)					
(Genant, H. K. et al. 2004) ¹⁴⁶	USA.	N/A	21.4±6.4	Oral 60 or 120mg Raloxifene daily for 2yrs	37	70.3±5.0	N/A
			21.3±6.8	Placebo	21	70.0±4.9	
(Boonen, S. et al. 2004) ¹⁴⁷	International	N/A	N/A	Oral 5mg Risedronate daily for 3yrs	704	83.0±3.1	24.9±4.6
				Placebo	688	83.0±3.0	24.5±4.1
(Barrett-Connor, E. et al. 2004) ¹⁴⁸	International	White (95.7)	N/A	Oral 60mg or 120mg Raloxifene daily for 4yrs	5129	66.4	25.2
				Placebo	2576	66.6	25.2
(Martino, S. et al. 2004) ¹⁴⁹	International	White (95.5)	18.4±8.2	Oral 60mg Raloxifene daily for 8yrs	2725	66.2±6.9	25.3±3.9
				Placebo	1286		
(Morii, H. et al. 2003) ¹⁵⁰	Japan	Japanese (100)	15.8±6.7	Oral 120mg Raloxifene daily for 52weeks	81	64.7±6.2	21.9±3
			14.4±6.3	Placebo	87	64.3±6.5	22±3
(Braga, V. et al. 2003) ¹⁵¹	Italy	N/A	17.4±10.3	IV 50mg Neridronate Q2M for 36M	39	63.4±8.7	23.6±3.7
			17.6±8.9	Placebo	39	65.7±6.6	23.5±3.4
(Hodsman, A. B. et al. 2003) ¹⁵²	USA, Canada	N/A	18±7	SC 100ug PTH(1-84) daily for 12M	51	64±6	N/A
			17±6	Placebo	53	64±6	
(Chailurkit, L. et al. 2003) ¹⁵³	Thailand	Thai (100)	12.6±7.0	Oral 10mg Alendronate daily for 12M	32	62.2±6.4	22.3±2.9
			12.8±6.6	Placebo	38	61.8±5.6	22.4±3.5
(Meunier, P. J. et al. 2002) ¹⁵⁴	European countries	Caucasian	17.5±8.3	Oral 2g Stronium ranelate daily for 24M	87	65.6±6.9	25.7±3.1
			19.1±7.7	Placebo	91	66.7±6.5	24.9±3.1
(Johnell, O. et al. 2002) ¹⁵⁵	International	N/A	15.6±7.7	Oral 60mg Raloxifene daily for 12M	82	63.4±6.3	24.8±3.8
			16.5±7.7	Oral 10mg Alendronate daily for 12M	83	63.7±6.0	24.8±3.8

			17.6±8.2	Placebo	82	63.8±5.3	24.3±3.9
(Body, J. J. et al. 2002) ¹⁵⁶	International	N/A	18±9	SC 40ug Teriparatide 1-34 daily for 12M	73	66±8	23.9±4.5
			19±10	Oral 10mg Alendronate daily for 12M	73	65±9	24.4±3.5
(Rubin, C. D. et al. 2001) ¹⁵⁷	USA.	N/A	26±8	Oral 25mg Sodium Fluoride daily for 42M	44	73±5	25.5±4.3
			26±10	Placebo	41	73±5	24.6±4.3
(Riis, B. J. et al. 2001) ¹⁵⁸	Denmark	N/A	18.8±6.8	IV 2.5mg Ibandronate daily for 12M	81	66.8±4.9	N/A
			17.8±6.7	Placebo	81	66.3±4.8	
(Neer, R. M. et al. 2001) ¹⁵⁹	International	White (99)	21±8	SC 40ug Teriparatide 1-34 daily for 24M	497	70±7	26.6±4.3
			21±8	Placebo	504	67±7	26.7±4.7
(Iwamoto, J. et al. 2001) ¹⁶⁰	Japan	Japanese	17.0±1.3	Oral 200mg Etidronate daily for 24M	25	64.3±1.3	21.2±0.7
			18.3±1.5	Oral 45mg Menatetrenone daily for 24M	23	65.4±1.2	20.6±0.7
			16.0±1.2	Placebo	24	66±1.1	20.9±0.6
(Guanabens, N. et al. 2000) ¹⁶¹	Spain	N/A	16.5	Oral 50mg Fluoride daily for 36M	31	64±7.96	26.6±3.73
			19	Oral 400mg Etidronate daily for 36M	47	65±6.92	27±5
(Bone, H. G. et al. 2000) ¹⁶²	USA.	Caucasian	22±8	Oral 10mg Alendronate daily for 24M	92	61±8	N/A
			21±8	Oral 0.625mg Estrogen daily for 24M	143	61±8	
			23±11	Placebo	50	62±9	
(Sahota, O. et al. 2000) ¹⁶³	UK.	N/A	17.4±5.1	Oral 10mg Alendronate daily for 12M	31	67.5±5.1	25.8±2.9
			17.2±4.2	Oral 250ng Calcitriol twice daily for 12M	33	67.2±4.2	26.8±3.1
(Downs, R. W. et al. 2000) ¹⁶⁴	USA.	White (98.3)	16.5±7.7	Oral 10mg Alendronate daily for 12M	118	64.6±6.8	25.6±4.2
			16.1±7.4	Intra-nasal 200 IU Calcitronin daily for 12M	123	64.1±7.2	25.9±4.6
			16.5±8.6	Placebo	58	64.6±6.8	25.4±4.2

(Chesnut, C. H. et al. 2000) ¹⁶⁵	USA, UK	N/A	21.9±8.4	Intra-nasal 400IU Calcitonin for 5yrs	127	67.9±6.9	24.9±3.6
			22±9.4	Placebo	128	68.2±7.7	24.7±3.9
(Boivin, G. Y. et al. 2000) ¹⁶⁶	France	N/A	N/A	Oral 10mg Alendronate daily for 2yrs	9	64±3	N/A
				Placebo	15	62±2	
(Reginster, J. Y. et al. 2000) ¹⁶⁷	International	N/A	25±8.6	Oral 5mg Risedronate daily for 1yr	251	71±7	N/A
			25±8.7	Placebo	221	71±7	
(Kung, A. W. C. et al. 2000) ¹⁶⁸	China	Chinese	15±4	Alendronate	35	64±5	23.2±3.3
			15±4	Placebo	35	65±4	23.1±2.3
(Tiras, M. B. et al. 2000) ¹⁶⁹	Turkey	N/A	4.9±4.6	Oral 2mg/1mg HRT daily for 12M	31	52.7±5.6	24.2±3.6
			6.5±5.6	Oral 10mg Alendronate daily for 12M	32	53.8±6.8	23.8±4.1
(Rossini, M. et al. 1999) ¹⁷⁰	Italy	N/A	14±3	IM 100mg Clodronate weekly for 24M	30	61±4	23.2±1.7
			13±4	Placebo	30	61±3	23.1±1.6
(Ringe, J. D. et al. 1999) ¹⁷¹	Germany	N/A	N/A	Oral 20mg MFP/Ca daily for 3yrs	30	65.5±6	N/A
				Placebo	33	63.7±6.1	
(Harris S. T. et al. 1999) ¹⁷²	USA	American	24±10.1	Oral 5mg Risedronate daily for 3yrs	425	69±7.7	N/A
			24±10.0	Placebo	398	68±7.2	
(Reginster, J. Y. et al. 1998) ¹⁷³	Belgium	N/A	N/A	Oral 10mg MFP/Ca daily for 4yrs	100	N/A	N/A
				Placebo	100		
(Meunier, P. J. et al. 1998) ¹⁷⁴	France	N/A	18.1	Oral 50mg/150mg Fluoride(NaF/MFP) daily for 2yrs	208	65.8	N/A
			18.8	Placebo	146	65.5	

(Lufkin, E. G. et al. 1998) ¹⁷⁵	USA.	N/A	22±6.24	Oral 60mg Raloxifene daily for 12M	48	69.9±3.46	24.8±4.23
			22.2±1	Placebo	48	68.2±4.85	25.3±3.81
(Felsenberg, D. et al. 1998) ¹⁷⁶	Germany	N/A	N/A	Oral 10mg Alendronate daily for 1yr	152	64.1±6.7	N/A
				Placebo	145	63.3±7.5	
(Gonnelli, S. et al. 1997) ¹⁷⁷	Italy	N/A	6.5±4.4	Patch 10mg Estrogen daily for 2yr	40	56.2±4.6	N/A
			65.2±3.5	Placebo	41	56.3±4.5	
(Thiébaud, D. et al. 1997) ¹⁷⁸	Switzerland,	N/A	18.3±1.6	IV 2mg Ibandronate Q3M for 12M	23	64±1.5	25.3±0.7
	Germany		17±1.3	Placebo	26	64.2±1.1	24.5±0.8
(Filipponi, P. et al. 1996) ¹⁷⁹	Italy	N/A	12.6±0.6	IM 200mg Clodronate every 3wk for 4yrs	44	62.1±0.6	N/A
			14.4±0.4	Placebo	37	63.9±0.7	
(Tucci, J. R. et al. 1996) ¹⁸⁰	USA.	N/A	17.1±8.5	Oral 10mg Alendronate daily for 3yrs	94	63.9±6.4	23.3±3
			17.8±8.2	Placebo	192	64.2±7.4	23.8±3.6
(Ravn, P. et al. 1996) ¹⁸¹	Denmark	N/A	N/A	Oral 2.5mg Ibandronate daily for 12M	30	65.2±5.7	N/A
				Placebo	30	63.9±6	
(Ellerington, M. C. et al. 1996) ¹⁸²	UK.	Caucasian	N/A	Intra-nasal 200IU Calcitonin daily for 2yrs	29	55.4±3.9	N/A
				Placebo	39	56.1±4.3	
(Devogelaer, J. P. et al. 1996) ¹⁸³	International	N/A	16±7.7	Oral 10mg Alendronate daily for 3 yrs	102	63.2±6.6	24±3.2
			15.2±8.1	Placebo	205	62.7±7.2	24.4±3.5
(Pak, C. Y. C. et al. 1995) ¹⁸⁴	USA.	N/A	18.5	Oral 25mg SR-NaF/Ca twice daily for 2yrs	48	66.5±8.6	N/A
			19	Placebo	51	68.7±8.9	
(Lieberman, U. A. et al. 1995) ¹⁸⁵	International	N/A	16	Oral 10mg Alendronate daily for 3yrs	196	64	24.2
			17	Placebo	397	64	24.1

(Chesnut, C. H. et al. 1995) ¹⁸⁶	USA.	N/A	15±6.9	Oral 10mg Alendronate daily for 24M	30	62.9±6.1	N/A
			16.9±7.7	Placebo	31	63.6±7.1	
(Adami, S. et al. 1995) ¹⁸⁷	Italy	N/A	12±7	Oral 10mg Alendronate daily for 24M	68	59±6	N/A
			11±6	Oral 100IU Calcitonin daily for 24M	75	60±6	
			11±8	Placebo	71	59±6	
(Thiébaud, D. et al. 1994) ¹⁸⁸	Switzerland	N/A	15.1±2.3	IV 30mg Pamidronate Q3M for 24M	16	64.6±2.7	N/A
			14.8±2.4	Oral 20-30mg Fluoride daily for 24M	16	67.2±2.1	
(IAN, R. R. et al. 1994) ¹⁸⁹	New Zealand	N/A	17±9	Oral 150mg Pamidronate daily for 2yrs	26	65±7	N/A
			19±10	Placebo	22	67±6	
(Rossini, M. et al. 1994) ¹⁹⁰	Italy	N/A	12±4	Oral 20mg Alendronate daily for 6M	15	63±3	25.6±3.9
			12±3	Placebo	15	62±2	23.6±3.8
(Adami, S. et al. 1993) ¹⁹¹	Italy	N/A	12±7	Oral 10mg Alendronate daily for 2yrs	68	59±6	N/A
			11±6	Intra-nasal 100IU Calcitonin daily for 2yrs	75	60±6	
			11±8	Placebo	71	59±6	

Abbreviation: N/A, not applicable; IM, intramuscularly; SC, subcutaneously; M, month; QM, once a month; QW, once a week; Q6M, every 6 month; Yr, year

Table S4: Concerned Adverse Events Reported in Previous Studies

Name	Intervention	Major reported adverse events	subject	Follow up
(Watts, N. B. et al. 2019) ⁹⁴	SC 60mg Denosumab Q6M for 7yrs Placebo for 3yrs and Denosumab for 7yrs	ONJ	2343 2207	10yrs
(Kendler, D. L. et al. 2018) ⁹⁶	SC 20ug Teriparatide daily for 24M Oral 35mg Risedronate weekly for 24M	Death, hip fracture, wrist fracture, atypical femoral fracture, ONJ	498 515	24M
(Saag, K. G. et al. 2017) ⁹⁸	SC 210mg Romosozumab QM for 12M PO 70mg Alendronate QW for 12M	Death, non-vertebral fracture, CVD, cancer, ONJ, hip fracture, atypical femoral fracture	1750 1757	12M
(Koh, J. M. et al. 2016) ¹⁰⁰	SC 60mg Denosumab Q6M for 6M Placebo	Death	68 66	6M
(Cosman, F. et al. 2016) ¹⁰²	Placebo PO 210mg Romosozumab QM for 12M	Death, cancer, CVD, ONJ, non-vertebral fracture, atypical femoral fracture	61 65	12M
(Miller, P. D. et al. 2016) ¹⁰³	SC 80ug Abaloparatide daily for 1yr SC 20ug Teriparatide daily for 1yr Placebo	Death, non-vertebral fracture	652 704 694	1yr
(Zhang, Z. L. et al. 2015) ¹⁰⁴	PO 70mg Alendronate with 5600 IU D3 QW for 6M 0.25µg Calcitonin daily for 6M	Death	95 101	6M

