

# Bone & Joint Research

## Supplementary Material

10.1302/2046-3758.1312.BJR-2024-0053.R1

**Table i.** Subgroup analysis of the effects of vitamin K supplementation on ultra distal radius bone mineral density, femoral Ward BMD.

Subgroup	Ultra distal radius BMD (g/cm <sup>2</sup> )				Femoral Ward BMD (g/cm <sup>2</sup> )			
	N	WMD (95% CI)	Heterogeneity		N	WMD (95% CI)	Heterogeneity	
		I <sup>2</sup>	p-value			I <sup>2</sup>	p-value	
<b>Intervention</b>								
Vitamin K1								
Vitamin K2								
Vitamin K1								
Vitamin K2								
<b>Dose, mg/day</b>								
≤ 1	2	0.00 (-0.02 to 0.03)	0.0%	0.708	2	-0.00 (-0.02 to 0.02)	0.0%	0.814
> 1	1	-0.00 (-0.10 to 0.09)	N/A	0.992	1	0.03 (-0.02 to 0.08)	N/A	0.269
<b>Duration, yrs</b>								
≤ 1								
> 1								
Vitamin K1								
Vitamin K2								
<b>Country</b>								
Asia								
Other continents								
Vitamin K1								
Vitamin K2								
<b>Health status</b>								
Healthy	2	0.00 (-0.02 to 0.03)	0.0%	0.708	2			
Unhealthy*	1	-0.00 (-0.10 to 0.09)	N/A	0.992	1			

\*Participants with osteoporosis or osteopenia.

BMD, bone mineral density; N/A, only one document included, not shown; WMD, weighted mean difference.

**Table ii.** Subgroup analysis of the effects of vitamin K supplementation on carboxylated osteocalcin: uncarboxylated osteocalcin (ucOC), ucOC: total osteocalcin, cross-linked telopeptide of type 1 collagen.

Subgroup	cOC: ucOC				ucOC: tOC			
	N	WMD (95% CI)	Heterogeneity		N	WMD (95% CI)	Heterogeneity	
			I <sup>2</sup>	p-value			I <sup>2</sup>	p-value
<b>Intervention</b>								
Vitamin K1					2	-0.00 (-0.03 to 0.03)	0.0%	0.902
Vitamin K2					3	-0.29 (-0.48 to -0.10)	87.5%	0.003
<b>Dose, mg/day</b>								
≤ 1					4	-0.21 (-0.44 to 0.03)	93.8%	0.083
>1					1	-0.14 (-0.20 to -0.07)	N/A	< 0.001
<b>Duration, yrs</b>								
≤ 1								
>1								
<b>Country</b>								
Asia					1	-0.14 (-0.20 to -0.07)	N/A	< 0.001
Other continents					4	-0.21 (-0.44 to 0.03)	93.8%	0.083
<b>Sex</b>								
Female	1	1.48 (0.82 to 2.14)	N/A	< 0.001	1	-0.14 (-0.20 to -0.07)	N/A	< 0.001
Female & male	2	2.80 (-0.56 to 6.16)	86.8%	0.102	4	-0.21 (-0.44 to 0.03)	93.8%	0.083
<b>Health status</b>								
Healthy					4	-0.21 (-0.44 to 0.03)	93.8%	0.083
Unhealthy*					1	-0.14 (-0.20 to -0.07)	N/A	< 0.001

