SUPPLEMENTAL TABLES FOR

Effect of vitamin D supplementation or fortification on bone turnover markers in women: A systematic review and meta-analysis

Nasrin Nasimi^{1,2}, Sanaz Jamshidi³, Aida Askari¹, Nazanin Zolfaghari¹, Erfan Sadeghi⁴, Mehran Nouri¹, Nick Bellissimo⁵, Shiva Faghih^{2*}

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Table S1. Summary findings of comparison of uNTX between the study treatments.

Outcomes	N	Subgroup Analysis	;	Meta-Regression 1	Meta-Regression 2	Non-linear Meta Regression
		MD (95%CI), <i>P-value</i>	l², P-value	B (95% CI), <i>P-value</i> , Res I ²	B (95% CI), <i>P-value</i> , Res I ²	S or NS
Total	6	- 8.138 (- 12.864, -3.413), 0.001	0.0% , 0.627	B (35% CI), <i>P-Value</i> , Res 1	B (95% CI), <i>P-Value</i> , Res I	3 01 103
Dose ≤ 600 IU/day		NA		Ref	0.0091 (-0.0050, 0.0232),	NS
Dose > 600 IU/day				6.9042 (-3.736, 17.544), <i>0.203</i> , 0.00%	<i>0.206,</i> 0.00%	NJ
Duration ≤ 12weeks	3	- 7.195 (- 13.050, -1.341), 0.016	12.2% , 0.345	Ref	-0.0044 (-0.1653, 0.1565),	NS
Duration > 12weeks	3	- 10.84 (- 20.193, - 1.488), 0.023	0.0% , 0.634	-3.6285 (-14.466, 7.209), 0.512, 0.00%	<i>0.957,</i> 1.88%	INS
Baseline vitD ≤ 20ng/ml		NA		NA	0.5277 (-2.3559, 3.4114),	NS
Baseline vitD > 20ng/ml		NA		NA	0.720, 2.18%	INS
Age ≤ 60 years		NA		NA	0.0236 (-0.4875, 0.5348),	NS
Age > 60 years		NA		NA	<i>0.904,</i> 0.00%	INS
Publication year < 2010		NA		NA	0.6358 (-0.6248, 1.8964),	NS
Publication year \geq 2010		NA		NA	<i>0.323,</i> 0.00%	INS
Sample Size ≤ 100		NA		NA	-0.0435 (-0.1909, 0.1038),	NS
Sample Size > 100		NA		NA	<i>0.563,</i> 0.00%	INS
Healthy postmeno		NA		NA		NA
Postmeno osteoporosis		NA		NA .	NA	NA
Region						
Asia						
Europe		NA		NA	NA	NA
America						
South America, Australia						
Risk of bias						
High		NA	NA		NA	
Some Concerns		NA		NA		NA
Low						

Meta-Regression 1: the subgrouping variable was included into the model as a categorized variable. **Meta-Regression 2**: the subgrouping variable was included into the model as a continuous variable. **Abbreviations**: N; Number of included interventions, B; Beta coefficient reflecting the effect of the subgrouping variable on the pooled effect size. vit; vitamin, postmeno; post-menopausal, CI; confidence interval, Res I²; Residual I², NA; Not Applicable, S; Singnificant, NS; Non-significant. *Italic*; P-values; **Bold**; significant P-value.

Table S2. Summary findings of comparison of BALP between the study treatments.

Outcomes	N	Subgroup Analysis	5	Meta-Regression 1	Meta-Regression 2	Non-linear Meta Regression
		MD (95%CI), <i>P-value</i>	l ² , <i>P-value</i>	$P(05\% Cl) P(cr) Post l^2$	P(05%)(1) $P(1)$ $P(1)$	S or NS
Total	6	- 1.487 (- 9.772, 6.797), 0.725	95.3% <i>, <0.001</i>	B (95% CI), <i>P-value</i> , Res I ²	B (95% CI), <i>P-value</i> , Res I ²	5 OF INS
Dose ≤ 600 IU/day	4	-5.425 (-14.417. 3.568) <i>, 0.237</i>	71.1%, 0.058	Ref	0.0121 (-0.0097, 0.0340),	NS
Dose > 600 IU/day	2	5.058 (-8.760, 18.876), <i>0.473</i>	97.6%, <i><0.001</i>	10.941 (-5.068, 26.950), <i>0.180</i> , 91.42%	0.276, 94.04%	INS
Duration ≤ 12weeks				NA	-0.0806 (-0.4326, 0.2712),	NC
Duration > 12weeks		NA		NA	0.653, 93.98%	NS
Baseline vitD ≤ 20ng/ml	2	-11.496 (-33.484, 10.492), 0.305	82.5%, 0.017	Ref	0.6681 (-3.1657, 4.5021),	NG
Baseline vitD > 20ng/ml	3	1.761 (-10.280, 13.801), 0.774	96.7%, <0.001	12.071 (-10.016, 34.160), 0.284, 96.43%)	0.733, 96.61%	NS
Age ≤ 60 years					-0.8261 (-2.0006, 0.3482),	
Age > 60 years		NA		NA	0.168, 90.51%	NS
Publication year < 2010	3	-6.354 (-19.767, 7.058), <i>0.353</i>	86.9%, 0.025	Ref	0.6212 (-0.5198, 1.7622),	NG
Publication year ≥2010	3	2.729 (-8.447, 13.904), 0.632	94.5%, <0.001	8.6549 (-8.294, 25.604), 0.317, 92.59%	0.286, 91.82%	NS
Sample Size ≤ 100	3	-7.807 (-23.833, 8.219), 0.340	72.3%, 0.025	Ref	0.0288 (-0.0841, 0.1417),	
Sample Size > 100	3	2.004 (-7.917, 11.924), 0.692	97.6%, <0.001	9.2874 (-8.516, 27.090), <i>0.307</i> , 96.46%	0.617, 95.10%	NS
Healthy postmeno		NA		NA		NA
Postmeno osteoporosis		INA		NA	NA	INA
Region						
Asia						
Europe		NA		NA	NA	NA
America						
South America, Australia						
Risk of bias						NA
High		ΝΑ		NA		
Some Concerns		NA		NA	. 47 \	
Low						

