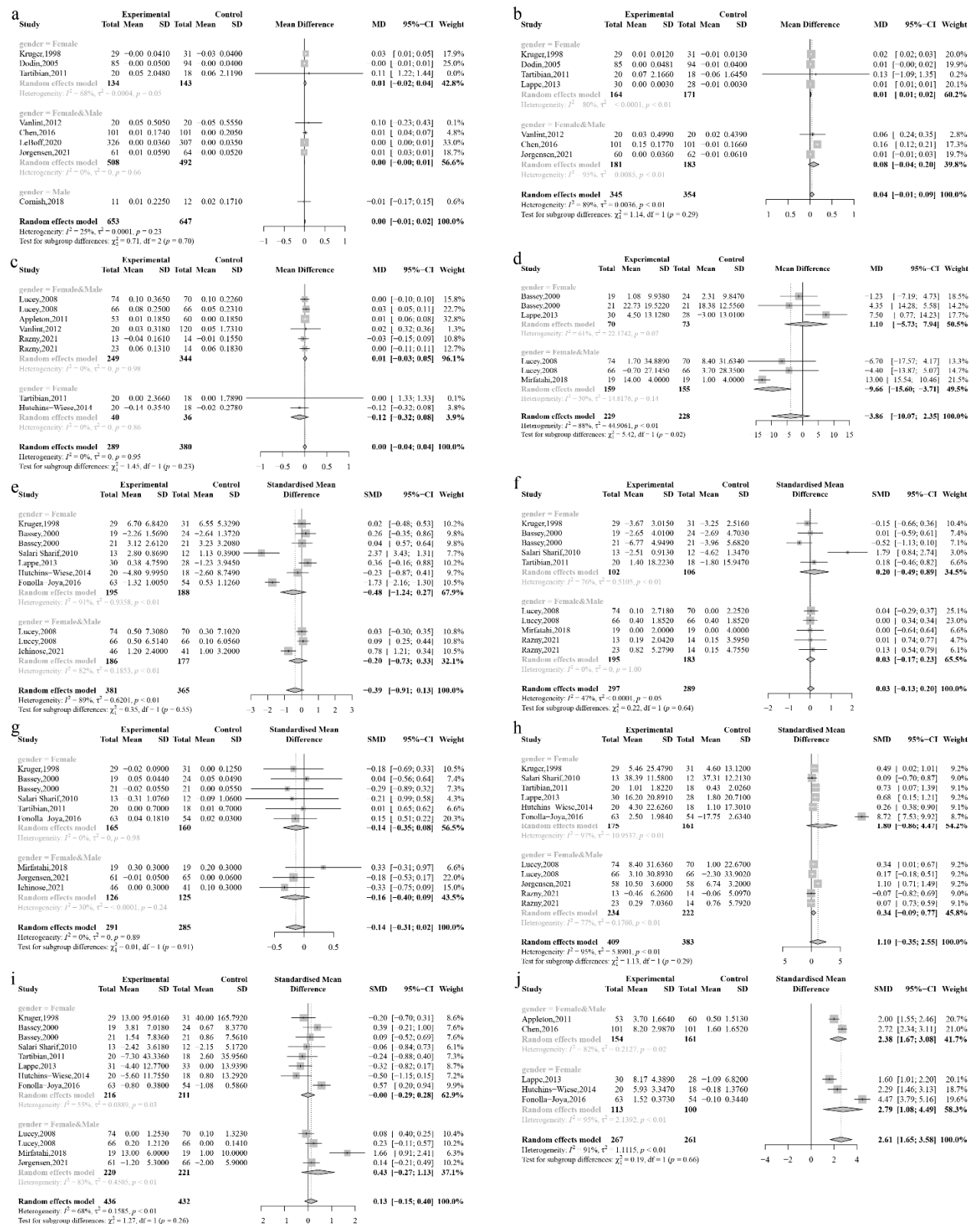# Supplementary Content

p 1: Search strategy

PubMed: (n-3 pufa[Title/Abstract] or omega-3, fatty acids[Title/Abstract] or fatty acids, omega-3[Title/Abstract] or "Fatty Acids, Omega-3"[Mesh] or "Fatty Acids, Unsaturated"[Mesh] or unsaturated fatty acids[Title/Abstract]) and ("Osteoporosis"[Mesh] or "Bone Density"[Mesh] or osteoporosis[Title/Abstract] or bone health[Title/Abstract] or bone density[Title/Abstract] or bone mineral density[Title/Abstract] or "Bone and Bones"[Mesh] or "Fractures, Bone"[Mesh] or fractures, bone[Title/Abstract] or bones[Title/Abstract])

Web of Science: (TS=n-3 pufa OR TS=omega-3, fatty acids OR AB=n-3 pufa OR AB=omega-3, fatty acids) AND (TS=osteoporosis OR TS=bone density OR TS=bone mineral density OR TS=bone OR TS=bone loss OR AB=osteoporosis OR AB=bone density OR AB=bone mineral density OR AB=bone OR AB=bone loss)

EBSCO: (TI n-3 pufa OR AB n-3 pufa OR TI (omega-3 fatty acids or omega 3 or fish oil) OR AB (omega-3 fatty acids or omega 3 or fish oil) OR TI fatty acids, omega 3 OR AB fatty acids, omega 3 OR (MM "Fatty Acids, Omega-3+") OR TI fatty acids, unsaturated OR AB fatty acids, unsaturated OR (MM "Fatty Acids, Unsaturated+")) AND (TI (osteoporosis or bone density or bone loss) OR AB (osteoporosis or bone density or bone loss) OR TI bone mineral density OR AB bone mineral density OR TI bone health OR AB bone health OR (MM "Osteoporosis+") OR (MM "Bone and Bones+"))

Supplemental Figure S1: Subgroup analysis for gender. a, lumbar spine BMD; b, femoral neck BMD; c, CTx-1; d, NTx-1; e, BAP; f, OC; g, serum calcium; h,25(OH)D; i, PTH; j, blood n-3 PUFA.

Supplemental Figure S2: Subgroup analysis for average age. a, lumbar spine BMD; b, femoral neck BMD; c, CTx-1; d, BAP; e, OC; f, serum calcium; g, 25(OH)D; h, PTH; i, IL-6; j, blood n-3 PUFA.

a

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	MD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	-0.00	0.0410	31	-0.03	0.0400	0.03	[0.01; 0.05]	17.9%
Tartibian,2011	20	0.05	2.0480	18	0.06	2.1190	0.11	[-1.22; 1.44]	0.0%
Chen,2016	101	0.01	0.1740	101	-0.00	0.2050	0.01	[-0.04; 0.07]	4.8%
Cornish,2018	11	0.01	0.2250	12	0.02	0.1710	-0.01	[-0.17; 0.15]	0.6%
LeBoff,2020	326	0.00	0.0360	307	0.00	0.0350	0.00	[0.00; 0.01]	33.0%
Random effects model	487			469			0.01	[-0.01; 0.03]	56.2%
Heterogeneity: I²=46%, τ²=0.0002, p=0.12									
ageclass = <60									
Dodin,2005	85	-0.00	0.0500	94	-0.00	0.0400	-0.00	[-0.01; 0.01]	25.0%
Vanlint,2012	20	0.05	0.5050	20	0.05	0.5550	0.10	[-0.23; 0.43]	0.1%
Jørgensen,2021	61	-0.01	0.0590	64	-0.00	0.0520	-0.01	[-0.03; 0.01]	18.7%
Random effects model	166			178			-0.00	[-0.01; 0.01]	43.8%
Heterogeneity: I²=0%, τ²=0, p=0.66									
Random effects model	653			647			0.00	[-0.01; 0.02]	100.0%
Heterogeneity: I²=25%, τ²=0.0001, p=0.23									
Test for subgroup differences: χ²₁=1.76, df=1 (p=0.18)									