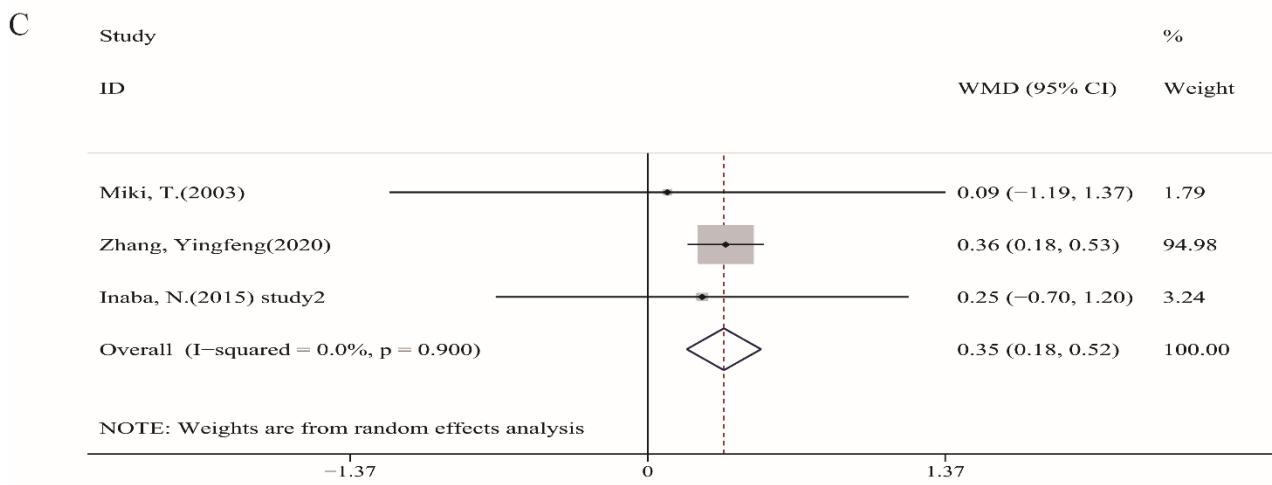
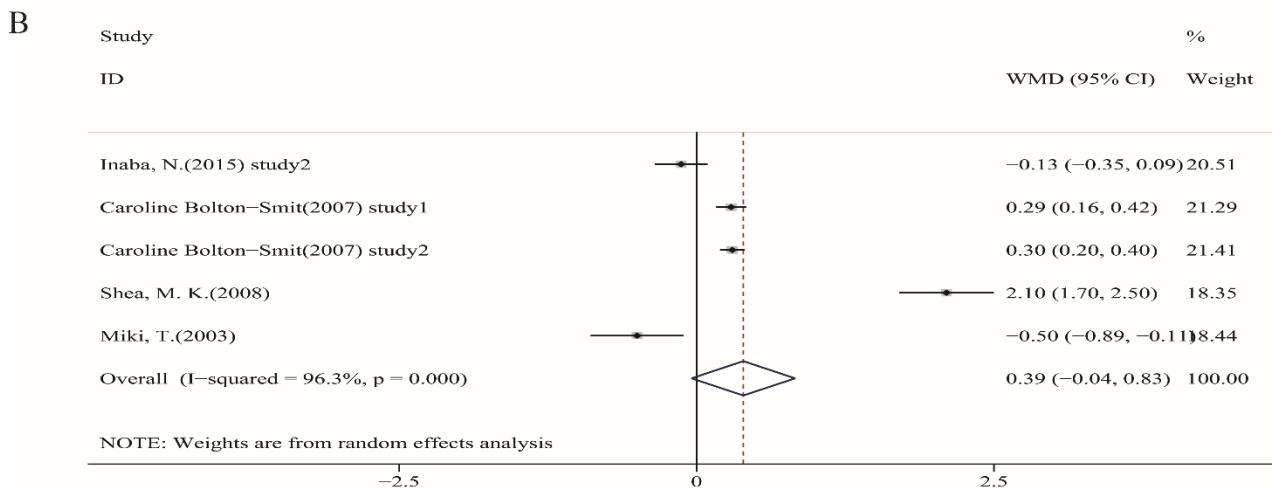
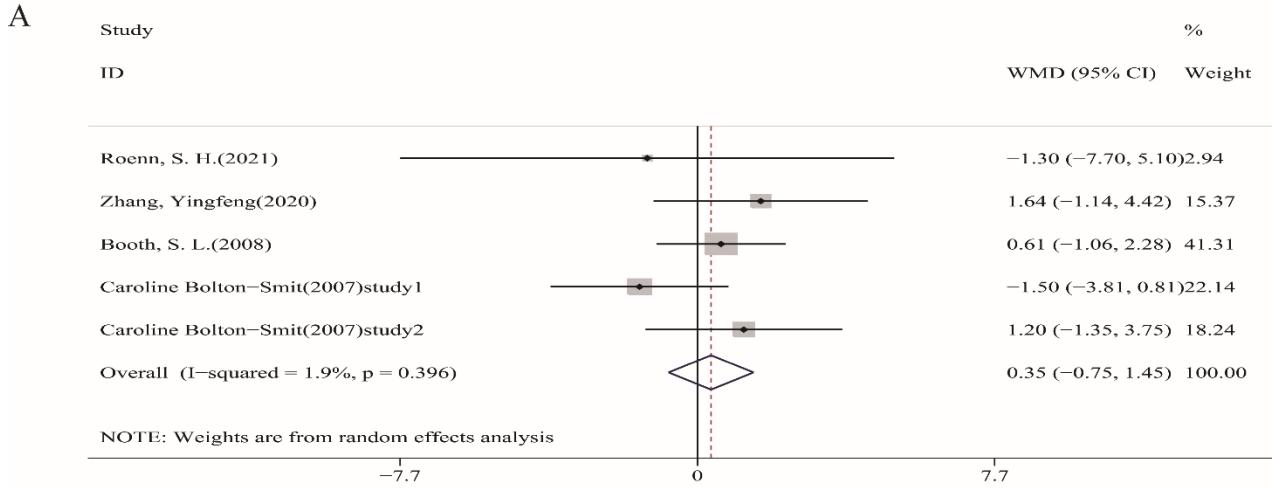
\*Participants with osteoporosis or osteopenia.