Meta-Regression 1: the subgrouping variable was included into the model as a categorized variable. **Meta-Regression 2**: the subgrouping variable was included into the model as a continuous variable. **Abbreviations**: N; Number of included interventions, B; Beta coefficient reflecting the effect of the subgrouping variable on the pooled effect size. vit; vitamin, postmeno; post-menopausal, CI; confidence interval, Res I²; Residual I², NA; Not Applicable, S; Singnificant, NS; Non-significant. *Italic*; P-values; **Bold**; significant P-value.

Table S3 GRADE evidence profile rating for the change in bone turnover markers in studies testing vitamin D supplementation in women.

Certainty assessment							№ of pati	ents		Effect		
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	vitamin D supplementation	control	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance

Overall effects of vitamin D supplementation on changes in sCTX level (All RCTs) (assessed with: MD)

15	randomized trials	not serious	serious ^a	not serious	not serious	all plausible residual confounding would reduce the demonstrated effect dose response gradient	1196	1453	-	MD 0.038 lower (0.058 lower to 0.018 lower)	⊕⊕⊕⊕ High	IMPORTANT
					1							

Overall effects of vitamin D supplementation on changes in uNTX level (All RCTs) (assessed with: MD)

4	randomized trials	very serious ^e	not serious	not serious	not serious	very strong association	167	167	-	MD 8.188 lower (12.898 lower to	⊕⊕⊕⊕ High	IMPORTANT
										3.479 lower)		

Overall effects of vitamin D supplementation on changes in OC level (All RCTs) (assessed with: MD)

18	randomized trials	very serious ^b	very serious ^c	not serious	not serious	strong association all plausible residual confounding would reduce the demonstrated effect dose response gradient	983	1140	-	MD 0.61 lower (1.151 lower to 0.07 lower)	⊕⊕⊕⊖ Moderate	IMPORTANT
						dose response gradient						

Overall effects of vitamin D supplementation on changes in P1NP level (All RCTs) (assessed with: MD)

11	randomized trials	not serious	serious ^d	not serious	not serious	dose response gradient	1007	1292	-	MD 0.191 lower (2.186 lower to 1.803 higher)	⊕⊕⊕⊕ High	IMPORTANT
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Overall effects of vitamin D supplementation on changes in BALP level (All RCTs) (assessed with: MD)

6	randomized trials	very serious ^f	very serious ^g	not serious	not serious	very strong association	416	403	-	MD 1.253 lower (8.888 lower to 6.381 higher)	⊕⊕⊖⊖ Low	IMPORTANT
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CI: confidence interval; MD: mean difference. Explanations: a. I2= 67.3 %, b. 27.7% of included studies had high risk of bias., c. I2= 80.3%, d. I2= 58.5%, e. 25% of included studies had high risk of bias., f. 33.3% of included studies had high risk of bias., g. I2= 94.5%.

SUPPLEMENTAL FIGURES FOR

Effect of vitamin D supplementation or fortification on bone turnover markers in women: A systematic review and meta-analysis