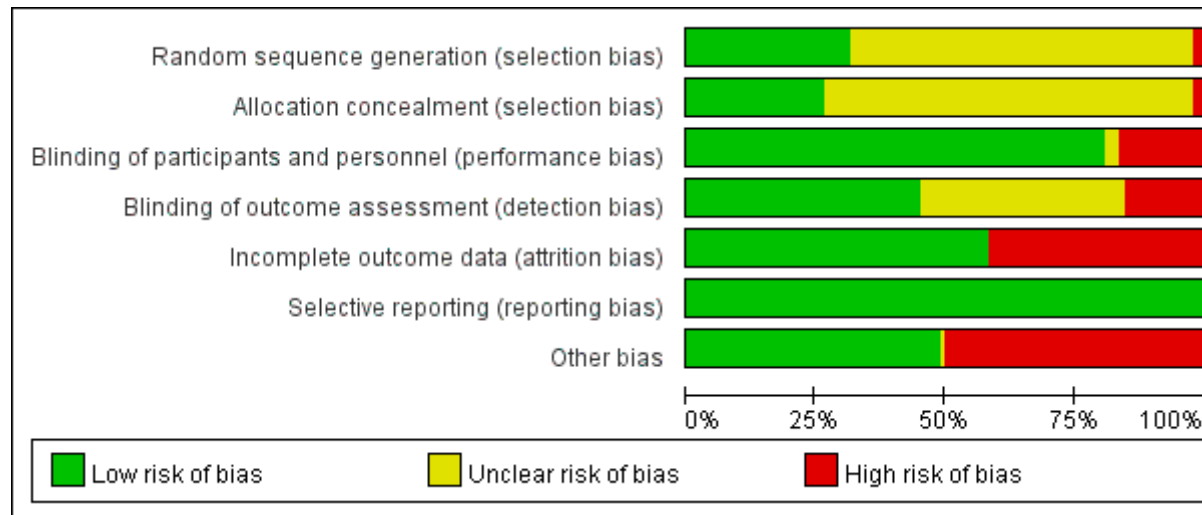
(Palacios, S. et al. 2015) ¹⁰⁵	Oral 20mg Bazedoxifene daily for 7yrs Placebo	Death, CVD, breast cancer	421 441	7yrs
(Ensrud, K. et al. 2010) ¹¹⁶	Oral 0.5mg Lasofoxifene daily for 5yrs Placebo	CVD	2852 2852	5yrs
(Cummings, S. R. et al. 2010) ¹¹⁷	Oral 0.5mg Lasofoxifene daily for 5yrs Placebo	Death	2852 2852	5yrs
(LaCroix, A. Z. et al. 2010) ¹¹⁸	Oral 0.5mg Lasofoxifene daily for 5yrs Placebo	Breast cancer	2099 2112	5yrs
(Christiansen, C. et al. 2010) ¹¹⁹	Oral 20mg Bazedoxifene daily for 3yrs Placebo	Breast cancer	1254 1256	3yrs
(Cummings, S. R. et al. 2009) ¹²¹	SC 60mg Denosumab Q6M for 36M Placebo	Death, cancer, ONJ, CVD, non-vertebral fracture, hip fracture	N/A	36M
(Silverman, S. L. et al. 2008) ¹²²	Oral 20mg Bazedoxifene daily for 36M Placebo	Death, breast cancer, non-vertebral fracture, venous thromboembolic event	1254 1256	36M
(Black, D. M. et al. 2007) ¹²⁸	IV(15min) 5mg Zoledronic acid yearly for 3yrs Placebo	Death, stroke, non-vertebral fracture, hip fracture	3248 3269	3yrs
(Ensrud, K. et al. 2006) ¹³³	Oral 60mg or 120mg Raloxifene daily for 4yrs Placebo	CVD, death (myocardial cause)	2336 1106	4yrs

(Martino, S. et al. 2005) ¹³⁴	Oral 60mg Raloxifene daily for 8yrs Placebo	Death, cancer, breast cancer, venous thromboembolic event	2725 1286	8yrs
(Adami, S. et al. 2004) ¹⁴²	IV 2mg Ibandronate Q3M for 12M Placebo	CVD	221 118	12M
(Boonen, S. et al. 2004) ¹⁴⁷	Oral 5mg Risedronate daily for 3yrs Placebo	Death	704 688	3yrs
(Barrett-Connor, E. et al. 2004) ¹⁴⁸	Oral 60mg or 120mg Raloxifene daily for 4yrs Placebo	Hip fracture, death, invasive breast cancer	5129 2576	4yrs
(Martino, S. et al. 2004) ¹⁴⁹	Oral 60mg Raloxifene daily for 8yrs Placebo	Breast cancer, death	2725 1286	8yrs
(Mori, H. et al. 2003) ¹⁵⁰	Oral 120mg Raloxifene daily for 52weeks Placebo	CVD	81 87	52wks
(Neer, R. M. et al. 2001) ¹⁵⁹	SC 40ug Teriparatide 1-34 daily for 24M Placebo	Non-vertebral fracture, wrist fracture, hip fracture	497 504	24M
(Chesnut, C. H. et al. 2000) ¹⁶⁵	Intra-nasal 400IU Calcitonin for 5yrs Placebo	Non-vertebral fracture, hip fracture	127 128	5yrs
(Reginster, J. Y. et al. 2000) ¹⁶⁷	Oral 5mg Risedronate daily for 1yr Placebo	CVD, non-vertebral fracture, cancer	251 221	1yr
(Ringe, J. D. et al. 1999) ¹⁷¹	Oral 20mg MFP/Ca daily for 3yrs Placebo	Hip fracture, non-vertebral fracture	30 33	3yrs
(Meunier, P. J. et al. 1998) ¹⁷⁴	Oral 50mg/150mg Fluoride daily for 2yrs Placebo	Hip fracture, non-vertebral fracture	208 146	2yrs

(Lufkin, E. G. et al. 1998) ¹⁷⁵	Oral 60mg Raloxifene daily for 12M Placebo	Non-vertebral fracture, hip fracture, wrist fracture	48 48	12M
(Pak, C. Y. C. et al. 1995) ¹⁸⁴	Oral 25mg SR-NaF/Ca twice daily for 2yrs Placebo	Hip fracture	48 51	2yrs
(Lieberman, U. A. et al. 1995) ¹⁸⁵	Oral 10mg Alendronate daily for 3yrs Placebo	Non-vertebral fracture, hip fracture	196 397	3yrs

Abbreviation: N/A, not applicable; SC, subcutaneously; M, month; QM, once a month; QW, once a week; Q6M, every 6 month; Yr, year

Figure S1. Risk of Bias Assessment Summary Graph (Review Authors' Judgment as Low, Unclear, or High for Each Risk of Bias Item) Shown as Percentages Across All Included Studies



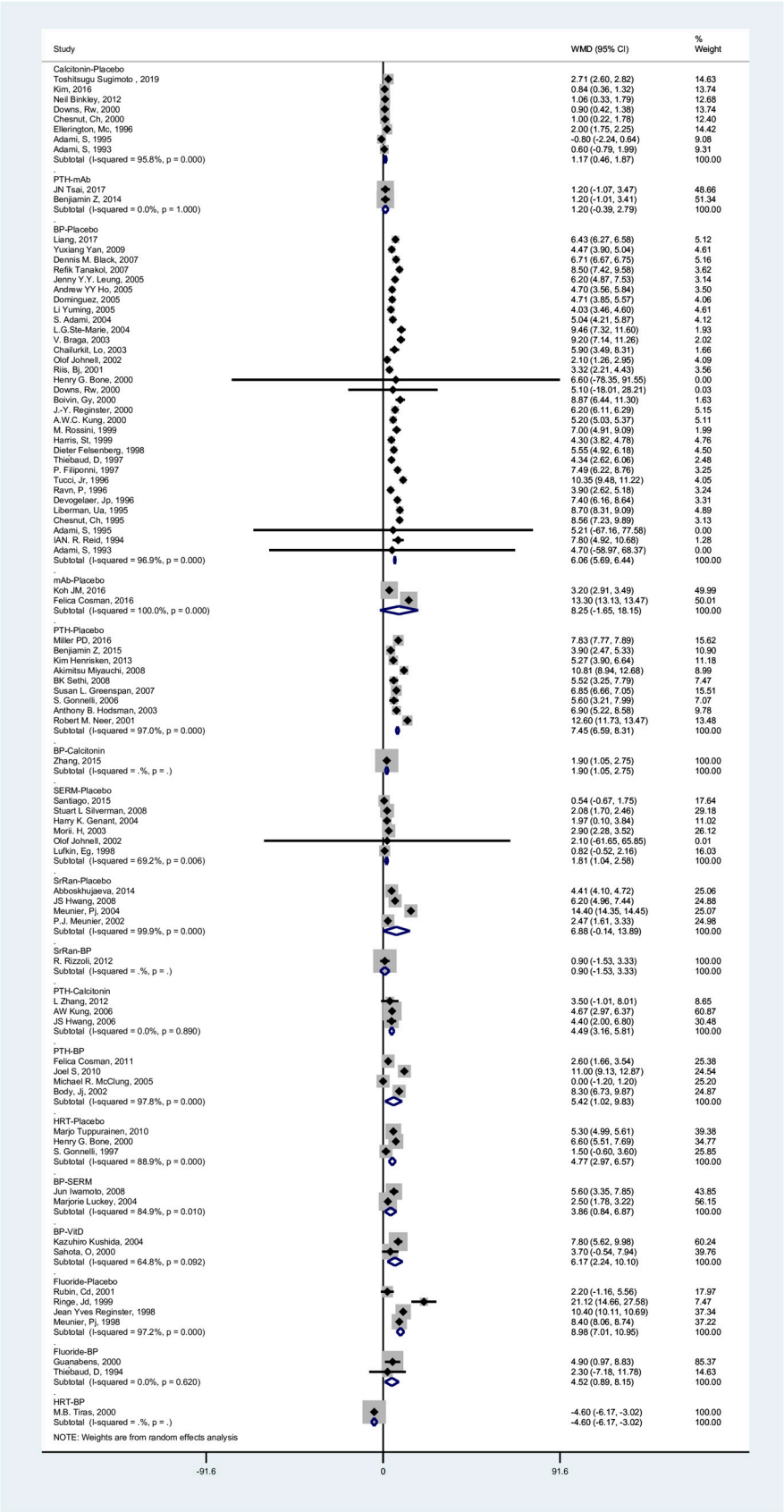
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Abboskhujaeva, L. S. 2014	+	+	?	?	+	+	+
Adami, S. 1993	?	?	+	?	+	+	+
Adami, S. 1995	?	?	+	?	+	+	+
Adami, S. 2004	+	?	+	+	+	+	+
Barrett-Connor, E. 2004	+	?	+	+	+	+	+
Binkley, N. 2012	?	+	+	+	+	+	+
Black, D. M. 2007	+	+	+	+	+	+	+
Body, J. J. 2002	?	?	+	?	+	+	+
Boivin, G. Y. 2000	?	?	+	?	+	+	+
Bone, H. G. 2000	+	?	+	?	+	+	+
Boonen, S. 2004	?	?	+	+	+	+	+
Braga, V. 2003	?	?	+	+	+	+	+
Chailurkit, L. 2003	?	?	+	?	+	+	+
Chesnut, C. H. 1995	+	?	+	?	+	+	+
Chesnut, C. H. 2000	+	+	+	+	+	+	+
Christiansen, C. 2010	?	?	+	+	+	+	+
Cosman, F. 2011	+	?	+	?	+	+	+
Cosman, F. 2016	+	?	+	?	+	+	+
Cummings, S. R. 2009	?	?	+	+	+	+	?
Cummings, S. R. 2010	?	?	+	+	+	+	+
Devogelaer, J. P. 1996	?	?	+	+	+	+	+
Dominguez, L. J. 2005	?	?	+	?	+	+	+
Downs, R. W. 2000	?	?	+	+	+	+	+
Ellerington, M. C. 1996	?	+	+	?	+	+	+
Ensrud, K. 2006	?	+	+	+	+	+	+
Ensrud, K. 2010	+	+	+	+	+	+	+
Felsenberg, D. 1998	?	?	+	+	+	+	+
Filipponi, P. 1996	?	?	+	+	+	+	+
Finkelstein, J. S. 2010	+	+	+	?	+	+	+
Genant, H. K. 2004	?	?	+	?	+	+	+
Gonnelli, S. 1997	?	?	+	?	+	+	+
Gonnelli, S. 2006	?	?	+	+	+	+	+
Greenspan, S. L. 2007	+	+	+	?	+	+	+
Guanabens, N. 2000	?	?	+	?	+	+	+
Harris S. T. 1999	+	?	+	+	+	+	+
Ho, A. Y. Y. 2005	?	?	+	+	+	+	+
Hodsman, A. B. 2003	?	?	+	?	+	+	+
Hwang, J. S. 2006	?	?	+	+	+	+	+
Hwang, J. S. 2008	?	+	+	?	+	+	+