N/A, only one document included, not shown; WMD, weighted mean difference.

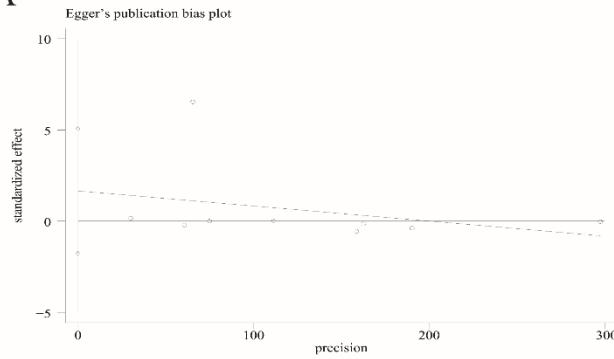
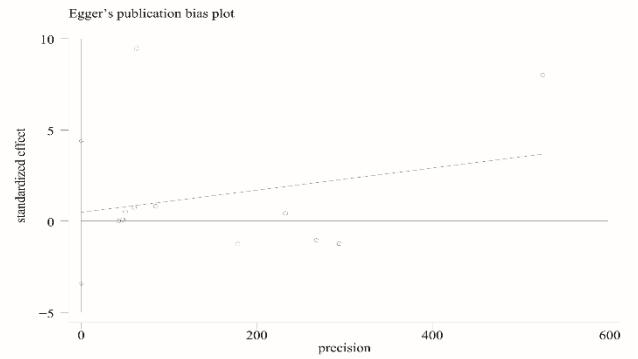
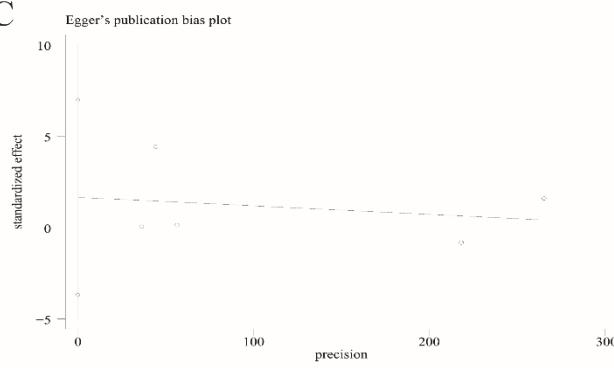
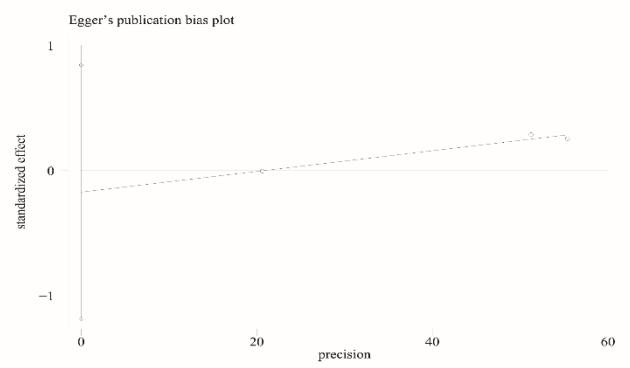
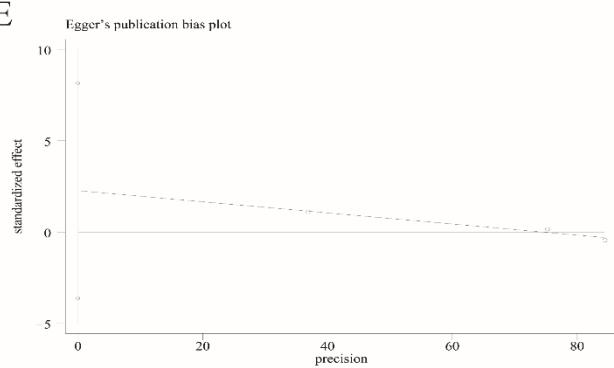
**Table iii.** Subgroup analysis of the effects of vitamin K supplementation on cross-linked telopeptide of type 1 collagen, bone alkaline phosphatase.