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Study	T N	reatme Mean		N	Control Mean			MD with 95% CI	Weight (%)
< 60 years old		mean	00		mourr	00			(70)
Nahas-Neto et al. (2018)	80	08	.14	80	02	.15		-0.06 [-0.10, -0.02]	5.72
Aloia et al. c (2013)	46	01	.12	35	.04	.15		-0.05 [-0.11, 0.01]	4.66
Aloia et al. d (2013)	47	07	.12	31	02	.13		-0.05 [-0.11, 0.01]	4.84
Gronborg et al. a (2019)	31	05	.1	35	006	.1		-0.04 [-0.09, 0.00]	5.45
Gronborg et al. b (2019)	33	02	.1	37	03	.1		0.01 [-0.04, 0.06]	5.56
Cheng et al. (2018)	75		.14	66		.33		0.04 [-0.05, 0.12]	3.28
Heterogeneity: $\tau^2 = 0.00$, I^2	= 36.3			57			•	-0.03 [-0.06, -0.00]	
Test of $\theta_i = \theta_j$: Q(5) = 8.20,		15							
> 60 years old							_		
Gao et al. f (2015)	109	1	.16		.04	.16		-0.14 [-0.18, -0.10]	6.47
Gao et al. e (2015)	101	03	.15	251	.04	.16		-0.07 [-0.11, -0.03]	6.45
Olmos et al. (2012)	73	41	.27	67	35	.26		-0.06 [-0.15, 0.03]	3.00
Manios et al. (2009)	39	08	.14	36	03	.12		-0.05 [-0.11, 0.01]	4.63
Zhang et al. a (2020)	34	24	.27	35	19	.28		-0.05 [-0.18, 0.08]	1.70
Cho et al. (2015)	101	2	.16	98	17	.16		-0.03 [-0.07, 0.01]	5.76
Välimäki et al. f (2016)	19	06	.29	18	03	.23		-0.03 [-0.20, 0.14]	1.09
Macdonald et al. e (2013)	84	01	.15	90	.01	.17		-0.02 [-0.07, 0.03]	5.50
Chung et al. (2013)	63	32	.25	65	31	.2		-0.01 [-0.09, 0.07]	3.46
Macdonald et al. f (2013)	90	0	.16	90	.01	.17		-0.01 [-0.06, 0.04]	5.46
Zhang et al. b (2020)	25	26	.19	26	26	.23		0.00 [-0.12, 0.12]	2.03
Bin Lee et al. (2022)	47	1	.1	44	1	.2		0.00 [-0.06, 0.06]	4.28
Välimäki et al. e (2016)	17	0	.24	18	03	.23		— 0.03 [-0.13, 0.19]	1.26
Heterogeneity: $\tau^2 = 0.00$, I^2	= 61.3	89%, H ²	= 2.	59			•	-0.04 [-0.07, -0.01]	
Test of $\theta_i = \theta_j$: Q(12) = 34.9	4, p =	0.00							
Overall 2 2							•	-0.04 [-0.06, -0.02]	
Heterogeneity: $\tau^2 = 0.00$, I^2			= 2.	36					
Test of $\theta_i = \theta_j$: Q(18) = 45.8	4, p =	0.00							
Test of group differences: C	Q _b (1) =	0.31, p	o = 0.	58					
							21 0 .1	.2	
Random-effects REML mode	əl								

Figure S1. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on sCTX (subgrouping participants' age). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CIs). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different participant groups; c, d: different intervention/ control groups; e, f: different dose of vitamin D.

	T	reatme	nt		Contro	l		MD	Weight
Study	Ν	Mean	SD	Ν	Mean	SD		with 95% CI	(%)
Europe									
Olmos et al. (2012)	73	41	.27	67	35	.26		-0.06 [-0.15, 0.03]	3.00
Manios et al. (2009)	39	08	.14	36	03	.12		-0.05 [-0.11, 0.01]	4.63
Gronborg et al. a (2019)	31	05	.1	35	006	.1		-0.04 [-0.09, 0.00]	5.45
Välimäki et al. f (2016)	19	06	.29	18	03	.23		-0.03 [-0.20, 0.14]	1.09
Macdonald et al. e (2013)	84	01	.15	90	.01	.17		-0.02 [-0.07, 0.03]	5.50
Macdonald et al. f (2013)	90	0	.16	90	.01	.17		-0.01 [-0.06, 0.04]	5.46
Bislev et al. (2019)	40	.01	.04	41	.02	.05		-0.01 [-0.03, 0.01]	7.73
Gronborg et al. b (2019)	33	02	.1	37	03	.1		0.01 [-0.04, 0.06]	5.56
Välimäki et al. e (2016)	17	0	.24	18	03	.23		0.03 [-0.13, 0.19]	1.26
Heterogeneity: $\tau^2 = 0.00$, I^2			: 1.00				•	-0.02 [-0.03, -0.00]	
Test of $\theta_i = \theta_j$: Q(8) = 5.49,							•		
South America & Au	strali	а							
von Hurst et al. b (2010)	13	03	.037	13	.055	.046		-0.09 [-0.12, -0.05]	6.80
Nahas-Neto et al. (2018)	80	08	.14	80	02	.15	_	-0.06 [-0.10, -0.02]	5.72
von Hurst et al. a (2010)	29	011	.108	26	.002	.103		-0.01 [-0.07, 0.04]	4.87
Heterogeneity: $\tau^2 = 0.00$, I^2	= 59.3	88%, H ²	= 2.4	6			•	-0.06 [-0.10, -0.02]	
Test of $\theta_i = \theta_j$: Q(2) = 4.86,	p = 0.0	09							
America									
Aloia et al. c (2013)	46	01	.12	35	.04	.15		-0.05 [-0.11, 0.01]	4.66
Aloia et al. d (2013)	47	07	.12	31	02	.13		-0.05 [-0.11, 0.01]	4.84
Heterogeneity: $\tau^2 = 0.00$, I^2	= 0.02	2%, H ² =	= 1.00				-	-0.05 [-0.09, -0.01]	
Test of $\theta_i = \theta_j$: Q(1) = 0.00,	p = 1.0	00							
Asia									
Gao et al. f (2015)	109	1	.16	251	.04	.16		-0.14 [-0.18, -0.10]	6.47
Gao et al. e (2015)	101	03	.15	251	.04	.16		-0.07 [-0.11, -0.03]	6.45
Zhang et al. a (2020)	34	24	.27	35	19	.28		-0.05 [-0.18, 0.08]	1.70
Cho et al. (2015)	101	2	.16	98	17	.16		-0.03 [-0.07, 0.01]	5.76
Chung et al. (2013)	63	32	.25	65	31	.2		-0.01 [-0.09, 0.07]	3.46
Zhang et al. b (2020)	25	26	.19	26	26	.23		- 0.00 [-0.12, 0.12]	2.03
Bin Lee et al. (2022)	47	1	.1	44	1	.2		0.00 [-0.06, 0.06]	4.28
Cheng et al. (2018)	75	.018	.14	66	018	.33		- 0.04 [-0.05, 0.12]	3.28
Heterogeneity: $\tau^2 = 0.00$, I^2	= 75.7	$'1\%, H^2$	= 4.12	2				-0.04 [-0.08, 0.00]	
Test of $\theta_i = \theta_j$: Q(7) = 32.06									
Overall							•	-0.04 [-0.06, -0.02]	
Heterogeneity: $\tau^2 = 0.00$, I^2	= 64.2	28%, H ²	= 2.8	C					
Test of $\theta_i = \theta_j$: Q(21) = 64.2									
Test of group differences: 0	Q _b (3) =	6.23, p	= 0.1	0		r		T	
						:	21 0 .	.1 .2	
Random-effects REML mod Sorted by Mean Difference (el (MD)								