IAN, R. R. 1994	?	?	+	+	+	+	+
Ishida, Y. 2004	?	?	+	+	+	+	+
Iwamoto, J. 2001	?	?	+	+	+	+	+
Iwamoto, J. 2008	?	?	+	?	+	+	+
Johnell, O. 2002	+	+	+	?	+	+	+
Kendler, D. L. 2018	+	+	+	+	+	+	+
Kim, H. 2013	?	+	+	+	+	+	+
Kim, H. 2016	+	+	+	+	+	+	+
Koh, J. M. 2016	?	?	+	?	+	+	+
Kung, A. W. C. 2000	?	?	+	?	+	+	+
Kung, A. W. C. 2006	?	?	+	?	+	+	+
Kushida, K. 2004	?	?	+	?	+	+	+
LaCroix, A. Z. 2010	+	+	+	+	+	+	+
Leder, B. Z. 2014	?	?	+	+	+	+	+
Leder, B. Z. 2015	?	?	+	+	+	+	+
Leung, J. Y. Y. 2005	?	?	+	+	+	+	+
Li, Y. 2005	?	?	+	?	+	+	+
Liang, B. C. 2017	?	+	+	?	+	+	+
Lieberman, U. A. 1995	?	?	+	+	+	+	+
Luckey, M. 2004	+	+	+	+	+	+	+
Lufkin, E. G. 1998	+	?	+	?	+	+	+
Martino, S. 2004	?	+	+	+	+	+	+
Martino, S. 2005	?	?	+	+	+	+	+
McClung, M. R. 2005	?	?	+	?	+	+	+
Meunier, P. J. 1998	?	+	+	+	+	+	+
Meunier, P. J. 2002	+	+	+	?	+	+	+
Meunier, P. J. 2004	?	?	+	+	+	+	+
Miller, P. D. 2016	+	+	+	+	+	+	+
Miyauchi, A. 2008	+	+	+	+	+	+	+
Morii, H. 2003	+	+	+	+	+	+	+
Neer, R. M. 2001	?	?	?	?	+	+	+
Pak, C. Y. C. 1995	?	+	+	?	+	+	+
Palacios, S. 2015	?	?	+	+	+	+	+
Ravn, P. 1996	?	?	+	?	+	+	+
Reginster, J. Y. 1998	+	+	+	+	+	+	+
Reginster, J. Y. 2000	?	?	+	+	+	+	+
Riis, B. J. 2001	?	?	+	?	+	+	+
Ringe, J. D. 1999	?	?	+	+	+	+	+
Rizzoli, R. 2012	?	+	+	+	+	+	+
Rossini, M. 1994	?	?	+	?	+	+	+
Rossini, M. 1999	?	?	+	?	+	+	+
Rubin, C. D. 2001	?	?	+	?	+	+	+
Saag, K. G. 2017	+	?	+	+	+	+	+
Sahota, O. 2000	+	?	+	+	+	+	+
Sethi, B. K. 2008	+	?	+	+	+	+	+
Silverman, S. L. 2008	+	?	+	+	+	+	+
Ste-Marie, L. G. 2004	?	?	+	+	+	+	+
Sugimoto, T. 2019	+	?	+	+	+	+	+
Tanakol, R. 2007	?	?	+	+	+	+	+
Thiebaud, D. 1994	?	?	+	+	+	+	+

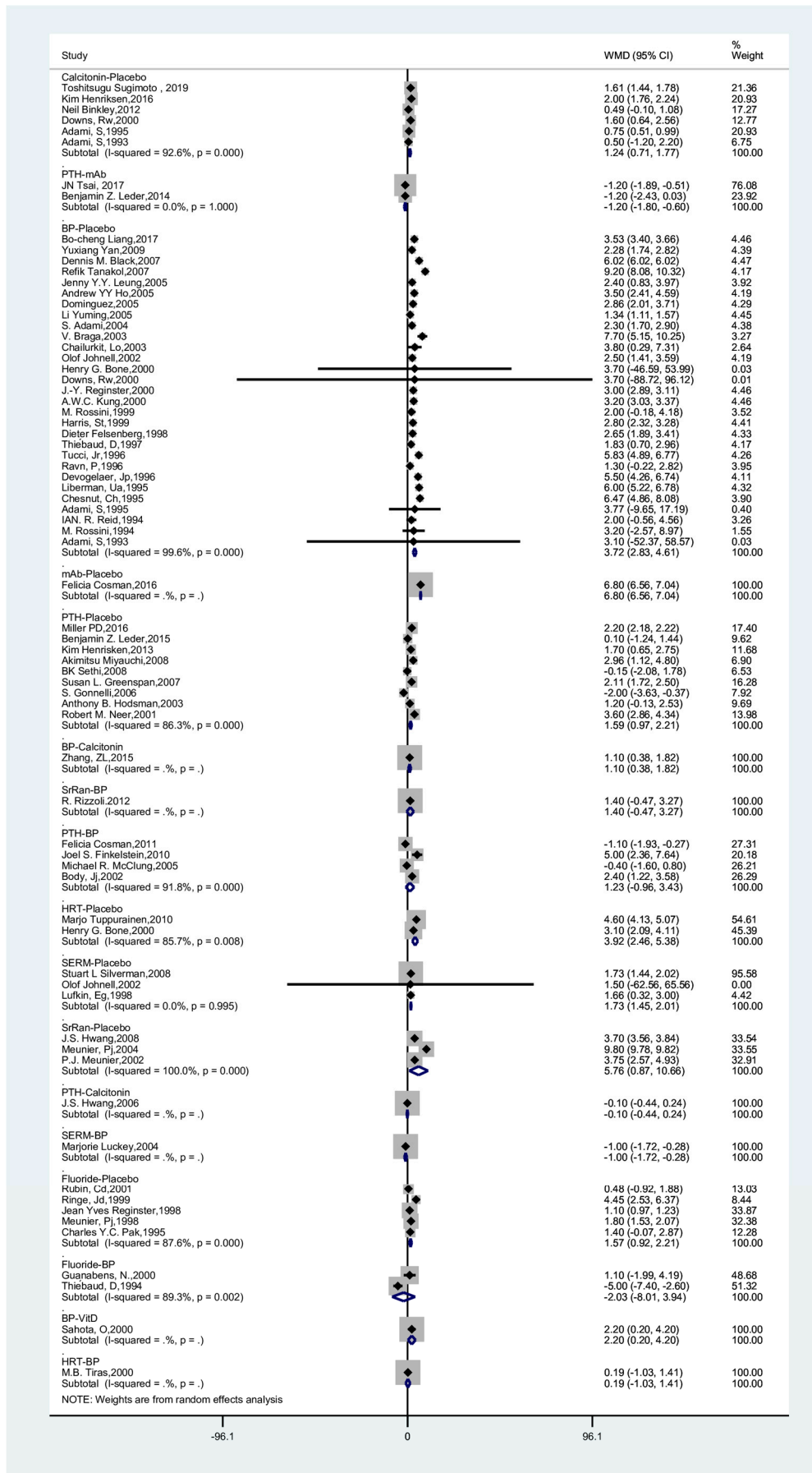
Thiebaud, D. 1997	+	?	+	+	+	+	+
Tiras, M. B. 2000	+	?	+	?	+	+	+
Tsai, J. N. 2017	?	?	?	?	+	+	+
Tucci, J. R. 1996	?	+	+	+	+	+	+
Tuppurainen, M. 2010	+	+	+	+	+	+	+
Watts, N. B. 2019	?	?	+	?	+	+	+
Yan, Y. 2009	+	?	+	+	+	+	+
Zhang, L. 2012	?	?	+	+	+	+	+
Zhang, Z. L. 2015	?	?	+	+	+	+	+

Figure S2. Forest Plots of Direct Pairwise Comparisons for BMD at (A) lumbar spine (LS) (B) total hip (TH) (C) radius (RU)

(A) Lumbar spine (LS)



(B) Total hip (TH)



(C) Radius (RU)

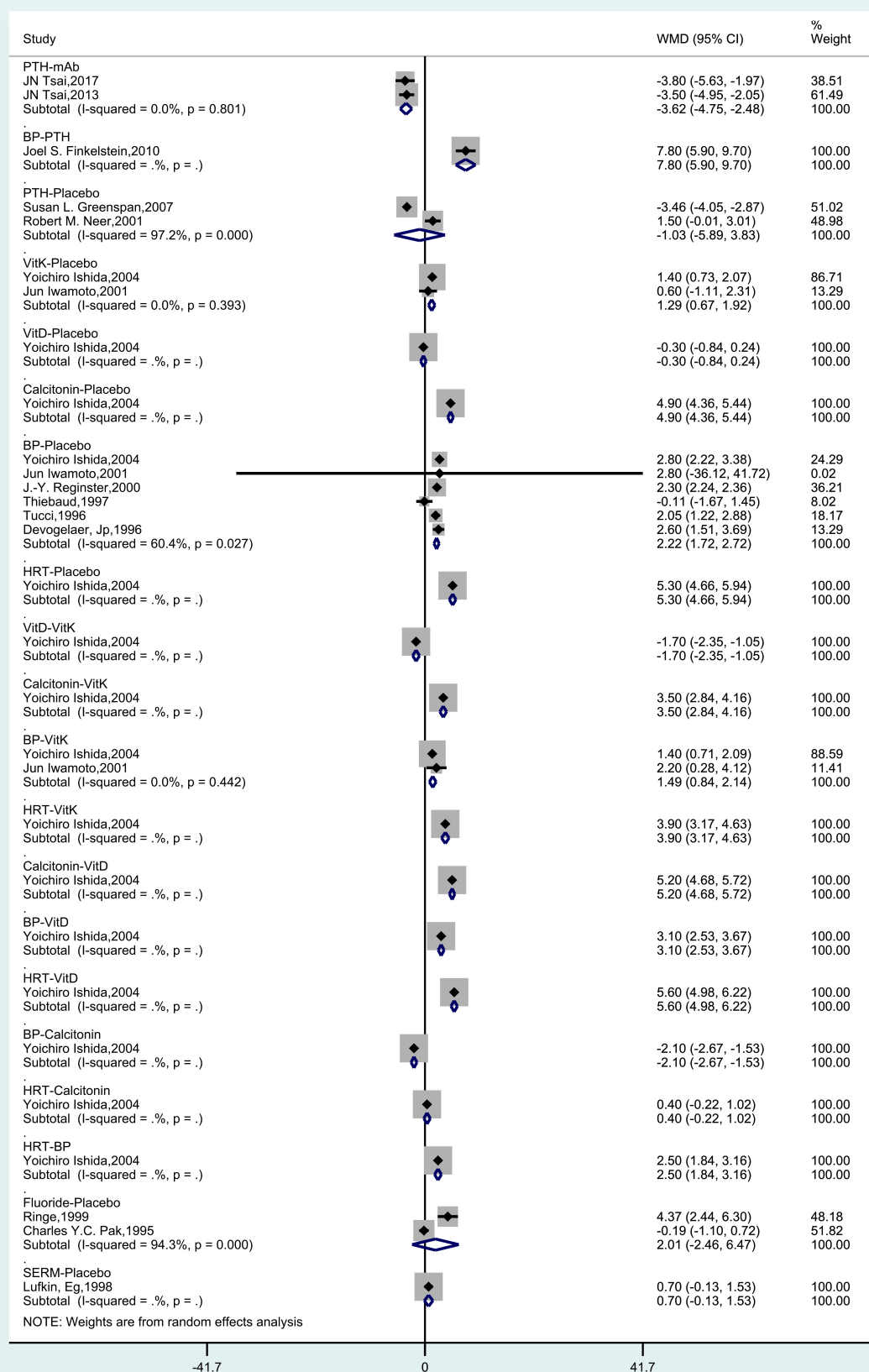
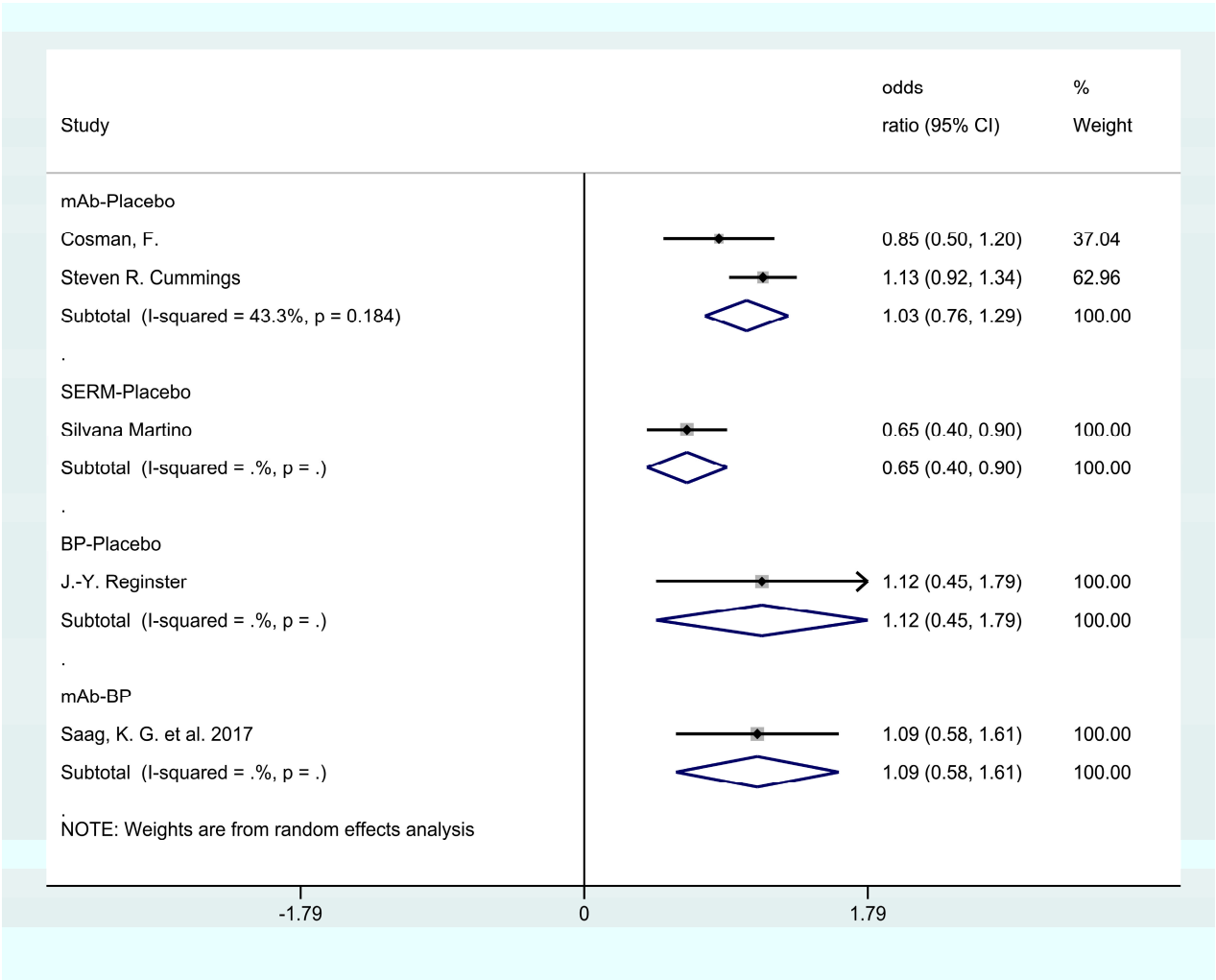
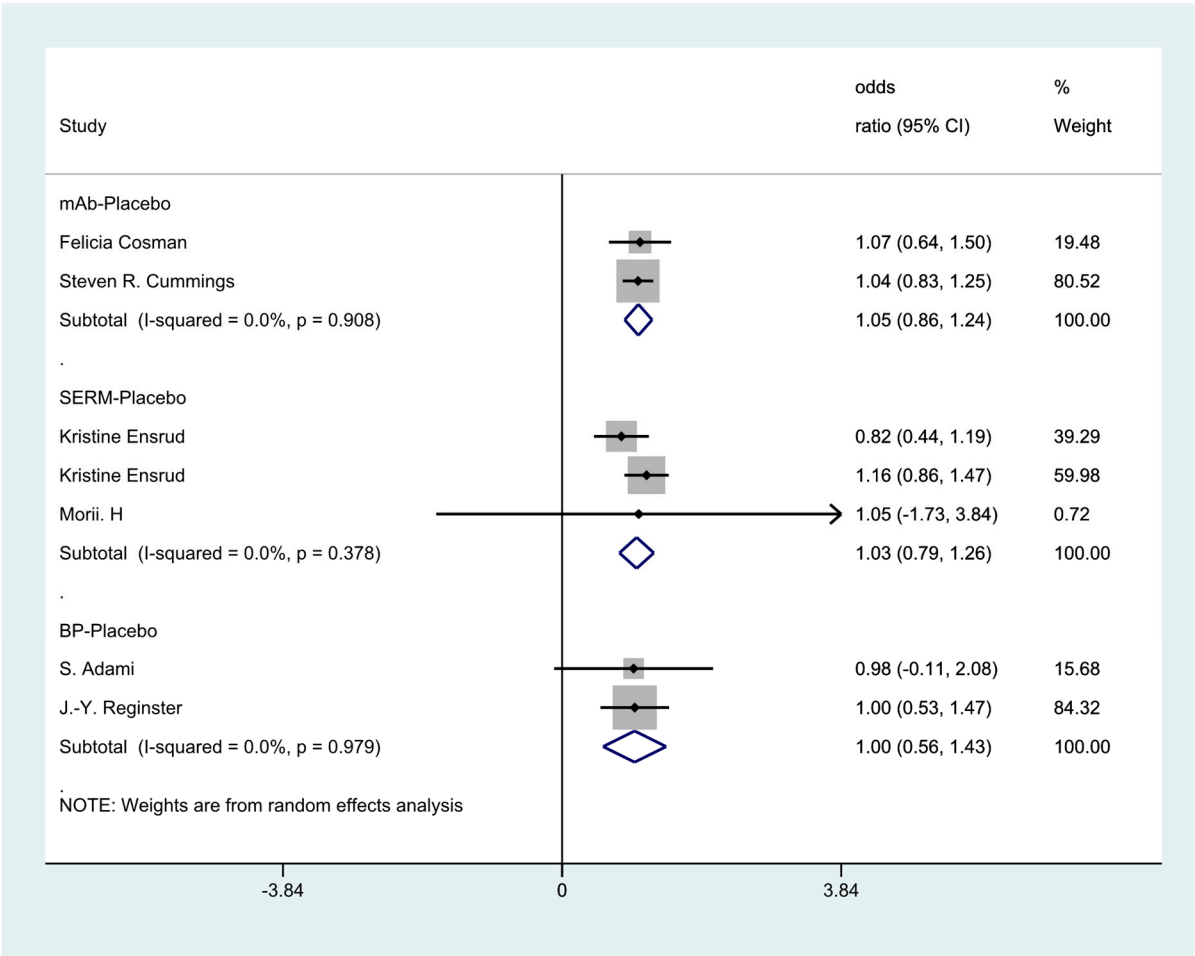