b

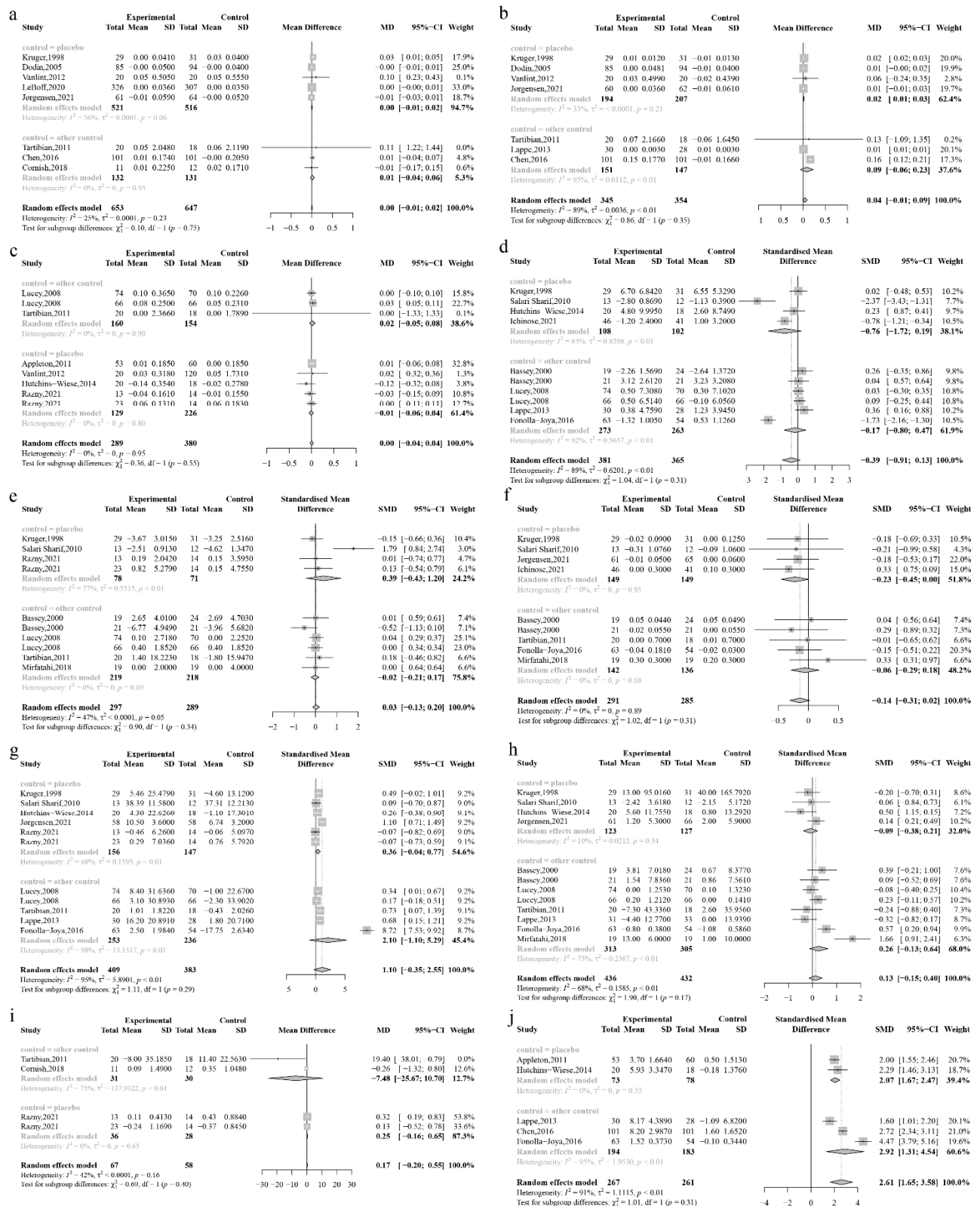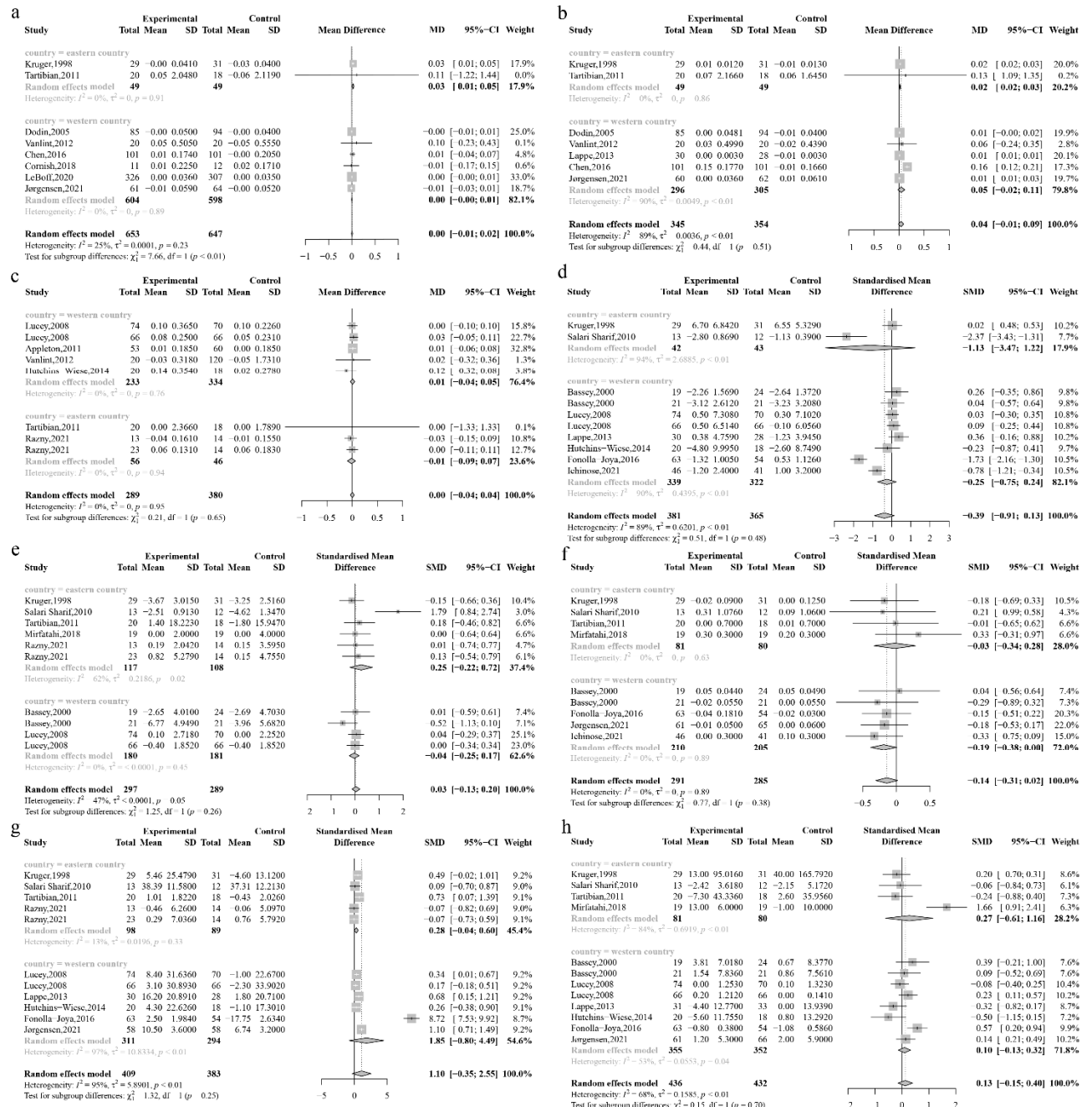| Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	MD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	0.01	0.0120	31	-0.01	0.0130	0.02	[0.02; 0.03]	20.0%
Tartibian,2011	20	0.07	2.1660	18	-0.06	1.6450	0.13	[-1.09; 1.35]	0.2%
Chen,2016	101	0.15	0.1770	101	-0.01	0.1660	0.16	[0.12; 0.21]	17.3%
Random effects model	150			150			0.09	[-0.04; 0.23]	37.5%
Heterogeneity: I²=94%, τ²=0.0094, p<0.01									
ageclass = <60									
Dodin,2005	85	0.00	0.0481	94	0.01	0.0400	0.01	[0.00; 0.02]	19.9%
Vanlint,2012	20	0.03	0.4990	20	-0.02	0.4390	0.06	[-0.24; 0.35]	2.8%
Lappe,2013	30	0.00	0.0030	28	-0.01	0.0030	0.01	[0.01; 0.01]	20.1%
Jørgensen,2021	60	0.00	0.0360	62	0.01	0.0610	0.01	[0.01; 0.03]	19.7%
Random effects model	195			204			0.01	[0.01; 0.01]	62.5%
Heterogeneity: I²=0%, τ²=0, p=0.99									
Random effects model	345			354			0.04	[-0.01; 0.09]	100.0%
Heterogeneity: I²=89%, τ²=0.0036, p<0.01									
Test for subgroup differences: χ²₁=1.41, df=1 (p=0.23)									

c

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	MD	95%-CI	Weight
ageclass = <60									
Lucey,2008	74	0.10	0.3650	70	0.10	0.2260	0.00	[-0.10; 0.10]	15.8%
Lucey,2008	66	0.08	0.2500	66	0.05	0.2310	0.03	[-0.05; 0.11]	22.7%
Vanlint,2012	20	-0.03	0.3180	120	-0.05	1.7310	0.02	[-0.32; 0.36]	1.3%
Razny,2021	13	-0.04	0.1610	14	-0.01	0.1550	0.03	[-0.15; 0.09]	10.8%
Razny,2021	23	0.06	0.1310	14	0.06	0.1830	0.00	[-0.11; 0.11]	12.7%
Random effects model	196			284			0.01	[-0.04; 0.06]	63.3%
Heterogeneity: I²=0%, τ²=0, p=0.95									
ageclass = NA									
Appleton,2011	53	0.01	0.1850	60	0.00	0.1850	0.01	[-0.06; 0.08]	32.8%
ageclass = >=60									
Tartibian,2011	20	0.00	2.3660	18	0.00	1.7890	0.00	[-1.33; 1.33]	0.1%
Hutchins-Wiese,2014	20	-0.14	0.3540	18	-0.02	0.2780	-0.12	[-0.32; 0.08]	3.8%
Random effects model	40			36			-0.12	[-0.32; 0.08]	3.9%
Heterogeneity: I²=0%, τ²=0, p=0.86									
Random effects model	289			380			0.00	[-0.04; 0.04]	100.0%
Heterogeneity: I²=0%, τ²=0, p=0.95									
Test for subgroup differences: χ²₂=1.46, df=2 (p=0.48)									