Figure S2. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on sCTX (subgrouping region). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CIs). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different participant groups; c, d: different intervention/ control groups; e, f: different dose of vitamin D.

	-	reatme	nt		Contro	มี			MD	Weight
Study	Ν	Mean	SD	Ν	Mean	SD			with 95% CI	(%)
Low risk of bias										
von Hurst et al. b (2010)	13	03	.037	13	.055	.046			-0.09 [-0.12, -0.05]	6.80
Nahas-Neto et al. (2018)	80	08	.14	80	02	.15			-0.06 [-0.10, -0.02]	5.72
Gronborg et al. a (2019)	31	05	.1	35	006	.1			-0.04 [-0.09, 0.00]	5.45
Cho et al. (2015)	101	2	.16	98	17	.16		-	-0.03 [-0.07, 0.01]	5.76
Macdonald et al. e (2013)	84	01	.15	90	.01	.17		-	-0.02 [-0.07, 0.03]	5.50
von Hurst et al. a (2010)	29	011	.108	26	.002	.103			-0.01 [-0.07, 0.04]	4.87
Chung et al. (2013)	63	32	.25	65	31	.2			-0.01 [-0.09, 0.07]	3.46
Macdonald et al. f (2013)	90	0	.16	90	.01	.17			-0.01 [-0.06, 0.04]	5.46
Bislev et al. (2019)	40	.01	.04	41	.02	.05			-0.01 [-0.03, 0.01]	7.73
Gronborg et al. b (2019)	33	02	.1	37	03	.1		_	0.01 [-0.04, 0.06]	5.56
Cheng et al. (2018)	75	.018	.14	66	018	.33			0.04 [-0.05, 0.12]	3.28
Heterogeneity: $\tau^2 = 0.00$, I^2	= 55.9	95%, H ²	= 2.27	7			•		-0.03 [-0.05, -0.01]	
Test of $\theta_i = \theta_j$: Q(10) = 23.5	8, p =	0.01								
Some concerns										
Olmos et al. (2012)	73	41	.27	67	35	.26			-0.06 [-0.15, 0.03]	
Manios et al. (2009)	39	08	.14	36	03	.12		-1	-0.05 [-0.11, 0.01]	4.63
Aloia et al. c (2013)	46	01	.12	35	.04	.15		5	-0.05 [-0.11, 0.01]	4.66
Aloia et al. d (2013)	47	07	.12	31	02	.13			-0.05 [-0.11, 0.01]	
Zhang et al. a (2020)	34	24	.27	35	19	.28			-0.05 [-0.18, 0.08]	1.70
Välimäki et al. f (2016)	19	06	.29	18	03	.23			-0.03 [-0.20, 0.14]	1.09
Zhang et al. b (2020)	25	26	.19	26	26	.23		<u> </u>	0.00 [-0.12, 0.12]	2.03
Bin Lee et al. (2022)	47	1	.1	44	1	.2			0.00 [-0.06, 0.06]	4.28
Välimäki et al. e (2016)	17	0	.24	18	03	.23			— 0.03 [-0.13, 0.19]	1.26
Heterogeneity: $\tau^2 = 0.00$, I^2	= 0.01	1%, H ² =	= 1.00				•		-0.04 [-0.06, -0.01]	
Test of $\theta_i = \theta_j$: Q(8) = 3.26,	p = 0.9	92								
High risk of bias										
Gao et al. f (2015)	109	1	.16	251	.04	.16			-0.14 [-0.18, -0.10]	6.47
Gao et al. e (2015)	101	03		251	.04	.16			-0.07 [-0.11, -0.03]	6.45
Heterogeneity: $\tau^2 = 0.00$, I^2	= 86.1	12%, H ²	= 7.2	1					-0.11 [-0.17, -0.04]	
Test of $\theta_i = \theta_j$: Q(1) = 7.21,	p = 0.	01								
Overall							•		-0.04 [-0.06, -0.02]	
Heterogeneity: $\tau^2 = 0.00$, I^2			= 2.80	D						
Test of $\theta_i = \theta_j$: Q(21) = 64.2	9, p =	0.00								
Test of group differences: (Q _b (2) =	4.75, p	0.0	9						
						-	21 0	.1	.2	
Random-effects REML mode Sorted by Mean Difference (