Figure S3: Forest Plots of Direct Pairwise Comparisons for incidence of adverse events including (A) cancer (B) cardiovascular disease (CVD) (C) hip fracture and (D) death.

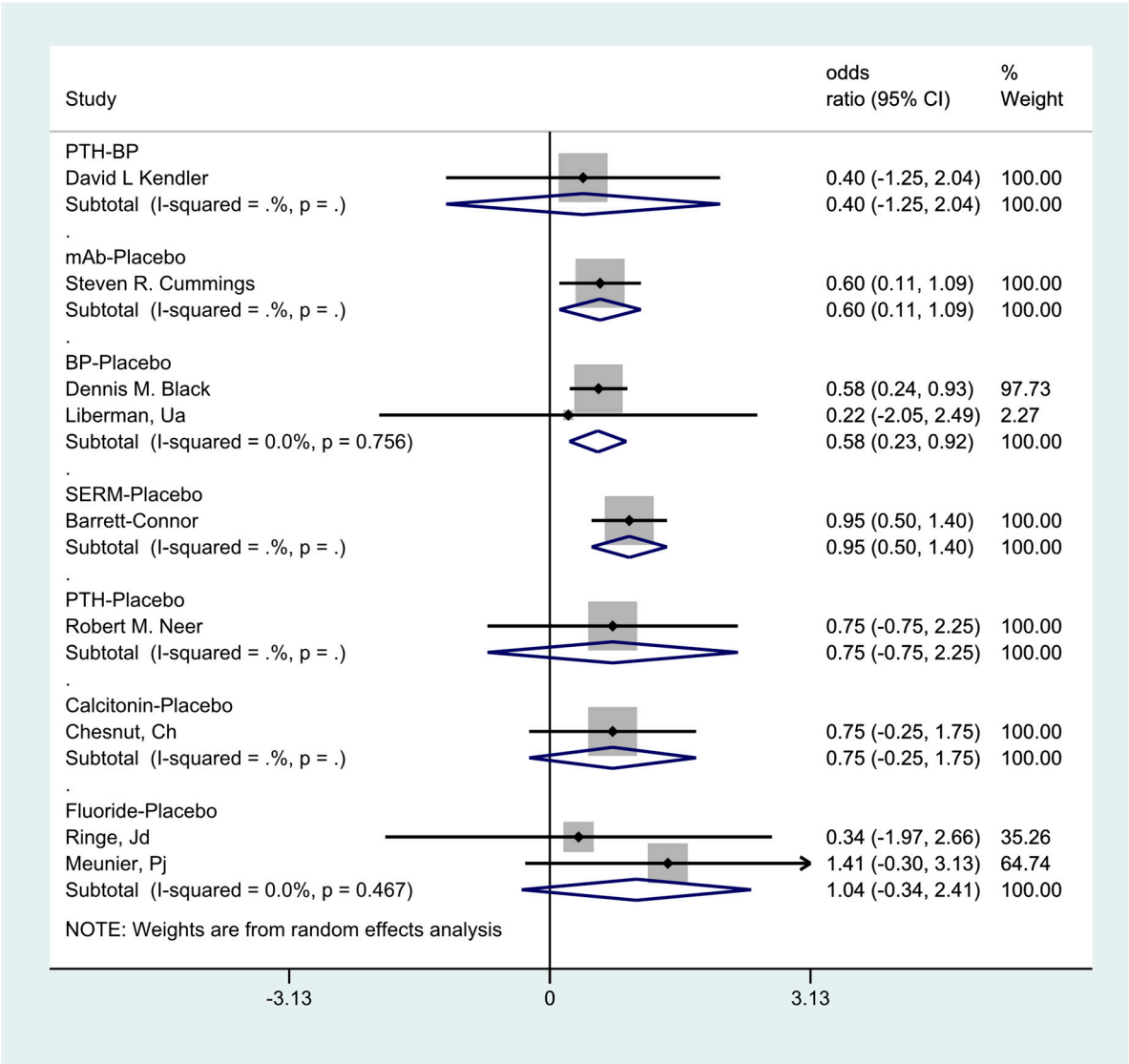
(A) Cancer



(B) Cardiovascular disease (CVD)



(C) Hip fracture



(D) Death

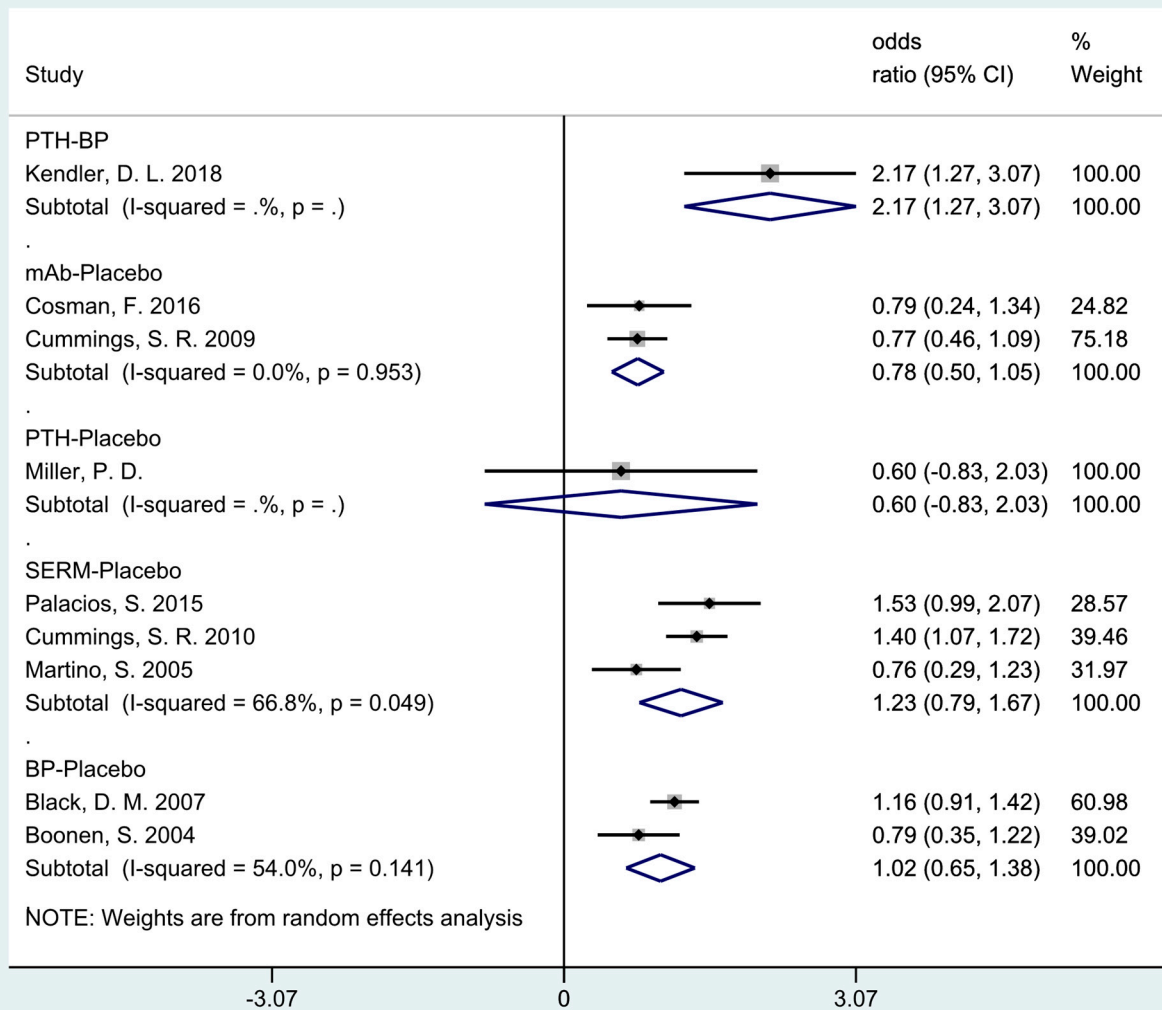


Figure S4: The Surface Under the Cumulative Ranking Curves (SUCRAs) for the outcomes of individual interventions including BMD **(A)** at lumbar spine (LS), **(B)** total hip (TH), **(C)** radius (RU) and incidence of **(D)** cancer, **(E)** cardiovascular disease (CVD), **(F)** hip fracture, and **(G)** death.