d

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	6.70	6.8420	31	6.55	5.3290	0.02	[-0.48; 0.53]	10.2%
Salari Sharif,2010	13	2.80	0.8690	12	1.13	0.3900	2.37	[3.43; 1.31]	7.7%
Hutchins-Wiese,2014	20	-4.80	9.9950	18	-2.60	8.7490	-0.23	[-0.87; 0.41]	9.7%
Ichinose,2021	46	-1.20	2.4000	41	1.00	3.2000	-0.78	[-1.21; -0.34]	10.5%
Random effects model	108			102			-0.76	[-1.72; 0.19]	38.1%
Heterogeneity: I²=84%, τ²=0.8298, p<0.01									
ageclass = <60									
Bassey,2000	19	2.26	1.5690	24	2.64	1.3720	0.26	[-0.35; 0.86]	9.8%
Bassey,2000	21	-3.12	2.6120	21	-3.23	3.2080	0.04	[-0.57; 0.64]	9.8%
Lucey,2008	74	0.50	7.3080	70	0.30	7.1020	0.03	[-0.30; 0.35]	10.8%
Lucey,2008	66	0.50	6.5140	66	-0.10	6.0560	0.09	[-0.25; 0.44]	10.8%
Lappe,2013	30	0.38	4.7590	28	-1.23	3.9450	0.36	[-0.16; 0.88]	10.2%
Fonolla Joya,2016	63	1.32	1.0050	54	0.53	1.1260	1.73	[2.16; 1.30]	6.3%
Random effects model	273			263			-0.17	[-0.80; 0.47]	61.9%
Heterogeneity: I²=92%, τ²=0.5657, p<0.01									
Random effects model	381			365			-0.39	[-0.91; 0.13]	100.0%
Heterogeneity: I²=89%, τ²=0.6201, p<0.01									
Test for subgroup differences: χ²₁=1.04, df=1 (p=0.31)									

e

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	-3.67	3.0150	31	-3.25	2.5160	-0.15	[-0.66; 0.36]	10.4%
Salari Sharif,2010	13	2.51	0.9130	12	4.62	1.3470	1.79	[0.84; 2.74]	3.0%
Tartibian,2011	20	1.40	18.2230	18	1.80	15.9470	0.18	[0.46; 0.82]	6.6%
Mirfatahi,2018	19	0.00	2.0000	19	0.00	4.0000	0.00	[0.64; 0.64]	6.6%
Random effects model	81			80			0.39	[-0.41; 1.18]	26.6%
Heterogeneity: I²=77%, τ²=0.5378, p<0.01									
ageclass = <60									
Bassey,2000	19	2.65	4.0100	24	2.69	4.7030	0.01	[0.59; 0.61]	7.4%
Bassey,2000	21	6.77	4.9490	21	3.96	5.6820	0.52	[1.13; 0.10]	7.1%
Lucey,2008	74	0.10	2.7180	70	0.00	2.2520	0.04	[0.29; 0.37]	25.1%
Lucey,2008	66	0.40	1.8520	66	0.40	1.8520	0.00	[0.34; 0.34]	23.0%
Razny,2021	13	0.19	2.0420	14	0.15	3.5950	0.01	[0.74; 0.77]	4.7%
Razny,2021	23	0.82	5.2790	14	0.15	4.7550	0.13	[-0.54; 0.79]	6.1%
Random effects model	216			209			-0.02	[-0.22; 0.17]	73.4%
Heterogeneity: I²=0%, τ²=0, p=0.72									
Random effects model	297			289			0.03	[-0.13; 0.20]	100.0%
Heterogeneity: I²=47%, τ²<0.0001, p=0.05									
Test for subgroup differences: χ²₁=0.97, df=1 (p=0.32)									

f

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	0.02	0.0900	31	0.00	0.1250	0.18	[0.69; 0.33]	10.5%
Salari Sharif,2010	13	-0.31	1.0760	12	-0.09	1.0600	-0.21	[-1.09; 0.67]	4.3%
Tartibian,2011	20	-0.00	0.7000	18	0.01	0.7000	-0.01	[-0.65; 0.62]	6.6%
Mirfatahi,2018	19	0.30	0.3000	19	0.20	0.3000	0.33	[-0.31; 0.97]	6.6%
Ichinose,2021	46	0.30	0.3000	41	0.10	0.3000	0.33	[0.75; 0.09]	15.0%
Random effects model	127			121			-0.13	[-0.38; 0.12]	43.0%
Heterogeneity: I²=0%, τ²=0, p=0.56									
ageclass = <60									
Bassey,2000	19	0.05	0.0440	24	0.05	0.0490	0.04	[-0.56; 0.64]	7.4%
Bassey,2000	21	-0.02	0.0550	21	0.00	0.0550	-0.29	[-0.89; 0.32]	7.3%
Fonolla Joya,2016	63	0.04	0.1810	54	0.02	0.0300	0.15	[0.51; 0.22]	20.3%
Jørgensen,2021	61	-0.01	0.0500	65	0.00	0.0600	-0.18	[-0.53; 0.17]	22.0%
Random effects model	164			164			-0.15	[-0.37; 0.06]	57.0%
Heterogeneity: I²=0%, τ²=0, p=0.89									
Random effects model	291			285			-0.14	[-0.31; 0.02]	100.0%
Heterogeneity: I²=0%, τ²=0, p=0.89									
Test for subgroup differences: χ²₁=0.02, df=1 (p=0.90)									

g

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	5.46	25.4790	31	-4.60	13.1200	0.49	[-0.02; 1.01]	9.2%
Salari Sharif,2010	13	38.39	11.5800	12	37.31	12.2130	0.09	[-0.70; 0.87]	9.0%
Tartibian,2011	20	1.01	1.8220	18	-0.43	2.0260	0.73	[0.07; 1.39]	9.1%
Hutchins-Wiese,2014	20	4.30	22.6260	18	1.10	17.3010	0.26	[0.38; 0.90]	9.1%
Random effects model	82			79			0.43	[0.11; 0.74]	36.4%
Heterogeneity: I²=0%, τ²=0, p=0.60									
ageclass = <60									
Lucey,2008	74	8.40	31.6360	70	-1.00	22.6700	0.34	[0.01; 0.67]	9.2%
Lucey,2008	66	3.10	30.8930	66	-2.30	33.9020	0.17	[-0.18; 0.51]	9.2%
Lappe,2013	30	16.20	20.8910	28	1.80	20.7100	0.68	[0.15; 1.21]	9.2%
Fonolla-Joya,2016	54	2.50	1.9840	54	-17.75	2.6340	8.72	[7.53; 9.92]	8.7%
Jørgensen,2021	58	10.50	3.6000	58	6.74	3.2000	1.10	[0.71; 1.49]	9.2%
Razny,2021	13	0.46	6.2600	14	0.06	5.0970	0.07	[0.82; 0.69]	9.0%
Razny,2021	23	0.29	7.0360	14	0.76	5.7920	0.07	[0.73; 0.59]	9.1%
Random effects model	327			304			1.52	[-0.79; 3.84]	63.6%
Heterogeneity: I²=97%, τ²=9.6290, p<0.01									
Random effects model	409			383			1.10	[-0.35; 2.55]	100.0%
Heterogeneity: I²=95%, τ²=5.8901, p<0.01									
Test for subgroup differences: χ²₁=0.85, df=1 (p=0.36)									