Sorted by Mean Difference (MD)

Figure S3. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on sCTX (subgrouping quality of studies). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CIs). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different participant groups; c, d: different intervention/ control groups; e, f: different dose of vitamin D.

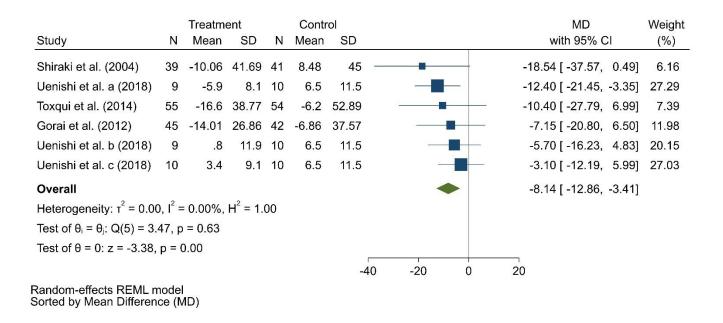
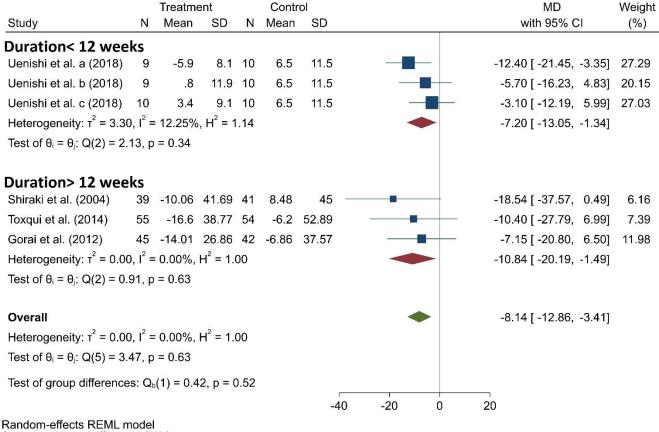


Figure S4. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on uNTX. Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the fixed effects model. Letters between parentheses represent: a, b, d: different dose of vitamin D.



Sorted by Mean Difference (MD)

Figure S5. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on uNTX (subgrouping study duration). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the fixed effects model. Letters between parentheses represent: a, b, d: different dose of vitamin D.