Subgroup	NTx (nM)				BAP ( $\mu\text{g/l}$ )			
	N	WMD (95% CI)	Heterogeneity		N	WMD (95% CI)	Heterogeneity	
		I <sup>2</sup>	p-value			I <sup>2</sup>	p-value	
<b>Intervention</b>								
Vitamin K1	2	0.01 (-0.33 to 0.36)	17.0%	0.936				
Vitamin K2	2	0.24 (-2.32 to 1.83)	95.3%	0.817				
<b>Dose, mg/day</b>								
$\leq 1$	2	0.01 (-0.33 to 0.36)	17.0%	0.936	1	-0.60 (-2.88 to 1.68)	N/A	0.606
$> 1$	2	-0.24 (-2.32 to 1.83)	95.3%	0.817	2	1.55 (-3.68 to 6.78)	8.5%	0.562
<b>Duration, yrs</b>								
$\leq 1$	3	-0.05 (-0.78 to 0.68)	98.1%	0.888	2	1.55 (-3.68 to 6.78)	8.5%	0.562
$> 1$	1	-0.55 (-0.50 to 1.59)	N/A	0.306	1	-0.60 (-2.88 to 1.68)	N/A	0.606
<b>Country</b>								
Asia					1	-0.60 (-2.88 to 1.68)	N/A	0.606
Other continents					2	1.55 (-3.68 to 6.78)	8.5%	0.562
<b>Sex</b>								
Female	3	-0.05 (-0.78 to 0.68)	98.7%	0.888				
Female & male	1	0.55 (-0.50 to 1.59)	N/A	0.306				