h

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = >=60									
Kruger,1998	29	13.00	95.0160	31	40.00	165.7920	-0.20	[-0.70; 0.31]	8.6%
Salari Sharif,2010	13	-2.42	3.6180	12	-2.15	5.1720	-0.06	[-0.84; 0.73]	6.1%
Tartibian,2011	20	-7.30	43.3360	18	2.60	35.9560	-0.24	[-0.88; 0.40]	7.3%
Hutchins-Wiese,2014	20	-5.60	11.7550	18	0.80	13.2920	-0.50	[-1.15; 0.15]	7.2%
Mirfatahi,2018	19	13.00	6.0000	19	-1.00	10.0000	1.66	[0.91; 2.41]	6.3%
Random effects model	101			98			0.12	[-0.63; 0.86]	35.5%
Heterogeneity: I²=82%, τ²=0.6004, p<0.01									
ageclass = <60									
Bassey,2000	19	3.81	7.0180	24	0.67	8.3770	0.39	[0.21; 1.00]	7.6%
Bassey,2000	21	1.54	7.8360	21	0.86	7.5610	0.09	[-0.52; 0.69]	7.6%
Lucey,2008	74	0.00	1.3230	70	0.10	1.3230	-0.08	[-0.40; 0.25]	10.4%
Lucey,2008	66	0.20	1.2120	66	0.00	0.1410	0.23	[-0.11; 0.57]	10.2%
Lappe,2013	31	-4.40	12.7700	33	0.00	13.9390	-0.32	[-0.82; 0.17]	8.7%
Fonolla Joya,2016	63	-0.80	0.3800	54	-1.08	0.5860	0.57	[0.20; 0.94]	9.9%
Jørgensen,2021	61	1.20	5.3000	66	2.00	5.9000	0.14	[0.21; 0.49]	10.2%
Random effects model	335			334			0.15	[-0.07; 0.37]	64.5%
Heterogeneity: I²=47%, τ²=0.0399, p=0.08									
Random effects model	436			432			0.13	[-0.15; 0.40]	100.0%
Heterogeneity: I²=68%, τ²=0.1585, p<0.01									
Test for subgroup differences: χ²₁=0.01, df=1 (p=0.93)									

i

Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	MD	95%-CI	Weight
ageclass = >=60									
Tartibian,2011	20	8.00	35.1850	18	11.40	22.5630	19.40	[38.01; 0.79]	0.0%
Cornish,2018	11	0.09	1.4900	12	0.35	1.0480	-0.26	[-1.32; 0.80]	12.6%
Random effects model	31			30			-7.48	[-25.67; 10.70]	12.7%
Heterogeneity: I²=75%, τ²=137.9322, p=0.04									
ageclass = <60									
Razny,2021	13	-0.11	0.4130	14	-0.43	0.8840	0.32	[-0.19; 0.83]	53.8%
Razny,2021	23	-0.24	1.1690	14	-0.37	0.8450	0.13	[-0.52; 0.78]	33.6%
Random effects model	36			28			0.25	[-0.16; 0.65]	87.3%
Heterogeneity: I²=0%, τ²=0, p=0.65									
Random effects model	67			58			0.17	[-0.20; 0.55]	100.0%
Heterogeneity: I²=42%, τ²<0.0001, p=0.16									
Test for subgroup differences: χ²₁=0.69, df=1 (p=0.40)									

j

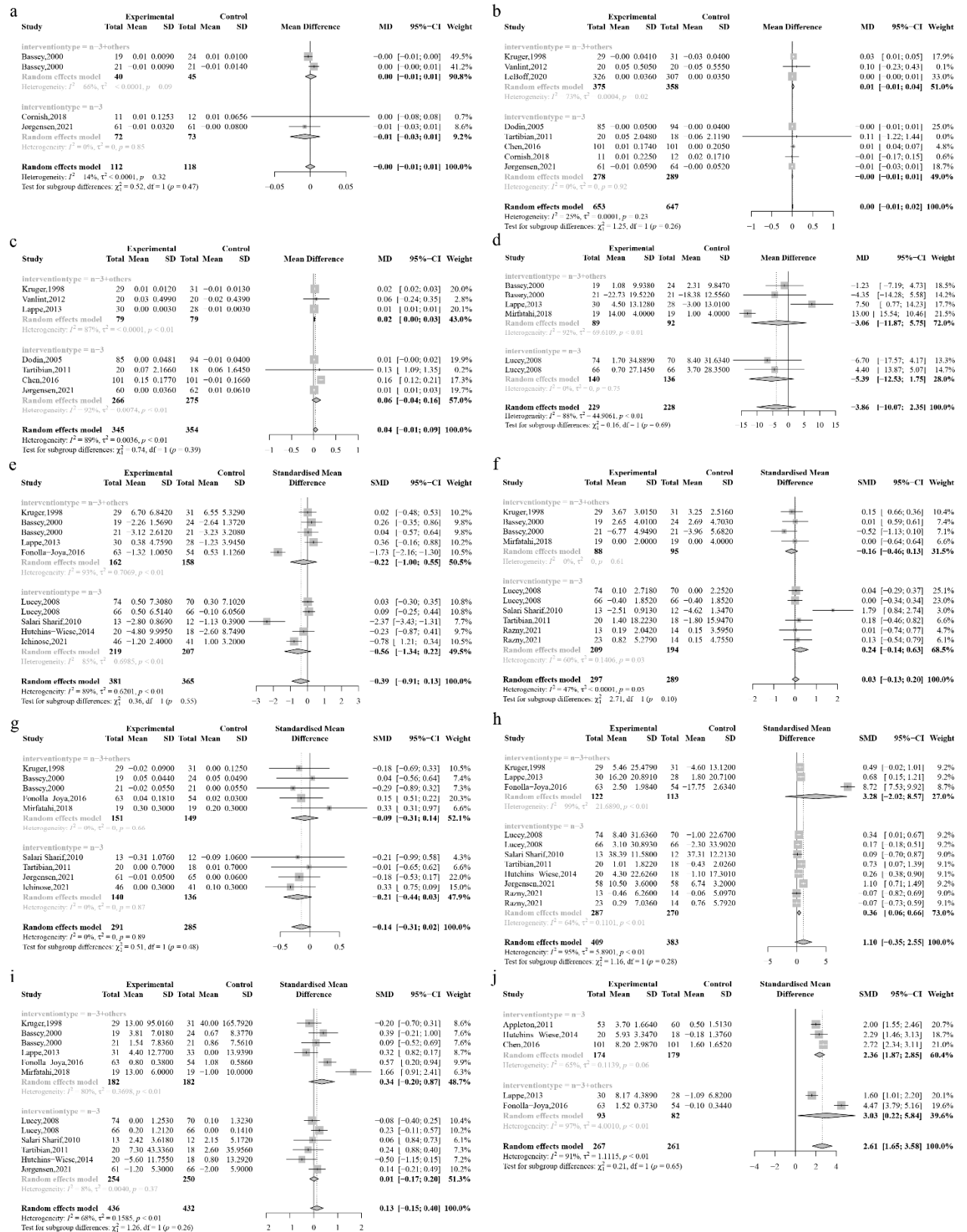| Study	Exp. Total	Exp. Mean	Exp. SD	Ctrl Total	Ctrl Mean	Ctrl SD	SMD	95%-CI	Weight
ageclass = NA									
Appleton,2011	53	3.70	1.6640	60	0.50	1.5130	2.00	[1.55; 2.46]	20.7%
ageclass = <60									
Lappe,2013	30	8.17	4.3890	28	-1.09	6.8200	1.60	[1.01; 2.20]	20.1%
Fonolla-Joya,2016	63	1.52	0.3730	54	-0.10	0.3440	4.47	[3.79; 5.16]	19.6%
Random effects model	93			82			3.03	[0.22; 5.84]	39.6%
Heterogeneity: I²=97%, τ²=4.0010, p<0.01									
ageclass = >=60									
Hutchins-Wiese,2014	20	5.93	3.3470	18	-0.18	1.3760	2.29	[1.46; 3.13]	18.7%
Chen,2016	101	8.20	2.9870	101	1.60	1.6520	2.72	[2.34; 3.11]	21.0%
Random effects model	121			119			2.65	[2.30; 3.00]	39.7%
Heterogeneity: I²=0%, τ²=0, p=0.36									
Random effects model	267			261			2.61	[1.65; 3.58]	100.0%
Heterogeneity: I²=91%, τ²=1.1115, p<0.01									
Test for subgroup differences: χ²₂=5.03, df=2 (p=0.08)									