		Treatm	ent		Contro	ol		MD	Weight
Study	Ν	Mean	SD	Ν	Mean	SD		with 95% CI	(%)
< 100 participants									
von Hurst et al. d (2010)	13	231	3.876	13	3.385	3.5		-3.62 [-6.45, -0.78]	2.41
Shiraki et al. (2004)	39	-1.88	5.45	41	1.05	6.07		-2.93 [-5.46, -0.40]	2.80
Ushiroyama et al. a (1995)	14	-3.05	.81	28	71	.79		-2.34 [-2.85, -1.83]	7.15
von Hurst et al. c (2010)	29	036	3.35	26	1.96	4.03		-2.00 [-3.95, -0.04]	3.78
Son et al. (2001)	20	-3.69	5.75	21	-1.83	5.6		-1.86 [-5.33, 1.61]	1.80
Gronborg et al. c (2019)	31	-2.3	4.6	35	-1.2	4.2		-1.10 [-3.22, 1.02]	3.45
Ushiroyama et al. a (2001)	41	2	4	31	.6	4.25		-0.80 [-2.72, 1.12]	3.84
Ushiroyama et al. b (1995)	14	32	.83	23	.42	.76		-0.74 [-1.26, -0.22]	7.13
Shiraki et al. (1996)	21	-1.91	3.55	20	-1.27	3.57		-0.64 [-2.82, 1.54]	3.35
Gorai et al. a (1999)	12	1.9	3.36	12	2.5	2.79		-0.60 [-3.07, 1.87]	2.89
Gronborg et al. d (2019)	33	5	2.9	37	2	4	-	-0.30 [-1.95, 1.35]	4.40
Ushiroyama et al. b (2001)	40	.1	3.95	52	.3	4.41	-	-0.20 [-1.94, 1.54]	4.22
Manios et al. (2009)	39	26	1.11	36	3	1.11		0.04 [-0.46, 0.54]	7.16
Gorai et al. b (1999)	13	-2.1	3.68	8	-2.4	4.44		0.30 [-3.20, 3.80]	1.78
Bislev et al. (2019)	40	2.5	1.48	41	1.2	1.48		1.30 [0.66, 1.94]	6.88
Ushiroyama et al. (2002)	31	.91	2.3	30	51	2.93		1.42 [0.10, 2.74]	5.21
Rodziewicz- Flis et al. d (2022)	9	-2.18	10.96	9	-4.54	21.78		— 2.36 [-13.57, 18.29]	0.11
Rodziewicz- Flis et al. c (2022)	10	-1.09	8.97	9	-9.79	16.07		8.70 [-2.84, 20.24]	0.21
Heterogeneity: $\tau^2 = 1.31$, $I^2 = 80$.	20%,	$H^2 = 5.0$	05				•	-0.66 [-1.37, 0.06]	
Test of $\theta_i = \theta_j$: Q(17) = 106.93, p	= 0.0	D							
> 100 participants									
Cheng et al. (2018)	75	47	3.35	66	3 74	17.07		-4.21 [-8.16, -0.26]	1.47
Gao et al. (2015)	101	68	6.22		.85	4.97		-1.53 [-2.77, -0.29]	5.42
Cooper et al. (2003)	73	.00	2.6	80	.00	2.1		-0.48 [-1.23, 0.27]	6.65
Hunter et al. (2000)	64	2.5	3.24	64	2.7	3.07		-0.20 [-1.29, 0.89]	5.79
Ooms et al. (1995)	148	4	1.55	135	2	1.33	-	-0.20 [-0.54, 0.14]	7.42
Pfeifer et al. (2000)	73	.15	1.88	72	38	6.44	T	0.53 [-1.01, 2.07]	4.67
Heterogeneity: $\tau^2 = 0.02$, $l^2 = 9.0$				12	00	0.44	T	-0.34 [-0.69, -0.00]	4.07
Test of $\theta_i = \theta_i$: Q(5) = 9.28, p = 0		- 1. IV	5				•	-0.04 [-0.09, -0.00]	
Test of $\theta_i = \theta_j$. Q(5) = 9.26, p = 0	.10								
Overall							٠	-0.61 [-1.15, -0.08]	
Heterogeneity: $\tau^2 = 0.97$, $I^2 = 79$.	95%,	$H^2 = 4.9$	99						
Test of $\theta_i = \theta_j$: Q(23) = 118.49, p	= 0.00	כ							
Test of group differences: $Q_b(1)$:	= 0.61	, p = 0.	44						
							-10 0 10	20	
Random-effects REML model									

Figure S6. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on OC (subgrouping study sample size). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different intervention/ control groups; c, d: different participant groups.

	Treatment				Contro	bl		MD	Weight
Study	Ν	Mean	SD	Ν	Mean	SD		with 95% CI	(%)
Nahas-Neto et al. (2018)	80	-7.4	22.63	80	3	25.07		-7.10 [-14.50, 0.30]	4.46
Gao et al. b (2015)	109	-4.27	21.4	251	11	18.65		-4.16 [-8.55, 0.23]	7.36
Gronborg et al. d (2019)	33	-1.7	10.4	37	1.7	10.3		-3.40 [-8.26, 1.46]	6.82
Olmos et al. (2012)	73	-26	22.71	67	-23	24.24		-3.00 [-10.78, 4.78]	4.19
Zhang et al. d (2020)	25	-14.61	15.66	26	-11.66	15.87		-2.95 [-11.61, 5.71]	3.64
Zhang et al. c (2020)	34	-17.1	15.51	35	-14.29	14.78		-2.81 [-9.96, 4.34]	4.65
Toxqui et al. (2014)	55	-4.9	21.96	54	-2.7	20.98		-2.20 [-10.27, 5.87]	4.00
Macdonald et al. a (2013)	84	-1.8	19.49	90	2	22.8		-1.60 [-7.92, 4.72]	5.33
Macdonald et al. b (2013)	90	-1.5	17.29	90	2	22.8		-1.30 [-7.21, 4.61]	5.72
Gronborg et al. c (2019)	31	-2.6	11	35	-2	7.9		-0.60 [-5.18, 3.98]	7.13
Gao et al. a (2015)	101	68	24.34	251	11	18.65		-0.57 [-5.29, 4.15]	6.97
Zhu et al. (2008)	123	-1.87	22.37	133	-1.51	23.44		-0.36 [-5.98, 5.26]	6.00
Bislev et al. (2019)	40	1.3	3.92	41	.4	5.33		0.90 [-1.14, 2.94]	10.16
Aloia et al. (2013)	47	2	5.2	31	-1.1	8.34		0.90 [-2.10, 3.90]	9.05
Välimäki et al. b (2016)	19	-3	20.45	18	-8	14.29		5.00 [-6.43, 16.43]	2.42
Aloia et al. (2013)	46	5.49	6.78	35	-2.55	8.63		8.04 [4.69, 11.39]	8.62
Välimäki et al. a (2016)	17	3	12.67	18	-8	14.29		— 11.00 [2.03, 19.97]	3.47
Overall							•	-0.20 [-2.21, 1.80]	
Heterogeneity: $\tau^2 = 9.21$, I^2	= 60.8	38%, H ²	= 2.56						
Test of $\theta_i = \theta_j$: Q(16) = 40.2	7, p =	0.00							
Test of θ = 0: z = -0.20, p =	0.84								
						-2	0 -10 0 10	20	
Random-effects REML mode	əl								

Figure S7. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on P1NP. Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different dose of vitamin D; c, d: different participant groups.