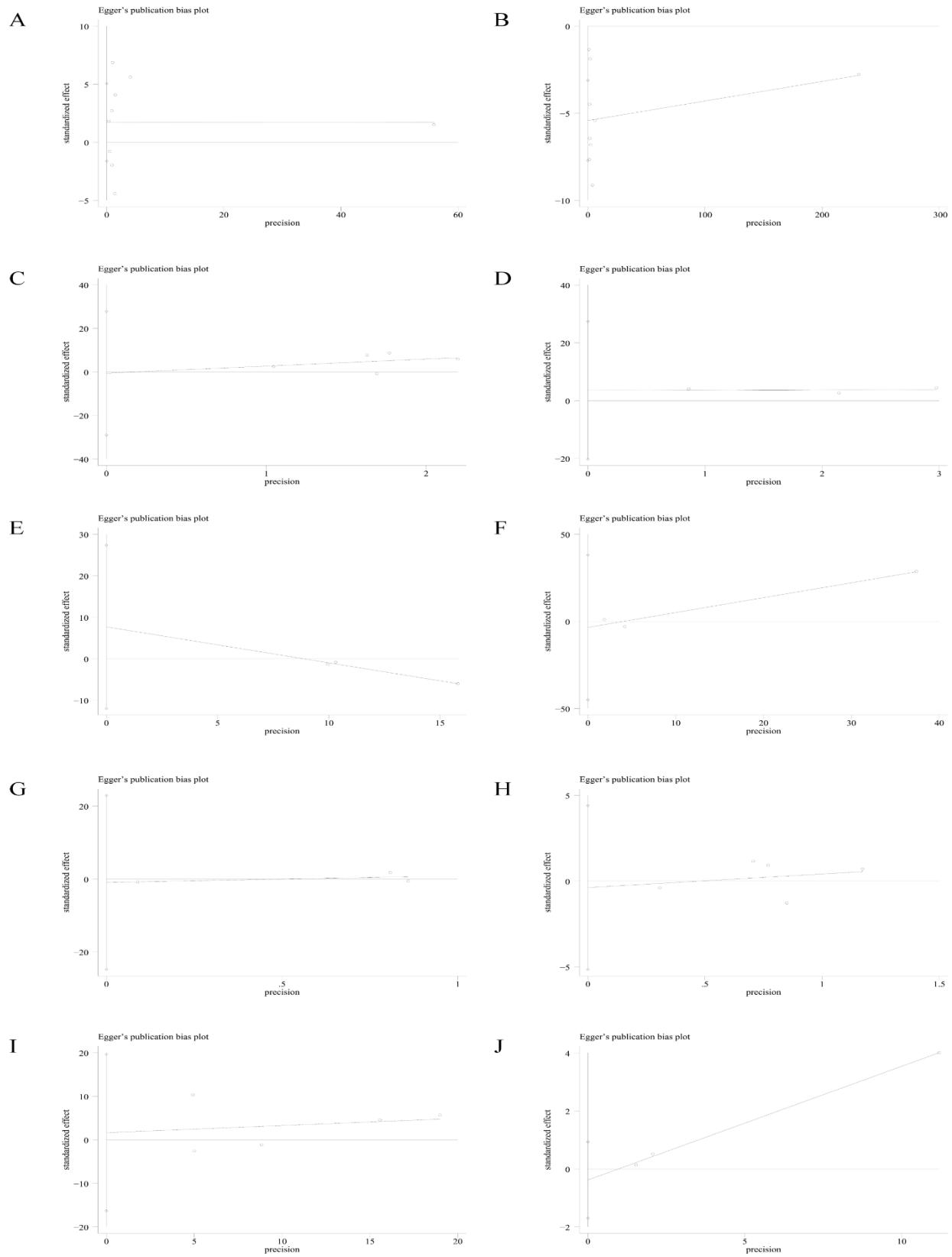
N/A, only one document included, not shown; WMD, weighted mean difference.