Supplemental Figure S3: Subgroup analysis for control type. a, lumbar spine BMD; b, femoral neck BMD; c, CTx-1; d, BAP; e, OC; f, serum calcium; g, 25(OH)D; h, PTH; i, IL-6; j, blood n-3 PUFA.
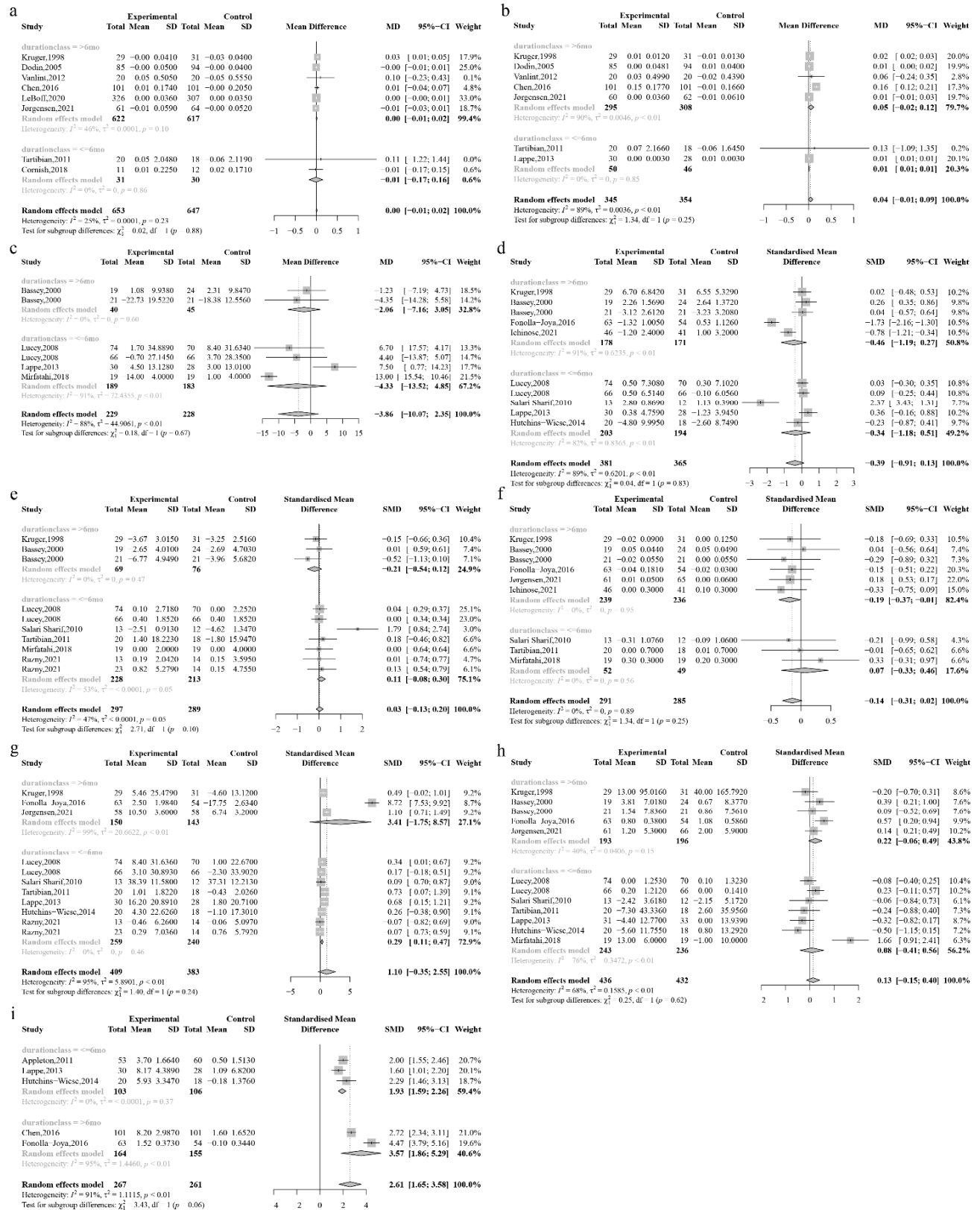
Supplemental Figure S4: Subgroup analysis for country. a, lumbar spine BMD; b, femoral neck BMD; c, CTx-1; d, BAP; e, OC; f, serum calcium; g, 25(OH)D; h, PTH.
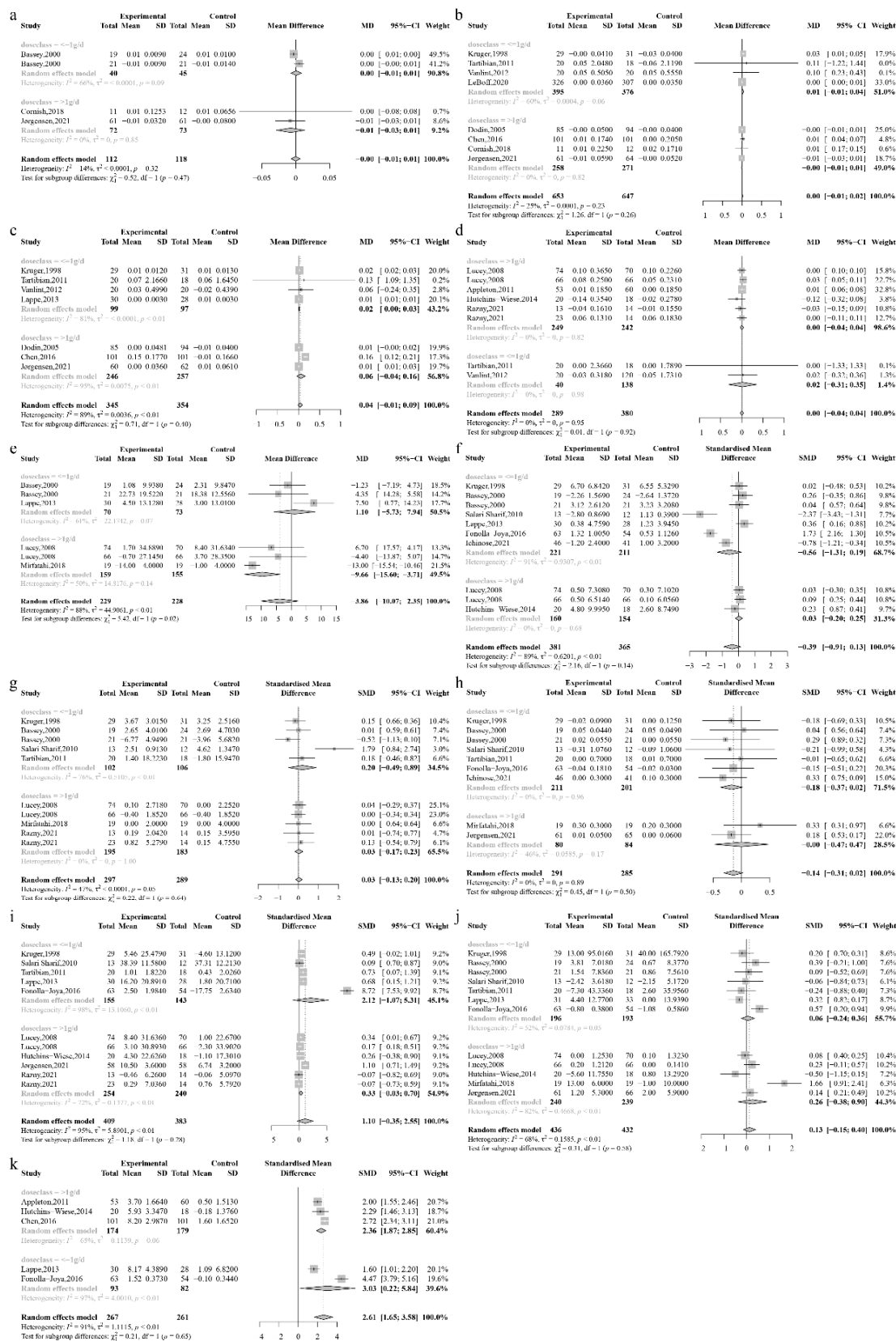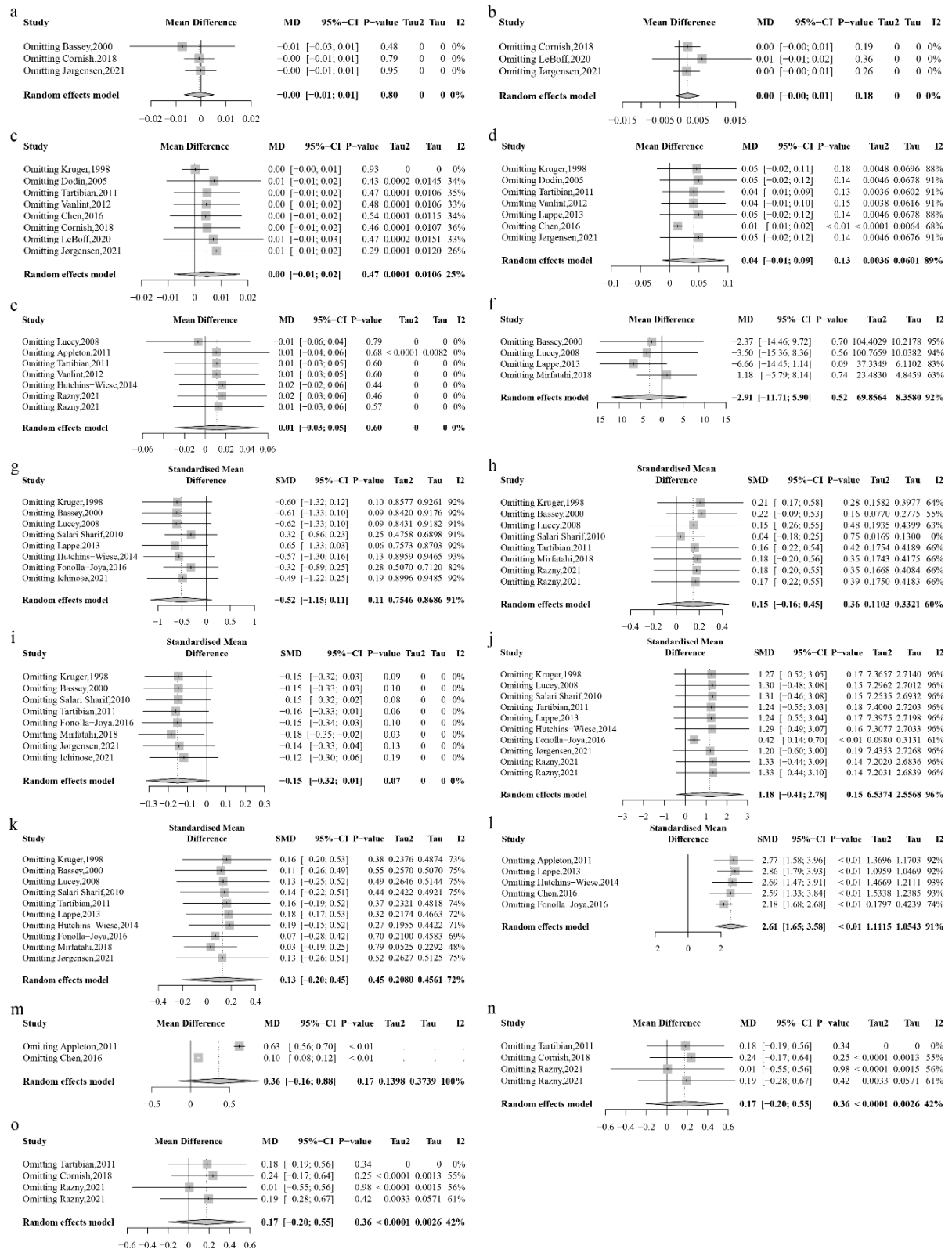
Supplemental Figure S5: Subgroup analysis for intervention type. a, TBMD; b, lumbar spine BMD; c, femoral neck BMD; d, NTx-1; e, BAP; f, OC; g, serum calcium; h, 25(OH)D; i, PTH; j, blood n-3 PUFA.