Study	N	Treatme Mean	ent SD	N	Contro Mean	ol SD		MD with 95% 0	CI	Weight (%)
Dosage< 600IU/day										
Gao et al. b (2015)	109	-4.27	21.4	251	11	18.65		-4.16 [-8.55,	0.23]	7.36
Zhang et al. d (2020)	25	-14.61	15.66	26	-11.66	15.87		-2.95 [-11.61,	5.71]	3.64
Zhang et al. c (2020)	34	-17.1	15.51	35	-14.29	14.78		-2.81 [-9.96,	4.34]	4.65
Toxqui et al. (2014)	55	-4.9	21.96	54	-2.7	20.98		-2.20 [-10.27,	5.87]	4.00
Macdonald et al. a (2013)	84	-1.8	19.49	90	2	22.8		-1.60 [-7.92,	4.72]	5.33
Heterogeneity: $\tau^2 = 0.00$, I^2	= 0.00	$0\%, H^2 =$	1.00				•	-3.07 [-5.89,	-0.24]	
Test of $\theta_i = \theta_j$: Q(4) = 0.50,	p = 0.	97								
Dosage> 600IU/day										
Nahas-Neto et al. (2018)	80	-7.4	22.63	80	3	25.07		-7.10 [-14.50,	0.30]	4.46
Gronborg et al. d (2019)	33	-1.7	10.4	37	1.7	10.3		-3.40 [-8.26,	1.46]	6.82
Olmos et al. (2012)	73	-26	22.71	67	-23	24.24		-3.00 [-10.78,	4.78]	4.19
Macdonald et al. b (2013)	90	-1.5	17.29	90	2	22.8		-1.30 [-7.21,	4.61]	5.72
Gronborg et al. c (2019)	31	-2.6	11	35	-2	7.9		-0.60 [-5.18,	3.98]	7.13
Gao et al. a (2015)	101	68	24.34	251	11	18.65		-0.57 [-5.29,	4.15]	6.97
Zhu et al. (2008)	123	-1.87	22.37	133	-1.51	23.44		-0.36 [-5.98,	5.26]	6.00
Bislev et al. (2019)	40	1.3	3.92	41	.4	5.33		0.90 [-1.14,	2.94]	10.16
Aloia et al. (2013)	47	2	5.2	31	-1.1	8.34		0.90 [-2.10,	3.90]	9.05
Välimäki et al. b (2016)	19	-3	20.45	18	-8	14.29		5.00 [-6.43,	16.43]	2.42
Aloia et al. (2013)	46	5.49	6.78	35	-2.55	8.63		8.04 [4.69,	11.39]	8.62
Välimäki et al. a (2016)	17	3	12.67	18	-8	14.29		— 11.00 [2.03,	19.97]	3.47
Heterogeneity: τ ² = 11.23, I	² = 68	.88%, H ⁱ	² = 3.21				+	0.67 [-1.80,	3.13]	
Test of $\theta_i = \theta_j$: Q(11) = 32.6	0, p =	0.00								
Overall 2							•	-0.20 [-2.21,	1.80]	
Heterogeneity: $\tau^2 = 9.21$, I^2			= 2.56							
Test of $\theta_i = \theta_j$: Q(16) = 40.2	7, p =	0.00								
Test of group differences: C	⊋₀(1) =	= 3.81, p	= 0.05							
						-2	0 -10 0 10	20		
Random-effects REML mode	əl									

Sorted by Mean Difference (MD)

Figure S8. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on P1NP (subgrouping dosage of supplementation). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different dose of vitamin D; c, d: different participant groups.