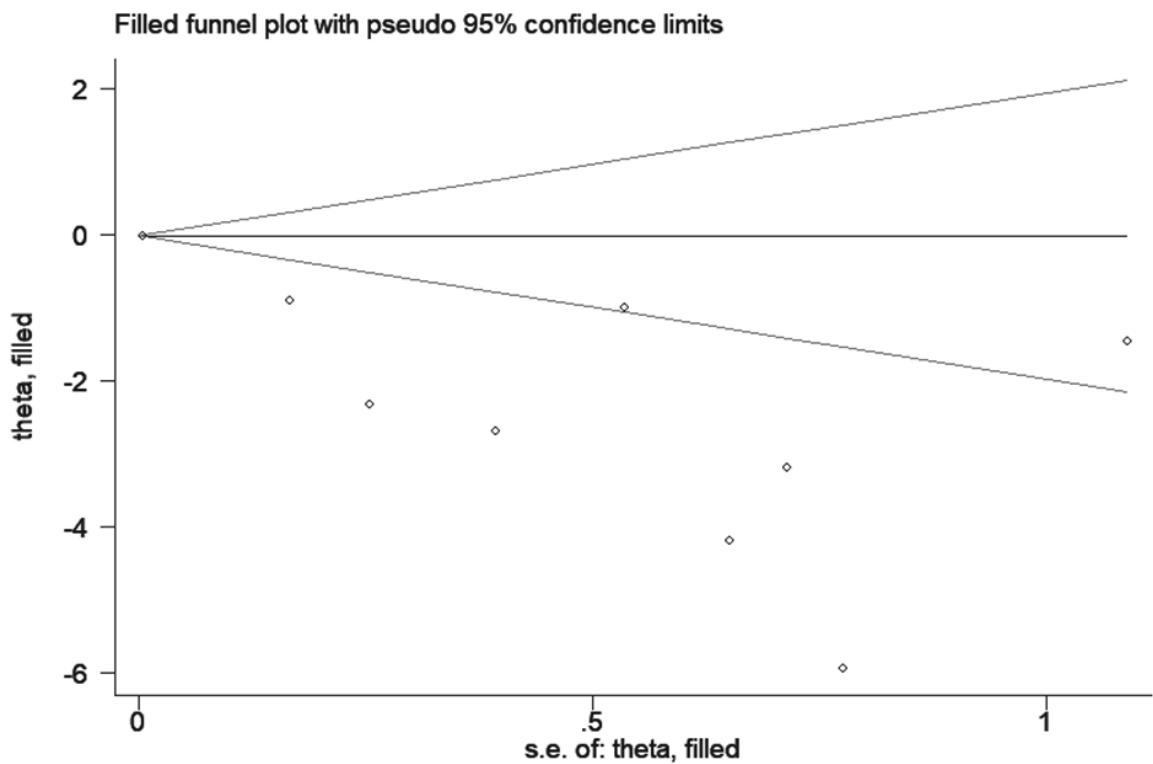
**Fig. a.** Forest plots of change in a) S-25-OH-vitamin D, b) serum vitamin K1, and c) serum MK-7.