Supplemental Figure S6: Subgroup analysis for duration. a, lumbar spine BMD; b, femoral neck BMD; c, NTx-1; d, BAP; e, OC; f, serum calcium; g, 25(OH)D; h, PTH; i, blood n-3 PUFA.
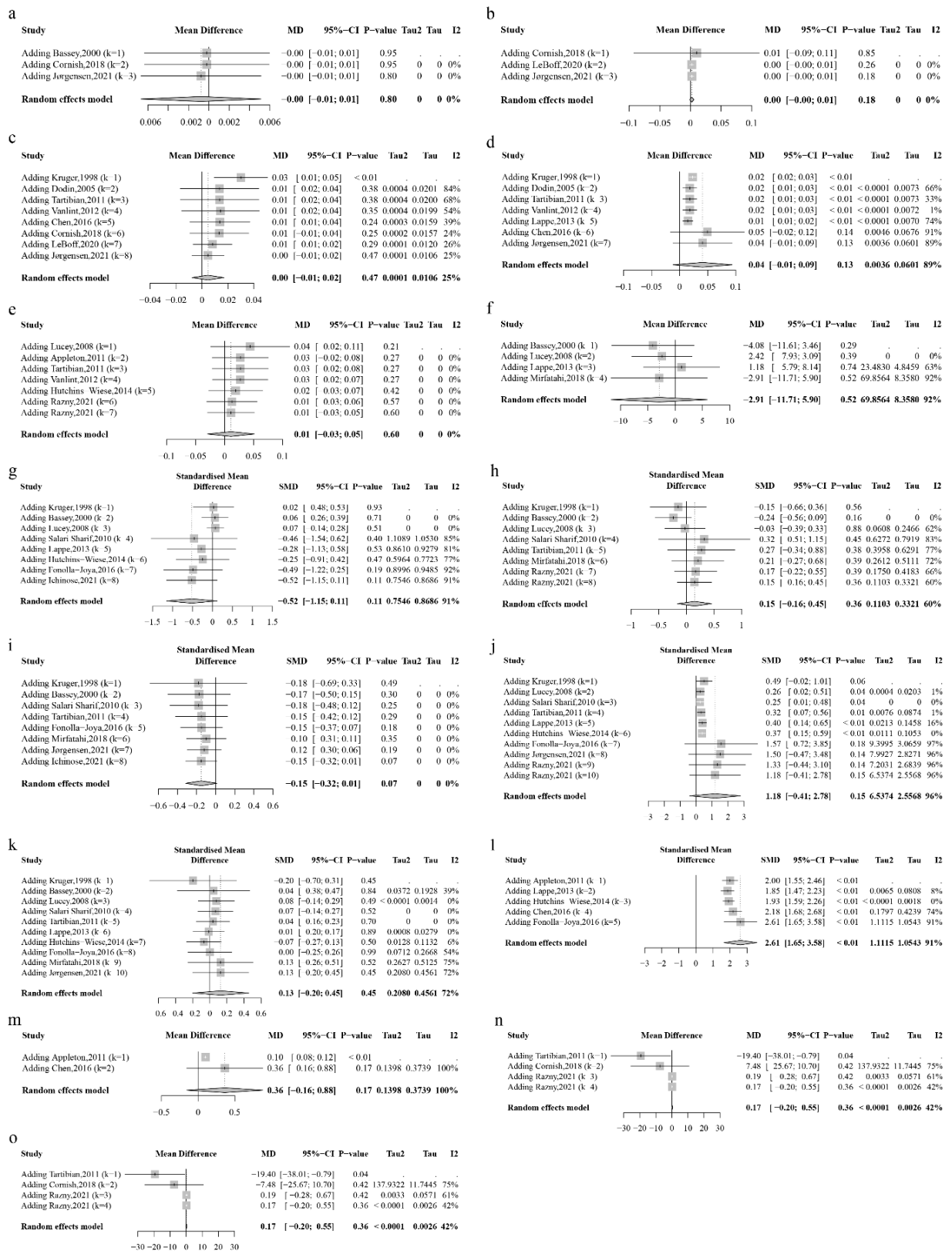
Supplemental Figure S7: Subgroup analysis for n-3 PUFAs' dose. a, TBMD; b, lumbar spine BMD; c, femoral neck BMD; d, CTx-1; e, NTx-1; f, BAP; g, OC; h, serum calcium; i, 25(OH)D; j, PTH; k, blood n-3 PUFA.

Supplemental Figure S8: Sensitivity analysis of the effects of n-3 PUFAs. a, TBMD; b, total hip BMD; c, lumbar spine BMD; d, femoral neck BMD; e, CTx-1; f, NTx-1; g, BAP; h, OC; i, serum calcium; j, 25(OH)D; k, PTH; l, blood n-3 PUFA; m, blood n-3 PUFA: n-6 PUFA ratio; n, CRP; o, IL-6.

Supplemental Figure S9: Cumulative meta-analysis of the effects of n-3 PUFAs. a, TBMD; b, total hip BMD; c, lumbar spine BMD; d, femoral neck BMD; e, CTx-1; f, NTx-1; g, BAP; h, OC; i, serum calcium; j, 25(OH)D; k, PTH; l, blood n-3 PUFA; m, blood n-3 PUFA: n-6 PUFA ratio; n, CRP; o, IL-6.

Supplemental Figure S10: Funnel plot for included studies. a, TBMD; b, lumbar spine BMD; c, total hip BMD; d, femoral neck BMD; e, CTx-1; f, NTx-1; g, BAP; h, OC; i, serum calcium; j, 25(OH)D; k, PTH; l, blood n-3 PUFA; m, blood n-3 PUFA: n-6 PUFA ratio; n, CRP; o, IL-6.