(A) BMD at lumbar spine (LS)

Treatment	SUCRA	PrBest	MeanRank
Placebo	6.5	0.0	9.4
BP	57.8	0.0	4.8
mAb	79.4	12.8	2.9
HRT	43.1	0.0	6.1
SERM	27.1	0.0	7.6
PTH	85.6	13.1	2.3
Calcitonin	27.0	0.0	7.6
SrRan	69.5	3.1	3.7
Fluoride	94.9	71.0	1.5
VitD	9.2	0.0	9.2

(B) BMD at total hip (TH)

Treatment	SUCRA	PrBest	MeanRank
Placebo	3.5	0.0	9.7
BP	70.3	0.0	3.7
mAb	86.8	26.6	2.2
HRT	70.7	4.2	3.6
SERM	37.7	0.0	6.6
PTH	47.9	0.0	5.7
Calcitonin	25.9	0.0	7.7
SrRan	95.6	66.6	1.4
Fluoride	31.4	0.0	7.2
VitD	30.1	2.6	7.3

(C) BMD at radius (RU)

Treatment	SUCRA	PrBest	MeanRank
Placebo	27.9	0.0	7.5
BP	68.8	0.9	3.8
mAb	50.9	2.7	5.4
HRT	93.0	55.2	1.6
SERM	41.8	1.1	6.2
PTH	3.3	0.0	9.7
Calcitonin	90.1	37.4	1.9
Fluoride	57.6	2.4	4.8
VitD	22.8	0.0	7.9
VitK	43.9	0.3	6.1

(D) Incidence of Cancer

Treatm~t	SUCRA	PrBest	MeanRank
Placebo	61.6	21.9	2.2
BP	62.6	39.3	2.1
mAb	73.4	38.8	1.8
SERM	2.4	0.0	3.9

(E) Incidence of cardiovascular disease (CVD)

Treatm~t	SUCRA	PrBest	MeanRank
Placebo	47.1	9.0	2.6
BP	47.4	33.7	2.6
mAb	65.1	39.3	2.0
SERM	40.4	18.0	2.8

(F) incidence of hip fracture

Treatment	SUCRA	PrBest	MeanRank
Placebo	81.2	25.0	2.1
BP	31.1	0.0	5.1
mAb	35.4	0.7	4.9
SERM	75.0	24.0	2.5
PTH	17.4	2.1	6.0
Calcitonin	54.2	21.3	3.8
Fluoride	55.8	26.9	3.7

(G) Incidence of Death

Treatm~t	SUCRA	PrBest	MeanRank
Placebo	47.2	2.5	3.1
BP	37.6	3.0	3.5
mAb	15.5	1.2	4.4
SERM	72.4	31.5	2.1
PTH	77.3	61.8	1.9

Figure S5. Assessment of Inconsistency Results Between Direct and Indirect Evidence for the Outcomes of BMD at **(A)** Lumbar Spine (LS) **(B)** Total Hip (TH) **(C)** Radius (RU) and Incidence of **(D)** Cancer **(E)** Hip fracture **(F)** Death within the Networks Using the Design-by-Treatment Interaction Models, Loop Inconsistency Models, and Side-splitting Models.

(A) BMD at lumbar spine (LS)

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

```
Testing for inconsistency:
( 1) [_y_B]des_ABD = 0
( 2) [_y_B]des_ABE = 0
( 3) [_y_B]des_ABG = 0
( 4) [_y_D]des_AD = 0
( 5) [_y_E]des_AE = 0
( 6) [_y_G]des_AG = 0
( 7) [_y_D]des_BD = 0
( 8) [_y_E]des_BE = 0
( 9) [_y_F]des_BF = 0
(10) [_y_G]des_BG = 0
(11) [_y_H]des_BH = 0
(12) [_y_I]des_BI = 0
(13) [_y_F]des_CF = 0
(14) [_y_F]des_FG = 0

      chi2( 14) =    15.43
Prob > chi2 =    0.3492
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B						
des_ABD	.2106389	2.655795	0.08	0.937	-4.994623	5.415901
des_ABE	-2.085361	2.607796	-0.80	0.424	-7.196547	3.025825
des_ABG	-1.382632	1.586424	-0.87	0.383	-4.491966	1.726702
_cons	6.389361	.5050656	12.65	0.000	5.399451	7.379271
_y_C						
_cons	8.257541	1.777056	4.65	0.000	4.774575	11.74051
_y_D						
des_AD	-3.027875	3.187885	-0.95	0.342	-9.276015	3.220266
des_BD	-4.80965	3.757999	-1.28	0.201	-12.17519	2.555893
_cons	6.6	2.590077	2.55	0.011	1.523542	11.67646
_y_E						
des_AE	-.4242197	2.810983	-0.15	0.880	-5.933644	5.085205
des_BE	.398245	3.221872	0.12	0.902	-5.916508	6.712998
_cons	2.104	2.558451	0.82	0.411	-2.910472	7.118472
_y_F						
des_BF	5.099325	1.726678	2.95	0.003	1.715099	8.483551
des_CF	2.129756	2.815275	0.76	0.449	-3.388082	7.647594
des_FG	-2.777251	2.450728	-1.13	0.257	-7.58059	2.026087
_cons	7.327771	.8861815	8.27	0.000	5.590887	9.064654
_y_G						
des_AG	1.275388	1.880271	0.68	0.498	-2.409874	4.960651
des_BG	4.235611	3.010028	1.41	0.159	-1.663936	10.13516
_cons	.2537345	1.502189	0.17	0.866	-2.690502	3.197971
_y_H						
des_BH	.3596695	3.191427	0.11	0.910	-5.895413	6.614752
_cons	6.929682	1.274097	5.44	0.000	4.432498	9.426867
_y_I						
des_BI	1.404938	3.31673	0.42	0.672	-5.095734	7.90561
_cons	9.287914	1.461523	6.35	0.000	6.423381	12.15245
_y_J						
_cons	.1934848	2.25647	0.09	0.932	-4.229115	4.616084

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

Testing for inconsistency:

```
( 1) [_y_D]groupB = 0
( 2) [_y_E]groupB = 0
( 3) [_y_F]groupB = 0
( 4) [_y_G]groupB = 0
( 5) [_y_H]groupB = 0
( 6) [_y_I]groupB = 0
( 7) [_y_F]groupC = 0
( 8) [_y_G]groupF = 0
```

```
      chi2( 8) =    13.32
Prob > chi2 =    0.1013
```

		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	_cons	6.160807	.4423097	13.93	0.000	5.293896	7.027718
_y_C	_cons	8.258042	1.721215	4.80	0.000	4.884523	11.63156
_y_D	groupB	-3.163401	2.969698	-1.07	0.287	-8.983903	2.657101
	_cons	4.725198	1.390939	3.40	0.001	1.999008	7.451387
_y_E	groupB	.3130226	2.130841	0.15	0.883	-3.863349	4.489394
	_cons	1.969962	1.002213	1.97	0.049	.0056604	3.934264
_y_F	groupB	4.84199	1.665609	2.91	0.004	1.577456	8.106524
	groupC	2.126076	2.737019	0.78	0.437	-3.238383	7.490536
	_cons	7.331952	.8611177	8.51	0.000	5.644192	9.019711
_y_G	groupB	3.028913	2.637923	1.15	0.251	-2.141321	8.199148
	groupF	1.799142	2.064046	0.87	0.383	-2.246314	5.844598
	_cons	1.23188	.8312695	1.48	0.138	-.3973784	2.861138
_y_H	groupB	.1272365	3.104391	0.04	0.967	-5.957258	6.211731
	_cons	6.933562	1.235132	5.61	0.000	4.512747	9.354377
_y_I	groupB	1.209236	3.251925	0.37	0.710	-5.16442	7.582892
	_cons	9.26654	1.42258	6.51	0.000	6.478334	12.05475
_y_J	_cons	-.0529302	2.197001	-0.02	0.981	-4.358973	4.253112

Side-Splitting Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT);
E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium
ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

Side	Direct		Indirect		Difference		P> z	tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.		
A B	6.196154	.4538203	4.132096	.9570798	2.064058	1.059516	0.051	2.455163
A C	8.257558	1.778173	7.045155	2.117893	1.212403	2.765392	0.661	2.511303
A D	4.606274	1.504086	2.129696	2.35353	2.476578	2.795795	0.376	2.49907
A E	1.750899	1.061037	2.459429	1.812532	-.7085292	2.099402	0.736	2.512755
A F	7.330105	.8719392	9.773941	1.054239	-2.443836	1.368277	0.074	2.46484
A G	1.065313	.8890846	3.778371	1.340119	-2.713057	1.610263	0.092	2.468347
A H	6.929513	1.275878	6.713392	2.916039	.2161202	3.182948	0.946	2.513355
A I	9.286751	1.459207	10.13511	2.96143	-.8483575	3.302089	0.797	2.505472
B D	-2.217559	1.864503	-1.667899	1.78944	-.5496591	2.586568	0.832	2.514939
B E	-3.294734	1.524342	-4.26139	1.215859	.9666563	1.949831	0.620	2.510031
B F	5.998816	1.332838	1.130306	.834634	4.86851	1.573804	0.002	2.386217
B G	-4.03145	1.29177	-3.846867	1.020269	-.1845824	1.64637	0.911	2.516907
B H	.9000007	2.88527	1.11611	1.344023	-.216109	3.182951	0.946	2.513357
B I	4.304115	2.931347	3.455575	1.518741	.8483655	3.302089	0.797	2.505472
B J *	-6.198922	2.190618	-11.57971	3896.614	5.380786	3896.614	0.999	2.495973
C F	1.200002	1.996633	-.0123734	1.913337	1.212375	2.765393	0.661	2.511304
F G	-4.298237	1.707496	-7.263246	1.070888	2.965008	2.015653	0.141	2.481604

(B) BMD at total hip (TH)

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT);
E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium
ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

Testing for inconsistency:

```
( 1) [_y_B]des_ABD = 0
( 2) [_y_B]des_ABE = 0
( 3) [_y_B]des_ABG = 0
( 4) [_y_D]des_AD = 0
( 5) [_y_E]des_AE = 0
( 6) [_y_G]des_AG = 0
( 7) [_y_D]des_BD = 0
( 8) [_y_E]des_BE = 0
( 9) [_y_F]des_BF = 0
(10) [_y_G]des_BG = 0
(11) [_y_H]des_BH = 0
(12) [_y_I]des_BI = 0
(13) [_y_F]des_CF = 0
(14) [_y_F]des_FG = 0
```

```
chi2( 14) = 11.48
Prob > chi2 = 0.6480
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	des_ABD	-.0690897	1.95869	-0.04	0.972	-3.908051 3.769872
	des_ABE	-1.26909	1.976752	-0.64	0.521	-5.143452 2.605272
	des_ABG	-.2143737	1.190988	-0.18	0.857	-2.548668 2.119921
	_cons	3.76909	.4070995	9.26	0.000	2.971189 4.56699
_y_C	_cons	6.799945	1.830474	3.71	0.000	3.212281 10.38761
_y_D	des_AD	1.5	2.66051	0.56	0.573	-3.714503 6.714503
	des_BD	.8590806	2.770526	0.31	0.757	-4.571051 6.289212
	_cons	3.1	1.915944	1.62	0.106	-.655182 6.855182
_y_E	des_AE	.1978133	2.338011	0.08	0.933	-4.384605 4.780231
	des_BE	1.269086	2.706993	0.47	0.639	-4.036522 6.574695
	_cons	1.5	1.910786	0.79	0.432	-2.245071 5.245071
_y_F	des_BF	3.496893	1.272521	2.75	0.006	1.002797 5.990989
	des_CF	4.205445	2.369122	1.78	0.076	-.4379488 8.848838
	des_FG	-.5267585	2.246476	-0.23	0.815	-4.92977 3.876253
	_cons	1.394485	.6547347	2.13	0.033	.111229 2.677742
_y_G	des_AG	.4071333	1.540162	0.26	0.792	-2.611529 3.425796
	des_BG	1.701332	2.218675	0.77	0.443	-2.647191 6.049856
	_cons	.9677511	1.116166	0.87	0.386	-1.219894 3.155396
_y_H	des_BH	-.6699296	2.422117	-0.28	0.782	-5.417192 4.077333
	_cons	5.839013	1.077182	5.42	0.000	3.727775 7.950252
_y_I	des_BI	-.2202793	1.956448	-0.11	0.910	-4.054847 3.614288
	_cons	1.767048	.8704673	2.03	0.042	.0609633 3.473132
_y_J	_cons	1.569086	2.198547	0.71	0.475	-2.739987 5.87816

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

Testing for inconsistency:

```
( 1) [_y_D]groupB = 0
( 2) [_y_E]groupB = 0
( 3) [_y_F]groupB = 0
( 4) [_y_G]groupB = 0
( 5) [_y_H]groupB = 0
( 6) [_y_I]groupB = 0
( 7) [_y_F]groupC = 0
( 8) [_y_G]groupF = 0

      chi2( 8) =    11.63
Prob > chi2 =    0.1685
```