**A****B****C****D****E**

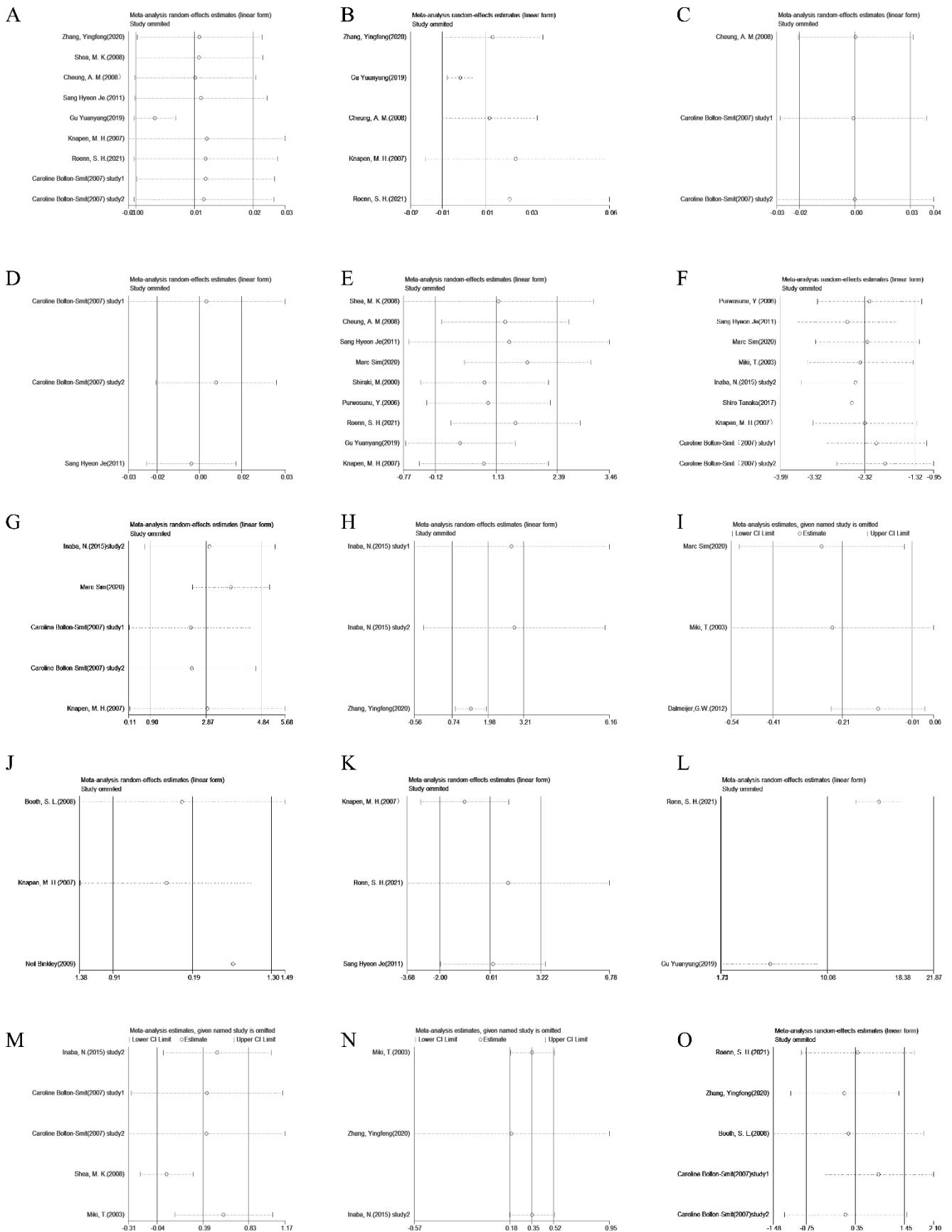
**Fig. b.** Publication bias tests for the pooled effect of a) femoral neck bone mineral density (BMD) change, b) lumbar spine BMD change, c) total hip BMD change, d) ultra distal radius BMD change, and e) femoral Ward BMD change.



**Fig. c.** Publication bias test for the pooled effect of a) total osteocalcin (tOC) change, b) uncarboxylated osteocalcin (ucOC) change, c) carboxylated osteocalcin (cOC) change, d) cOC to ucOC change, e) ucOC to tOC change, f) cross-linked telopeptide of type 1 collagen (NTx) change, g) BAP change, h) S-25-OH-vitamin D change, i) serum vitamin K1 change, and j) serum MK-7 change.



**Fig. d.** Trim-and-fill method for the pooled effect of uncarboxylated osteocalcin (ucOC) change. s.e., standard error.



**Fig. e.** Sensitivity analysis of the change in a) femoral neck bone mineral density (BMD), b) total hip BMD, c) ultra distal radius BMD, d) femoral Ward BMD, e) total osteocalcin (tOC), f) uncarboxylated osteocalcin (ucOC), g) carboxylated osteocalcin (cOC), h) cOC to ucOC, i) ucOC to tOC, j) cross-linked telopeptide of type 1 collagen (NTx), k) bone alkaline phosphatase (BAP), l) procollagen I N-terminal propeptide (PINP), m) serum vitamin K1, n) serum MK-7, and o) S-25-OH-vitamin D.