Supplemental Figure S11: Forest plot of trim-and-fill method for included studies. a, TBMD; b, total hip BMD; c, lumbar spine BMD; d, femoral neck BMD; e, CTx-1; f, NTx-1; g, BAP; h, OC; i, serum calcium; j, 25(OH)D; k, PTH; l, blood n-3 PUFA; m, CRP; n, IL-6.
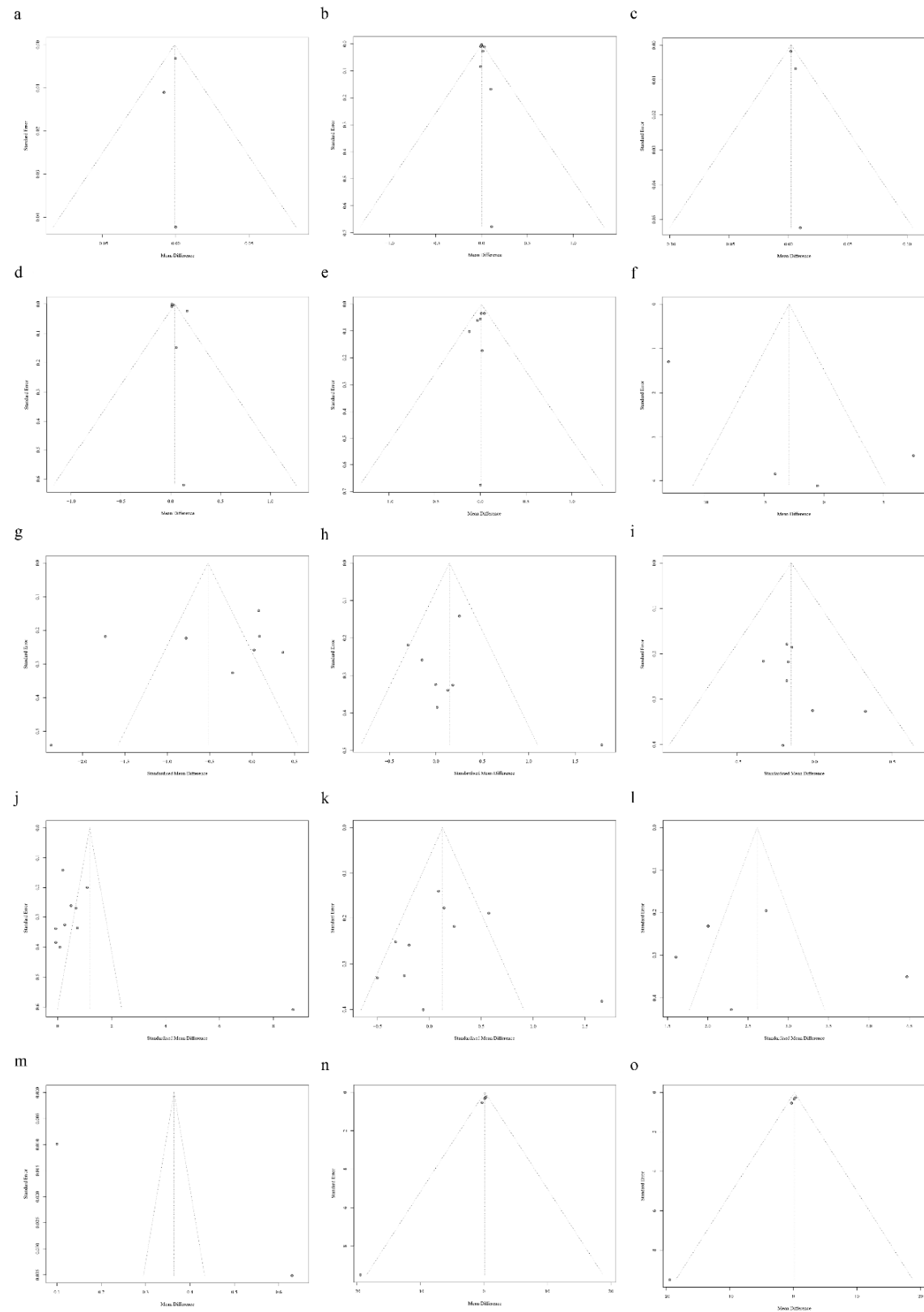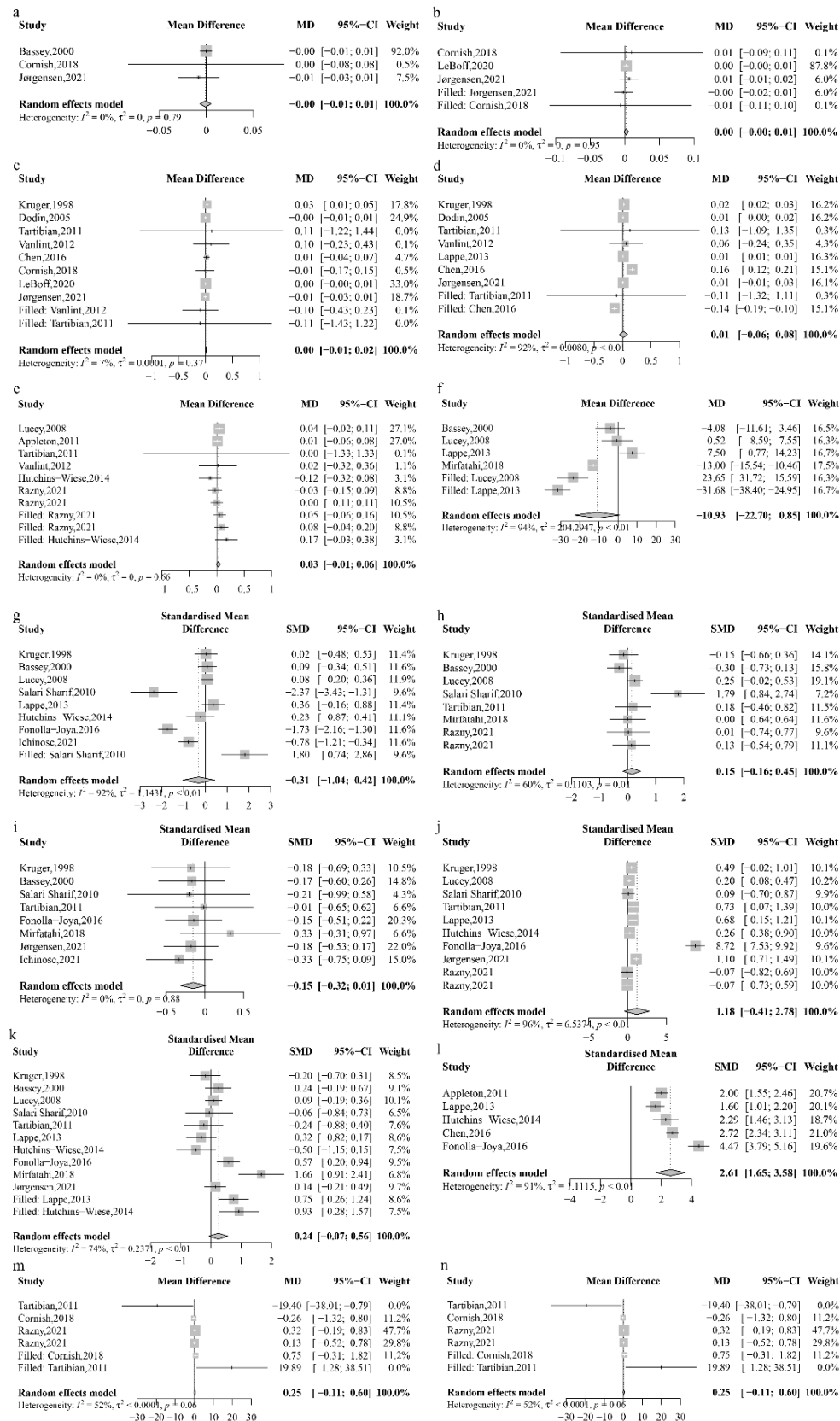
a

Study	Mean Difference	MD	95%−CI	Weight
Bassey,2000		−0.00	[−0.01; 0.01]	92.0%
Cornish,2018		0.00	[−0.08; 0.08]	0.5%
Jørgensen,2021		−0.01	[−0.03; 0.01]	7.5%
Random effects model		−0.00	[−0.01; 0.01]	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.79$

b

Study	Mean Difference	MD	95%−CI	Weight
Cornish,2018		0.01	[−0.09; 0.11]	0.1%
LeBoff,2020		0.00	[−0.00; 0.01]	87.8%
Jørgensen,2021		0.01	[−0.01; 0.02]	6.0%
Filled: Jørgensen,2021		−0.00	[−0.02; 0.01]	6.0%
Filled: Cornish,2018		−0.01	[0.11; 0.10]	0.1%
Random effects model		0.00	[−0.00; 0.01]	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.95$

c

Study	Mean Difference	MD	95%−CI	Weight
Kruger,1998		0.03	[0.01; 0.05]	17.8%
Dodin,2005		−0.00	[−0.01; 0.01]	24.9%
Tartibian,2011		0.11	[−1.22; 1.44]	0.0%
Vanlint,2012		0.10	[−0.23; 0.43]	0.1%
Chen,2016		0.01	[−0.04; 0.07]	4.7%
Cornish,2018		−0.01	[−0.17; 0.15]	0.5%
LeBoff,2020		0.00	[−0.00; 0.01]	33.0%
Jørgensen,2021		−0.01	[−0.03; 0.01]	18.7%
Filled: Vanlint,2012		−0.10	[−0.43; 0.23]	0.1%
Filled: Tartibian,2011		−0.11	[−1.43; 1.22]	0.0%
Random effects model		0.00	[−0.01; 0.02]	100.0%