		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	_cons	3.717969	.3433816	10.83	0.000	3.044953	4.390984
_y_C	_cons	6.799951	1.719434	3.95	0.000	3.429923	10.16998
_y_D	groupB	.1414085	2.198276	0.06	0.949	-4.167132	4.449949
	_cons	3.766552	1.156964	3.26	0.001	1.498944	6.03416
_y_E	groupB	.8636165	2.042042	0.42	0.672	-3.138711	4.865944
	_cons	1.854349	.9902935	1.87	0.061	-.0865906	3.795289
_y_F	groupB	3.405061	1.193896	2.85	0.004	1.065068	5.745054
	groupC	4.194764	2.230827	1.88	0.060	-.1775774	8.567105
	_cons	1.405175	.6199413	2.27	0.023	.1901119	2.620237
_y_G	groupB	1.419738	1.90636	0.74	0.456	-2.316659	5.156134
	groupF	.3069156	1.955892	0.16	0.875	-3.526561	4.140393
	_cons	1.198225	.6805293	1.76	0.078	-.1355877	2.532038
_y_H	groupB	-.7318574	2.300579	-0.32	0.750	-5.240909	3.777194
	_cons	5.849821	1.014107	5.77	0.000	3.862208	7.837433
_y_I	groupB	-.2829641	1.871088	-0.15	0.880	-3.950229	3.384301
	_cons	1.758951	.823268	2.14	0.033	.1453759	3.372527
_y_J							
	_cons	1.517965	2.095615	0.72	0.469	-2.589364	5.625295

Side-Splitting Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z	
A B	3.696167	.3519623	2.440064	.7261904	1.256102	.8070284	0.120	1.733721
A C	6.8	1.726267	3.441772	1.381626	3.358228	2.211083	0.129	1.720702
A D	3.873681	1.286719	3.342586	1.682254	.531095	2.127133	0.803	1.76342
A E	1.632294	1.064462	2.72948	1.632778	-1.097186	1.949113	0.573	1.759134
A F	1.410056	.6057899	4.211569	.8077713	-2.801513	1.010673	0.006	1.668444
A G	1.183228	.7425085	1.990229	1.123091	-.8070009	1.34618	0.549	1.758431
A H	5.84525	1.039477	4.837181	2.099256	1.008068	2.342481	0.667	1.758721
A I	1.762276	.8418495	1.206052	1.699594	.5562234	1.896449	0.769	1.757798
B D	-.2238181	1.310143	.8934242	1.611651	-1.117242	2.076984	0.591	1.759811
B E	-1.004332	1.301361	-1.961611	1.263921	.9572786	1.817276	0.598	1.759662
B F	1.08132	.9417747	-2.005059	.6356444	3.086379	1.137343	0.007	1.675916
B G	-2.195934	.932067	-1.872853	.8948605	-.3230808	1.29269	0.803	1.764301
B H	1.4	2.074132	2.408064	1.088665	-1.008064	2.34248	0.667	1.75872
B I	-2.23404	1.668257	-1.677821	.9026208	-.5562187	1.896451	0.769	1.757801
B J *	-2.2	2.094411	-6.842195	2873.939	4.642195	2873.94	0.999	1.746469
C F	-1.2	1.283596	-4.558203	1.80035	3.358203	2.21108	0.129	1.720699
F G	.1	1.769043	-1.23194	.8266983	1.33194	1.952676	0.495	1.757447

(C) BMD at radius (RU)

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: Fluoride; I: active vitamin D (VitD); J: vitamin K (VitK)

Testing for inconsistency:

```
( 1)  [_y_B]des_ABDGIJ = 0
( 2)  [_y_B]des_ABJ = 0
( 3)  [_y_J]des_ABJ = 0
( 4)  [_y_F]des_BF = 0

      chi2( 4) =      2.97
Prob > chi2 =      0.5621
```


	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B						
des_ABDGIJ	1.031458	2.250362	0.46	0.647	-3.379171	5.442087
des_ABJ	1.031458	2.438394	0.42	0.672	-3.747706	5.810622
_cons	1.768542	1.029362	1.72	0.086	-.248971	3.786055
_y_C						
_cons	2.468227	2.138485	1.15	0.248	-1.723127	6.659581
_y_D						
_cons	5.3	2.006328	2.64	0.008	1.36767	9.23233
_y_E						
_cons	.7	2.030781	0.34	0.730	-3.280257	4.680257
_y_F						
des_BF	-4.856083	2.887236	-1.68	0.093	-10.51496	.8027955
_cons	-1.175372	1.471968	-0.80	0.425	-4.060377	1.709632
_y_G						
_cons	4.9	1.996657	2.45	0.014	.9866234	8.813377
_y_H						
_cons	1.861939	1.519276	1.23	0.220	-1.115787	4.839664
_y_I						
_cons	-.3	1.996472	-0.15	0.881	-4.213013	3.613013
_y_J						
des_ABJ	-.8	2.987729	-0.27	0.789	-6.655841	5.055841
_cons	1.4	2.009785	0.70	0.486	-2.539105	5.339105

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT);
E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: Fluoride; I:
active vitamin D (VitD); J: vitamin K (VitK)

Testing for inconsistency:

```
( 1)  [_y_F]groupB = 0

      chi2( 1) =    3.39
Prob > chi2 =    0.0656
```

		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	_cons	2.113888	.7010388	3.02	0.003	.7398771	3.487899
_y_C	_cons	2.379368	1.8008	1.32	0.186	-1.150136	5.908871
_y_D	_cons	4.851498	1.43538	3.38	0.001	2.038206	7.664791
_y_E	_cons	.7	1.671868	0.42	0.675	-2.576801	3.976801
_y_F	groupB	-4.424314	2.402632	-1.84	0.066	-9.133386	.2847568
	_cons	-1.261796	1.225691	-1.03	0.303	-3.664107	1.140514
_y_G	_cons	4.451498	1.421832	3.13	0.002	1.664759	7.238237
_y_H	_cons	1.770134	1.280285	1.38	0.167	-.7391788	4.279446
_y_I	_cons	-.7485019	1.421571	-0.53	0.599	-3.534731	2.037727
_y_J	_cons	.7315285	1.139759	0.64	0.521	-1.502358	2.965415

Side-Splitting Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: Fluoride; I: active vitamin D (VitD); J: vitamin K (VitK)

Side	Direct		Indirect		Difference		P> z	tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.		
A B *	2.113887	.7010388	6.538194	2.296828	-4.424307	2.402629	0.066	1.599093
A D *	5.3	1.946608	4.233402	3.401374	1.066598	3.911008	0.785	1.910487
A E
A F	-1.261795	1.225691	-5.686086	2.065077	4.424291	2.402625	0.066	1.599094
A G *	4.9	1.93664	3.833402	3.39568	1.066598	3.911009	0.785	1.910488
A H
A I *	-.3	1.936449	-1.366598	3.395571	1.066598	3.911009	0.785	1.910488
A J *	1.043364	1.442688	.2259352	3.132171	.8174286	3.428409	0.812	1.904758
B D *	2.5	1.959608	2.633439	3.431117	-.1334387	3.946012	0.973	1.920996
B F	-7.8	1.942451	-3.375684	1.414044	-4.424316	2.402631	0.066	1.599093
B G *	2.1	1.949707	2.233438	3.425472	-.1334383	3.946014	0.973	1.920997
B I *	-3.1	1.949514	-2.966561	3.425359	-.1334391	3.946008	0.973	1.920993
B J *	-1.749244	1.462868	-.9318149	3.104718	-.8174287	3.428417	0.812	1.904763
C F *	-3.642489	1.431095	-4.742603	1614.783	1.100114	1614.784	0.999	1.781107
D G
D I
D J *	-3.9	1.942151	-5.482926	4.667951	1.582926	5.058605	0.754	1.894049
G I
G J *	-3.5	1.932156	-5.082925	4.663797	1.582925	5.058598	0.754	1.894046
I J *	1.7	1.931966	.1170741	4.66372	1.582926	5.058601	0.754	1.894047

(D) Incidence of Cancer

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM)

```
Testing for inconsistency:
( 1)  [_y_C]des_BC = 0

      chi2( 1) =      0.15
      Prob > chi2 =      0.6991
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B _cons	.1163682	.3669585	0.32	0.751	-.6028573	.8355938
_y_C des_BC	.1904792	.4928562	0.39	0.699	-.7755012	1.15646
	.0161595	.1456462	0.11	0.912	-.2693019	.3016209
_y_D _cons	-.4320222	.1865551	-2.32	0.021	-.7976635	-.0663809

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM)

```
Testing for inconsistency:
( 1)  [_y_C]groupB = 0

      chi2( 1) =      0.15
      Prob > chi2 =      0.6991
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B _cons	.1163682	.3669585	0.32	0.751	-.6028573	.8355938
_y_C groupB _cons	.1904792	.4928562	0.39	0.699	-.7755012	1.15646
	.0161595	.1456462	0.11	0.912	-.2693019	.3016209
_y_D _cons	-.4320222	.1865551	-2.32	0.021	-.7976635	-.0663809

Side-

Splitting Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM)

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z	
A B	.116367	.3669618	-.0741228	.3291707	.1904898	.4929648	0.699	.1344039
A C	.0161461	.1450142	.2066352	.4708476	-.1904891	.4926729	0.699	.1344012
A D
B C	.0902683	.2950202	-.1002212	.3947944	.1904894	.4928484	0.699	.1343997

(E) Incidence of hip fracture

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH); F: Calcitonin; G: Fluoride

Testing for inconsistency:

```
( 1)  [_y_E]des_BE = 0
```

```
      chi2( 1) =      0.73
Prob > chi2 =      0.3934
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B _cons	-.560394	.1743985	-3.21	0.001	-.9022089	-.2185792
_y_C _cons	-.5064632	.2494679	-2.03	0.042	-.9954112	-.0175152
_y_D _cons	-.0491759	.2307689	-0.21	0.831	-.5014746	.4031228
_y_E des_BE _cons	-.9368668	1.097788	-0.85	0.393	-3.088491	1.214757
	-.5442526	.6868526	-0.79	0.428	-1.890459	.8019537
_y_F _cons	-.2845401	.5105043	-0.56	0.577	-1.28511	.7160299
_y_G _cons	-.2914165	.6460761	-0.45	0.652	-1.557702	.9748694

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH); F: Calcitonin; G: Fluoride

Testing for inconsistency:

```
( 1)  [_y_E]groupB = 0
```

```
      chi2( 1) =      0.73
Prob > chi2 =      0.3934
```

		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	_cons	-.560394	.1743985	-3.21	0.001	-.9022089	-.2185792
_y_C	_cons	-.5064632	.2494679	-2.03	0.042	-.9954112	-.0175152
_y_D	_cons	-.0491759	.2307689	-0.21	0.831	-.5014746	.4031228
_y_E	groupB	-.9368668	1.097788	-0.85	0.393	-3.088491	1.214757
	_cons	-.5442526	.6868526	-0.79	0.428	-1.890459	.8019537
_y_F	_cons	-.2845401	.5105043	-0.56	0.577	-1.28511	.7160299
_y_G	_cons	-.2914165	.6460761	-0.45	0.652	-1.557702	.9748694

Side-Splitting Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH); F: Calcitonin; G: Fluoride

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z	
A B	-.560394	.1743985	.3764728	1.083847	-.9368667	1.097788	0.393	2.47e-06
A C
A D
A E	-.5442526	.6868526	-1.481119	.856371	.9368668	1.097788	0.393	2.57e-06
A F
A G
B E	-.9207253	.8384249	.0161415	.7086475	-.9368668	1.097788	0.393	3.05e-08

(F) Incidence of Death

Design-by-Treatment Interaction Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH)

Testing for inconsistency:

(1) [_y_E]des_BE = 0

chi2(1) = 1.91
Prob > chi2 = 0.1673

		Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B	_cons	-.0024594	.1887356	-0.01	0.990	-.3723744	.3674556
_y_C	_cons	-.2303769	.2040826	-1.13	0.259	-.6303714	.1696177
_y_D	_cons	.1724264	.1717063	1.00	0.315	-.1641118	.5089646
_y_E	des_BE	1.282465	.928733	1.38	0.167	-.5378186	3.102748
	_cons	-.5108256	.7583527	-0.67	0.501	-1.99717	.9755184

Loop Inconsistency Model

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH)

Testing for inconsistency:

```
( 1)  [_y_E]groupB = 0

      chi2( 1) =      1.91
      Prob > chi2 =    0.1673
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_y_B _cons	-.0024594	.1887356	-0.01	0.990	-.3723744	.3674556
_y_C _cons	-.2303769	.2040826	-1.13	0.259	-.6303714	.1696177
_y_D _cons	.1724264	.1717063	1.00	0.315	-.1641118	.5089646
_y_E groupB _cons	1.282465 -.5108256	.928733 .7583527	1.38 -0.67	0.167 0.501	-.5378186 -1.99717	3.102748 .9755184