Heterogeneity: $I^2 = 7\%$, $\tau^2 = 0.0001$, $p = 0.37$

d

Study	Mean Difference	MD	95%−CI	Weight
Kruger,1998		0.02	[0.02; 0.03]	16.2%
Dodin,2005		0.01	[0.00; 0.02]	16.2%
Tartibian,2011		0.13	[−1.09; 1.35]	0.3%
Vanlint,2012		0.06	[−0.24; 0.35]	4.3%
Lappe,2013		0.01	[0.01; 0.01]	16.3%
Chen,2016		0.16	[0.12; 0.21]	15.1%
Jørgensen,2021		0.01	[−0.01; 0.03]	16.1%
Filled: Tartibian,2011		−0.11	[−1.32; 1.11]	0.3%
Filled: Chen,2016		−0.14	[−0.19; −0.10]	15.1%
Random effects model		0.01	[−0.06; 0.08]	100.0%

Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.0080$, $p < 0.01$

e

Study	Mean Difference	MD	95%−CI	Weight
Lucey,2008		0.04	[−0.02; 0.11]	27.1%
Appleton,2011		0.01	[−0.06; 0.08]	27.0%
Tartibian,2011		0.00	[−1.33; 1.33]	0.1%
Vanlint,2012		0.02	[−0.32; 0.36]	1.1%
Hutchins−Wiese,2014		−0.12	[−0.32; 0.08]	3.1%
Razny,2021		0.03	[0.15; 0.09]	8.8%
Razny,2021		0.00	[0.11; 0.11]	10.5%
Filled: Razny,2021		0.05	[−0.06; 0.16]	10.5%
Filled: Razny,2021		0.08	[−0.04; 0.20]	8.8%
Filled: Hutchins−Wiese,2014		0.17	[−0.03; 0.38]	3.1%
Random effects model		0.03	[−0.01; 0.06]	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.56$

f

Study	Mean Difference	MD	95%−CI	Weight
Bassey,2000		−4.08	[−11.61; 3.46]	16.5%
Lucey,2008		0.52	[8.59; 7.55]	16.3%
Lappe,2013		7.50	[0.77; 14.23]	16.7%
Mirfatahi,2018		13.00	[15.54; 10.46]	17.5%
Filled: Lucey,2008		23.65	[31.72; 15.59]	16.3%
Filled: Lappe,2013		−31.68	[−38.40; −24.95]	16.7%
Random effects model		−10.93	[−22.70; 0.85]	100.0%

Heterogeneity: $I^2 = 94\%$, $\tau^2 = 204.2947$, $p < 0.01$

g

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Kruger,1998		0.02	[−0.48; 0.53]	11.4%
Bassey,2000		0.09	[0.34; 0.51]	11.6%
Lucey,2008		0.08	[0.20; 0.36]	11.9%
Salari Sharif,2010		−2.37	[−3.43; −1.31]	9.6%
Lappe,2013		0.36	[−0.16; 0.88]	11.4%
Hutchins Wiese,2014		0.23	[0.87; 0.41]	11.1%
Fonolla−Joya,2016		−1.73	[−2.16; −1.30]	11.6%
Ichinose,2021		−0.78	[−1.21; −0.34]	11.6%
Filled: Salari Sharif,2010		1.80	[0.74; 2.86]	9.6%
Random effects model		−0.31	[−1.04; 0.42]	100.0%

Heterogeneity: $I^2 = 92\%$, $\tau^2 = 1.1431$, $p < 0.01$

h

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Kruger,1998		−0.15	[−0.66; 0.36]	14.1%
Bassey,2000		0.30	[0.73; 0.13]	15.8%
Lucey,2008		0.25	[−0.02; 0.53]	19.1%
Salari Sharif,2010		1.79	[0.84; 2.74]	7.2%
Tartibian,2011		0.18	[−0.46; 0.82]	11.5%
Mirfatahi,2018		0.00	[0.64; 0.64]	11.6%
Razny,2021		0.01	[−0.74; 0.77]	9.6%
Razny,2021		0.13	[−0.54; 0.79]	11.1%
Random effects model		0.15	[−0.16; 0.45]	100.0%

Heterogeneity: $I^2 = 60\%$, $\tau^2 = 0.1103$, $p = 0.01$

i

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Kruger,1998		−0.18	[−0.69; 0.33]	10.5%
Bassey,2000		−0.17	[−0.60; 0.26]	14.8%
Salari Sharif,2010		−0.21	[−0.99; 0.58]	4.3%
Tartibian,2011		−0.01	[−0.65; 0.62]	6.6%
Fonolla−Joya,2016		−0.15	[−0.51; 0.22]	20.3%
Mirfatahi,2018		0.33	[−0.31; 0.97]	6.6%
Jørgensen,2021		−0.18	[−0.53; 0.17]	22.0%
Ichinose,2021		0.33	[−0.75; 0.09]	15.0%
Random effects model		−0.15	[−0.32; 0.01]	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.88$

j

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Kruger,1998		0.49	[−0.02; 1.01]	10.1%
Lucey,2008		0.20	[0.08; 0.47]	10.2%
Salari Sharif,2010		0.09	[−0.70; 0.87]	9.9%
Tartibian,2011		0.73	[0.07; 1.39]	10.0%
Lappe,2013		0.68	[0.15; 1.21]	10.1%
Hutchins Wiese,2014		0.26	[0.38; 0.90]	10.0%
Fonolla−Joya,2016		8.72	[7.53; 9.92]	9.6%
Jørgensen,2021		1.10	[0.71; 1.49]	10.1%
Razny,2021		−0.07	[−0.82; 0.69]	10.0%
Razny,2021		−0.07	[0.73; 0.59]	10.0%
Random effects model		1.18	[−0.41; 2.78]	100.0%

Heterogeneity: $I^2 = 96\%$, $\tau^2 = 6.5374$, $p < 0.01$

k

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Kruger,1998		−0.20	[−0.70; 0.31]	8.5%
Bassey,2000		0.24	[−0.19; 0.67]	9.1%
Lucey,2008		0.09	[−0.19; 0.36]	10.1%
Salari Sharif,2010		−0.06	[−0.84; 0.73]	6.5%
Tartibian,2011		−0.24	[−0.88; 0.40]	7.6%
Lappe,2013		0.32	[0.82; 0.17]	8.6%
Hutchins−Wiese,2014		−0.50	[−1.15; 0.15]	7.5%
Fonolla−Joya,2016		0.57	[0.20; 0.94]	9.5%
Mirfatahi,2018		1.66	[0.91; 2.41]	6.8%
Jørgensen,2021		0.14	[−0.21; 0.49]	9.7%
Filled: Lappe,2013		0.75	[0.26; 1.24]	8.6%
Filled: Hutchins−Wiese,2014		0.93	[0.28; 1.57]	7.5%
Random effects model		0.24	[−0.07; 0.56]	100.0%

Heterogeneity: $I^2 = 74\%$, $\tau^2 = 0.2371$, $p < 0.01$

l

Study	Standardised Mean Difference	SMD	95%−CI	Weight
Appleton,2011		2.00	[1.55; 2.46]	20.7%
Lappe,2013		1.60	[1.01; 2.20]	20.1%
Hutchins Wiese,2014		2.29	[1.46; 3.13]	18.7%
Chen,2016		2.72	[2.34; 3.11]	21.0%
Fonolla−Joya,2016		4.47	[3.79; 5.16]	19.6%
Random effects model		2.61	[1.65; 3.58]	100.0%

Heterogeneity: $I^2 = 91\%$, $\tau^2 = 1.1115$, $p < 0.01$

m

Study	Mean Difference	MD	95%−CI	Weight
Tartibian,2011		−19.40	[−38.01; −0.79]	0.0%
Cornish,2018		−0.26	[−1.32; 0.80]	11.2%
Razny,2021		0.32	[−0.19; 0.83]	47.7%
Razny,2021		0.13	[−0.52; 0.78]	29.8%
Filled: Cornish,2018		0.75	[−0.31; 1.82]	11.2%
Filled: Tartibian,2011		19.89	[1.28; 38.51]	0.0%
Random effects model		0.25	[−0.11; 0.60]	100.0%

Heterogeneity: $I^2 = 52\%$, $\tau^2 < 0.0001$, $p = 0.06$

n

Study	Mean Difference	MD	95%−CI	Weight
Tartibian,2011		−19.40	[−38.01; −0.79]	0.0%
Cornish,2018		−0.26	[−1.32; 0.80]	11.2%
Razny,2021		0.32	[0.19; 0.83]	47.7%
Razny,2021		0.13	[−0.52; 0.78]	29.8%
Filled: Cornish,2018		0.75	[−0.31; 1.82]	11.2%
Filled: Tartibian,2011		19.89	[1.28; 38.51]	0.0%
Random effects model		0.25	[−0.11; 0.60]	100.0%

Heterogeneity: $I^2 = 52\%$, $\tau^2 < 0.0001$, $p = 0.06$

Supplemental Figure S12: Funnel plot of trim-and-fill method for included studies. a, TBMD; b, lumbar spine BMD; c, total hip BMD; d, femoral neck BMD; e, CTx-1; f, NTx-1; g, BAP; h, OC; i, serum calcium; j, 25(OH)D; k, PTH; l, blood n-3 PUFA; m, CRP; n, IL-6.