Side-Splitting Model

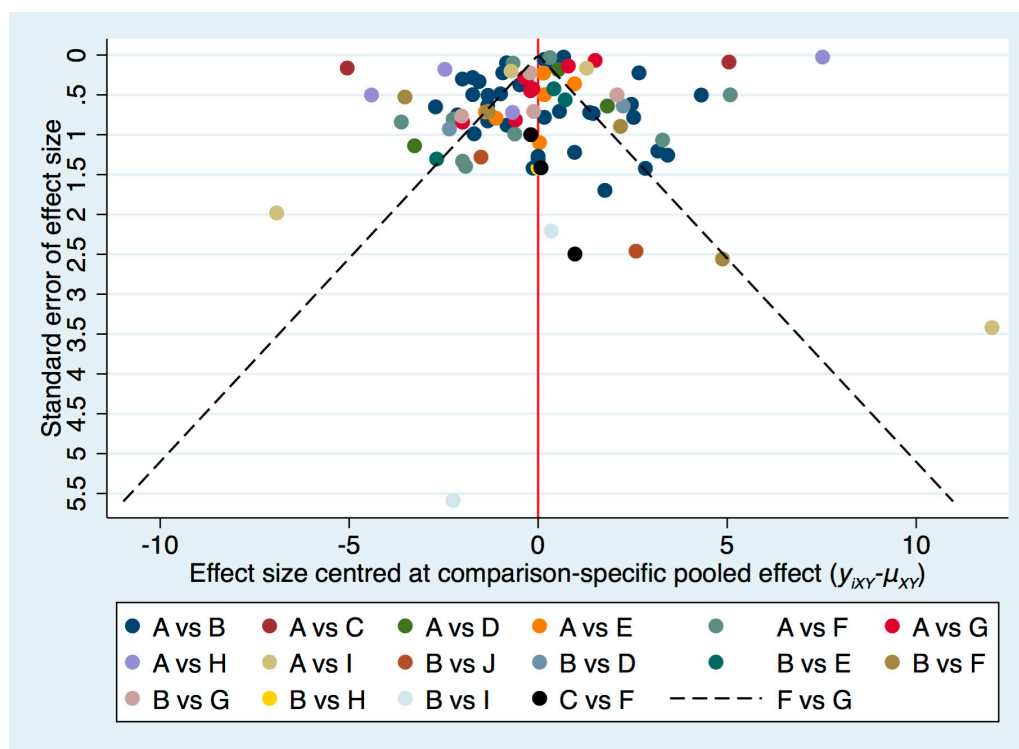
A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH)

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	P> z	
A B	-.0024594	.1887395	-1.284924	.9093537	1.282464	.928734	0.167	.1982714
A C
A D
A E	-.5108256	.7583526	.771639	.5361399	-1.282465	.9287328	0.167	.1982711
B E	.7740984	.5018233	-.5083651	.7814814	1.282463	.9287302	0.167	.1982754

Figure S6. Comparison-Adjusted Funnel Plots for the Outcomes of BMD at (A) lumbar spine (LS) (B) total hip (TH) (C) radius (RU) and incidence of (D) cancer (E) cardiovascular disease (CVD) (F) hip fracture (G) death. The red line represents the null hypothesis that the study-specific effect sizes do not differ from the respective comparison-specific pooled effect estimates.

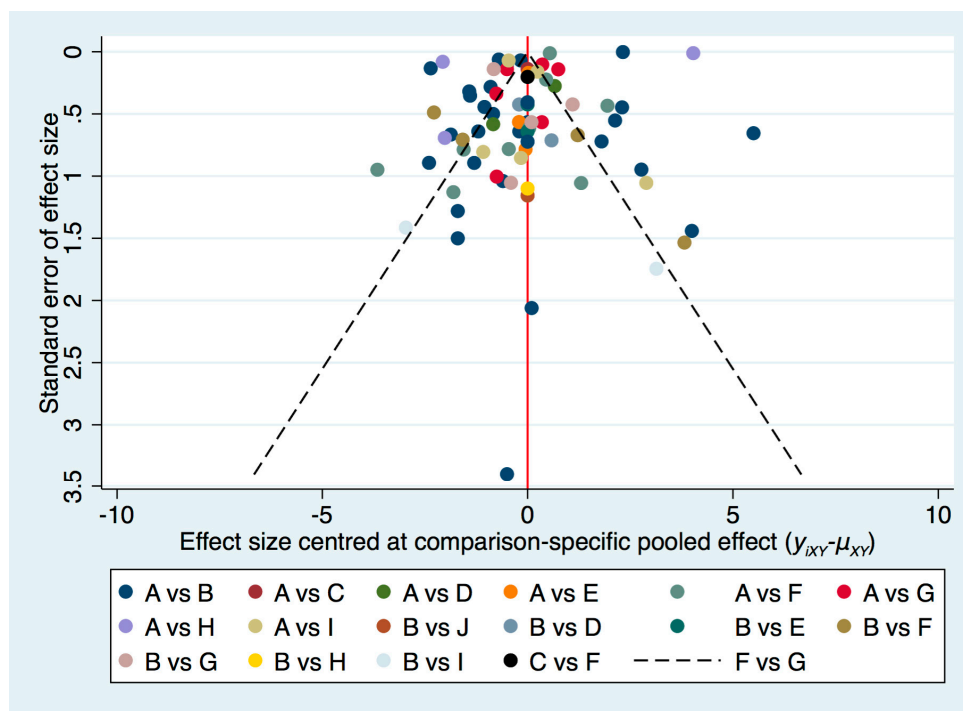
(A) BMD at lumbar spine (LS)

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)



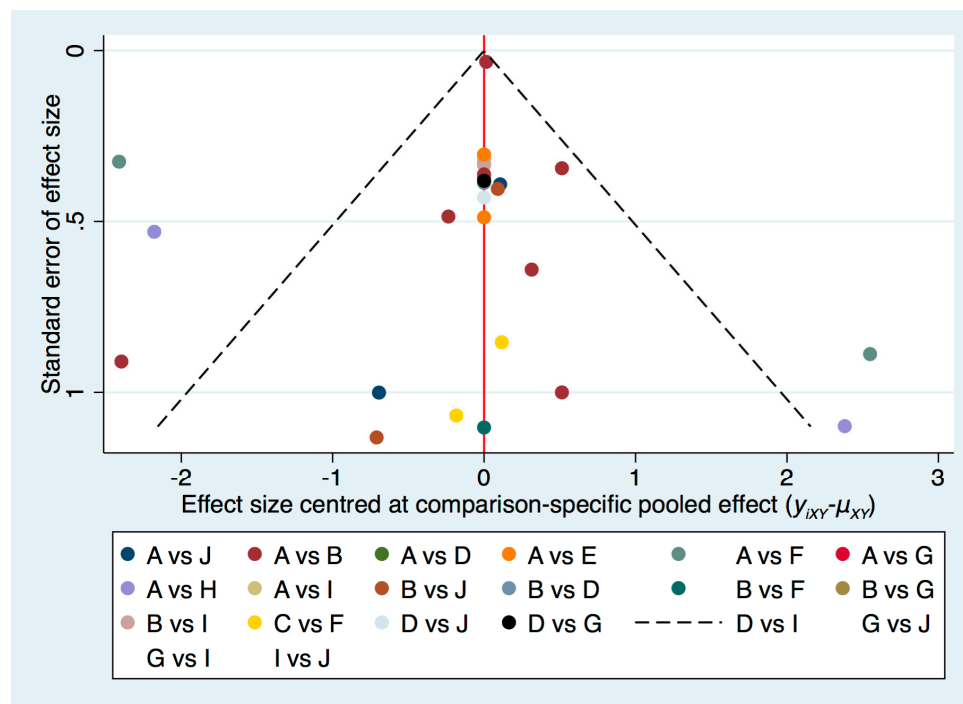
(B) BMD at total hip (TH)

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: strontium ranelate (SrRan); I: Fluoride; J: active vitamin D (VitD)



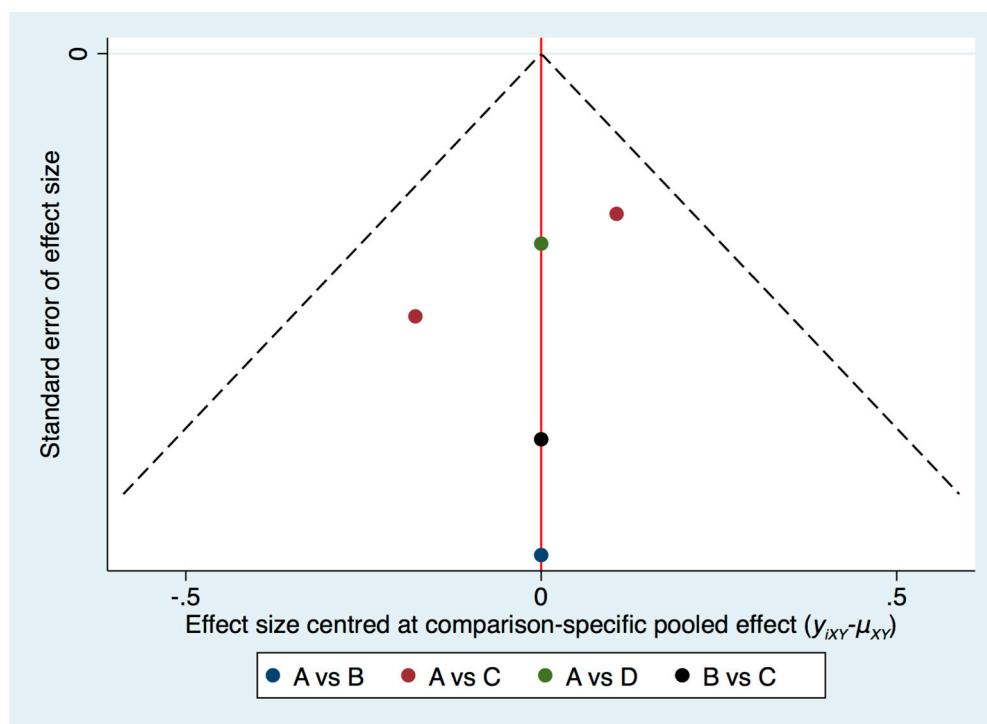
(C) BMD at radius (RU)

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: hormone replacement therapy (HRT); E: selective estrogen receptor modulator (SERM); F: parathyroid hormone (PTH); G: Calcitonin; H: Fluoride; I: active vitamin D (VitD); J: vitamin K (VitK)



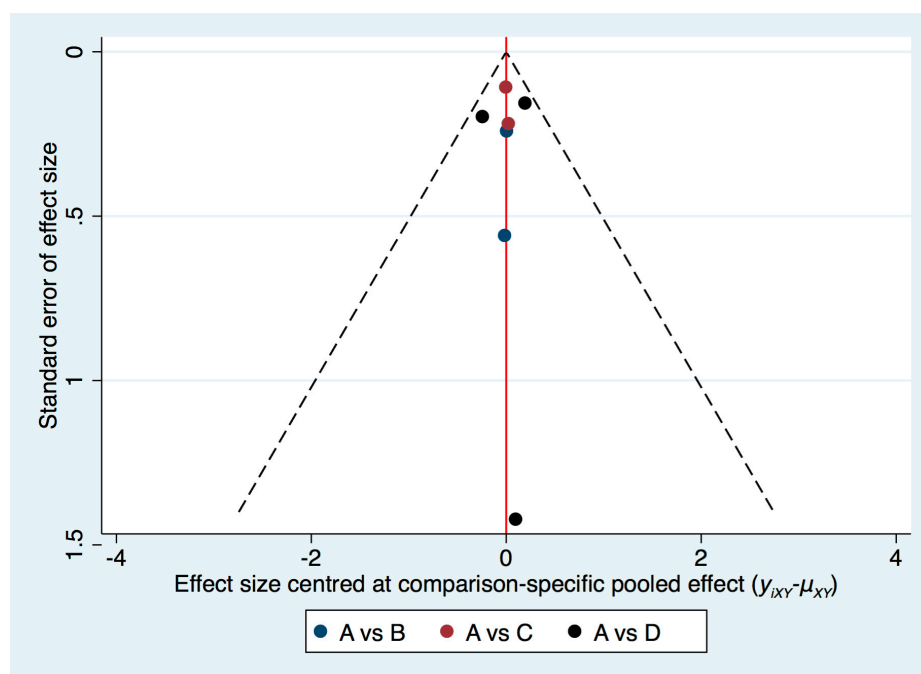
(D) Incidence of Cancer

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM)



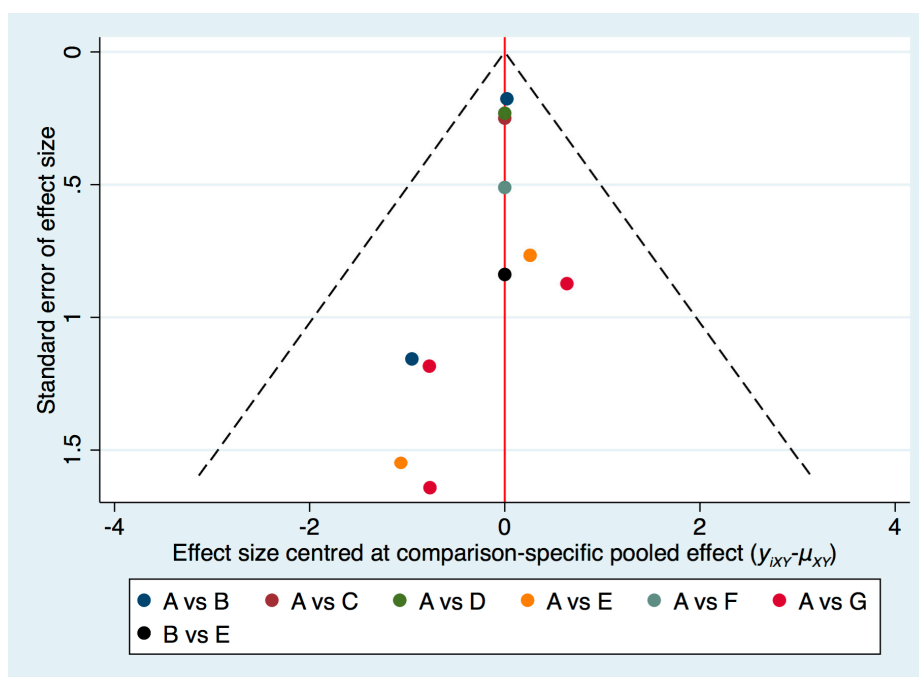
(E) Incidence of cardiovascular disease (CVD)

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM)



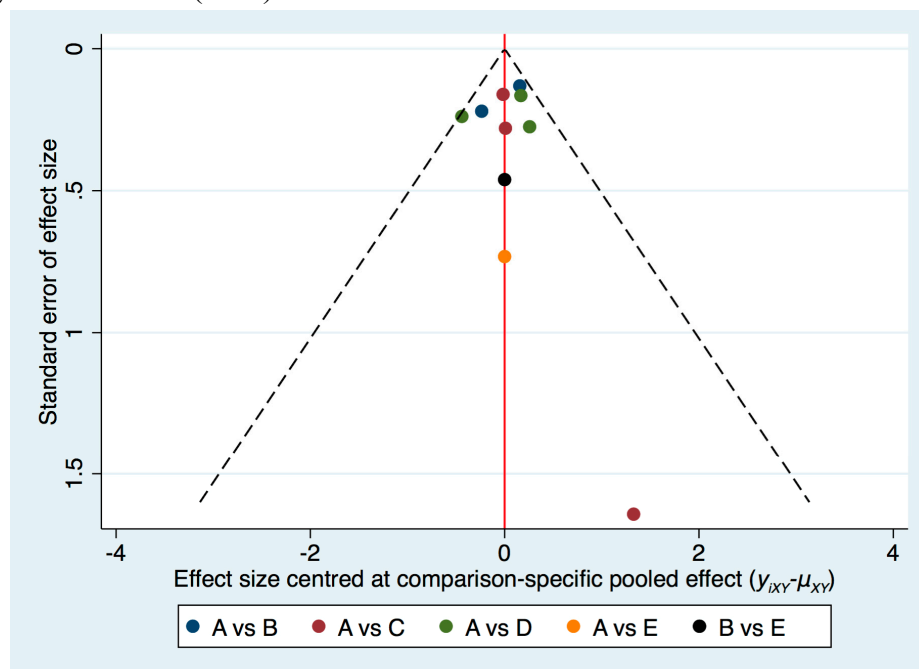
(F) Incidence of hip fracture

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH); F: Calcitonin; G: Fluoride

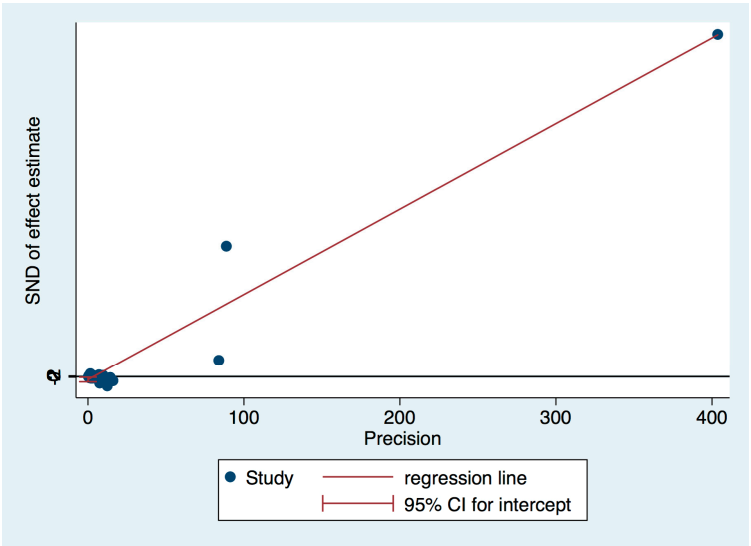


(G) Incidence of death

A: Placebo; B: bisphosphonate (BP); C: monoclonal antibody (mAb); D: selective estrogen receptor modulator (SERM); E: parathyroid hormone (PTH)



(B) BMD at total hip (TH)

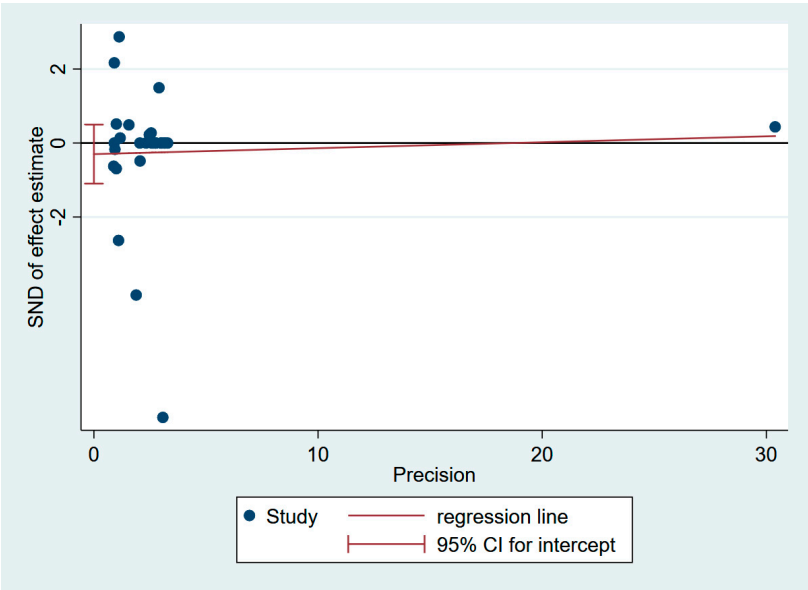


Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies = 77				Root MSE = 26.97		
Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	2.335164	.0652112	35.81	0.000	2.205257	2.465071
bias	-8.023912	3.148003	-2.55	0.013	-14.29505	-1.752769

Test of H0: no small-study effects P = 0.013

(C) BMD at radius (RU)

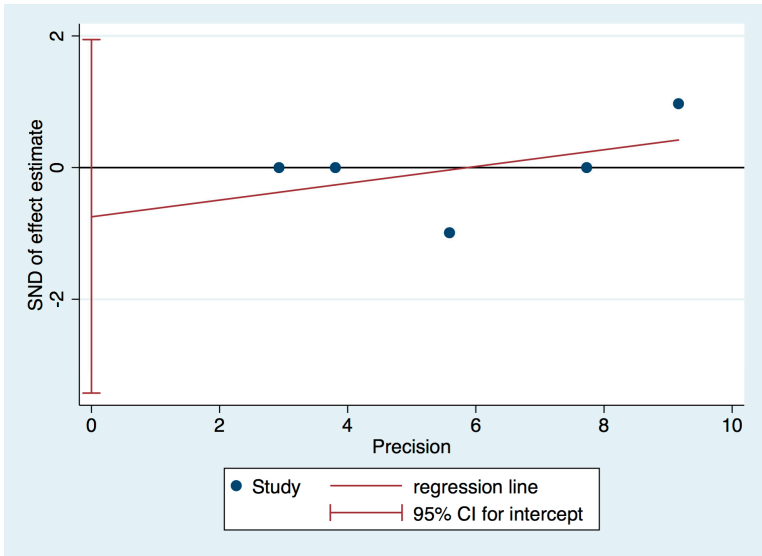


Egger's test for small-study effects:
 Regress standard normal deviate of intervention
 effect estimate against its standard error

Number of studies = 30				Root MSE = 1.831		
Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	.0160382	.0650207	0.25	0.807	-.1171507	.1492272
bias	-.3001536	.3892059	-0.77	0.447	-1.097406	.4970984

Test of H0: no small-study effects P = 0.447

(D) Incidence of Cancer

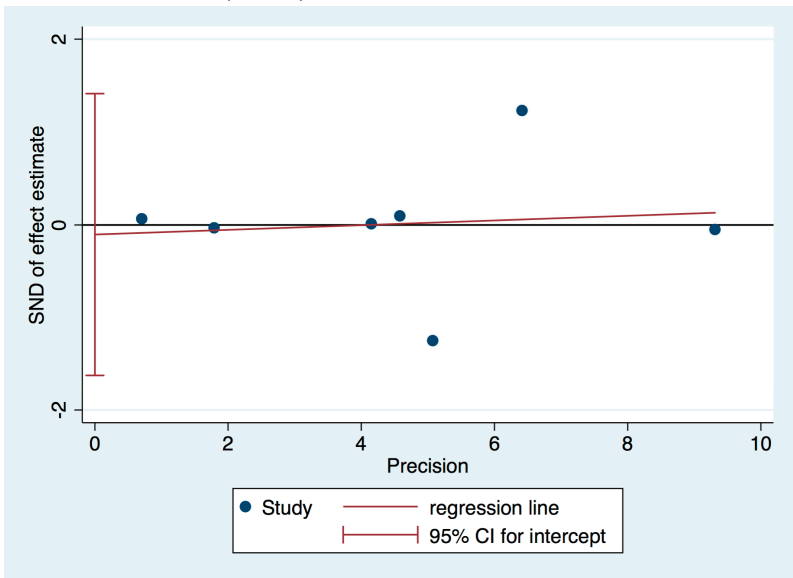


Egger's test for small-study effects:
 Regress standard normal deviate of intervention
 effect estimate against its standard error

Number of studies = 5				Root MSE = .702		
Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	.127339	.1344146	0.95	0.413	-.3004284	.5551064
bias	-.7477861	.8458527	-0.88	0.442	-3.439667	1.944095

Test of H0: no small-study effects P = 0.442

(E) Incidence of cardiovascular disease (CVD)

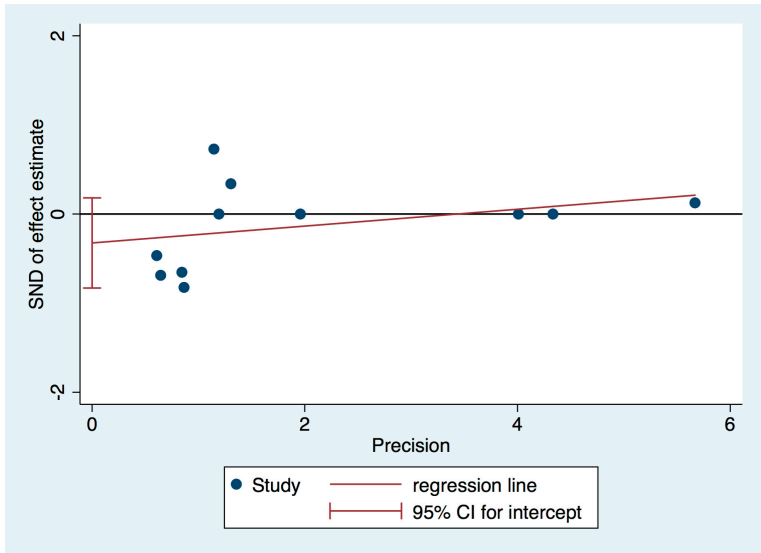


Egger's test for small-study effects:
 Regress standard normal deviate of intervention
 effect estimate against its standard error

Number of studies = 7				Root MSE = .7813		
Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	.0252207	.1116302	0.23	0.830	-.2617339	.3121753
bias	-.1027587	.5898883	-0.17	0.869	-1.619115	1.413597

Test of H0: no small-study effects P = 0.869

(F) Incidence of hip fracture

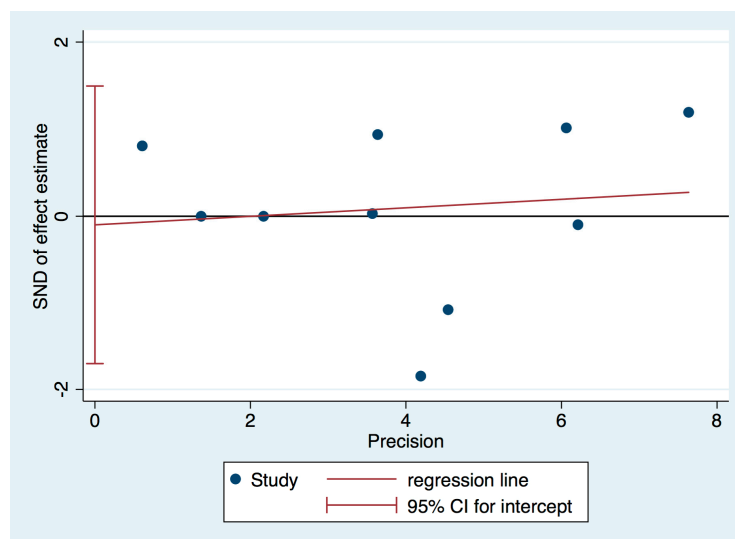


Egger's test for small-study effects:
 Regress standard normal deviate of intervention
 effect estimate against its standard error

Number of studies = 11				Root MSE = .4703		
Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	.0945217	.0842401	1.12	0.291	-.0960427	.2850861
bias	-.3244908	.2236007	-1.45	0.181	-.8303107	.1813292

Test of H0: no small-study effects P = 0.181

(G) Incidence of death



Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error

Number of studies = 10 Root MSE = 1.022

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
slope	.0488426	.1527248	0.32	0.757	-.3033413	.4010265
bias	-.0983542	.6909909	-0.14	0.890	-1.691782	1.495074

Test of H0: no small-study effects P = 0.890

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