Study	N	Treatme Mean	ent SD	N	Contro Mean	I SD		MD with 95% (CI	Weight (%)
< 100 participants		Moun			Would	00		With 0070		(70)
Gronborg et al. d (2019)	33	-1.7	10.4	37	1.7	10.3		-3.40 [-8.26,	1.46]	6.82
Zhang et al. d (2020)	25	-14.61	15.66	26	-11.66	15.87		-2.95 [-11.61,	1.50	3.64
Zhang et al. c (2020)	34	-17.1	15.51	35	-14.29	14.78		-2.81 [-9.96,	4.34]	4.65
Gronborg et al. c (2019)	31	-2.6	11	35	-2	7.9		-0.60 [-5.18,	3.98]	7.13
Bislev et al. (2019)	40	1.3	3.92	41	.4	5.33	-	0.90 [-1.14,	2.94]	10.16
Aloia et al. (2013)	47	2	5.2	31	-1.1	8.34	-	0.90 [-2.10,	3.90]	9.05
Välimäki et al. b (2016)	19	-3	20.45	18	-8	14.29		5.00 [-6.43,	16.43]	2.42
Aloia et al. (2013)	46	5.49	6.78	35	-2.55	8.63		8.04 [4.69,	11.39]	8.62
Välimäki et al. a (2016)	17	3	12.67	18	-8	14.29		— 11.00 [2.03,	19.97]	3.47
Heterogeneity: $\tau^2 = 13.47$, I	2 = 74	.04%, H	² = 3.85				-	1.53 [-1.51,	4.57]	
Test of $\theta_i = \theta_j$: Q(8) = 26.86,	p = (0.00								
> 100 participants										
Nahas-Neto et al. (2018)	80	-7.4	22.63	80	3	25.07		-7.10 [-14.50,	0.30]	4.46
Gao et al. b (2015)	109	-4.27	21.4	251	11	18.65		-4.16 [-8.55,	0.23]	7.36
Olmos et al. (2012)	73	-26	22.71	67	-23	24.24		-3.00 [-10.78,	4.78]	4.19
Toxqui et al. (2014)	55	-4.9	21.96	54	-2.7	20.98		-2.20 [-10.27,	5.87]	4.00
Macdonald et al. a (2013)	84	-1.8	19.49	90	2	22.8		-1.60 [-7.92,	4.72]	5.33
Macdonald et al. b (2013)	90	-1.5	17.29	90	2	22.8		-1.30 [-7.21,	4.61]	5.72
Gao et al. a (2015)	101	68	24.34	251	11	18.65		-0.57 [-5.29,	4.15]	6.97
Zhu et al. (2008)	123		22.37	133	-1.51	23.44		-0.36 [-5.98,	5.26]	6.00
Heterogeneity: $\tau^2 = 0.00$, I^2	= 0.00	0%, H ² =	1.00				•	-2.34 [-4.41,	-0.26]	
Test of $\theta_i = \theta_j$: Q(7) = 3.47, μ	o = 0.	84								
Overall							•	-0.20 [-2.21,	1.80]	
Heterogeneity: $\tau^2 = 9.21$, I^2	= 60.8	88%, H ²	= 2.56							
Test of $\theta_i = \theta_j$: Q(16) = 40.2	7, p =	0.00								
Test of group differences: C	_b (1) =	= 4.24, p	= 0.04							
						-2	0 -10 0 10	20		
Random-effects REML mode	el									

Figure S9. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on P1NP (subgrouping study sample size). Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the random effects model. Letters between parentheses represent: a, b: different dose of vitamin D; c, d: different participant groups.

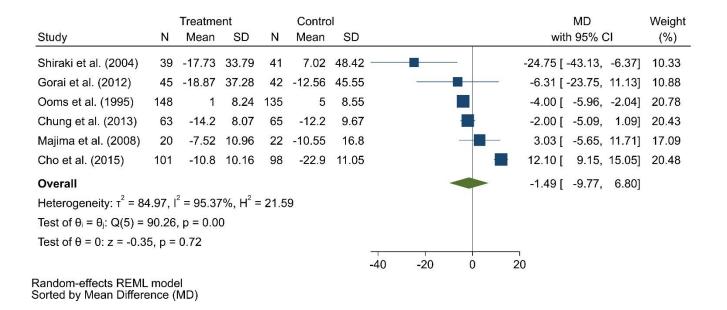


Figure S10. Forest plot of the Randomized Clinical Trials (RCTs) examining the effect of vitamin D supplementation on BALP. Data have been expressed as mean differences (MDs) between intervention and control groups with 95% confidence intervals (CI). Estimates were pooled using the random effects model.

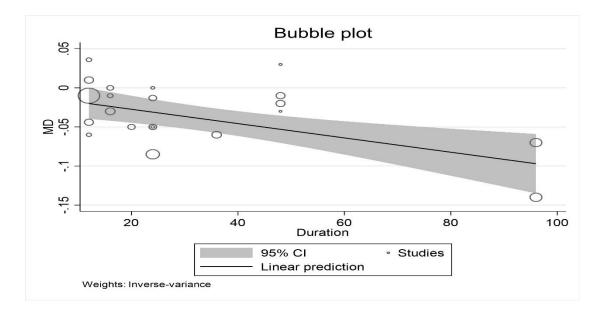


Figure S11. Meta-regression analysis revealed a significant association between sCTX level and study duration.

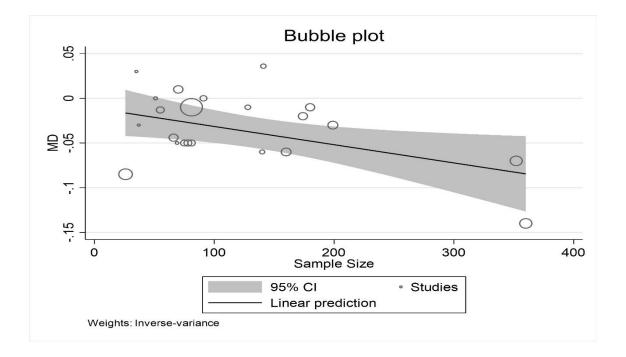


Figure S12. Meta-regression analysis revealed a significant association between sCTX level and study sample size.

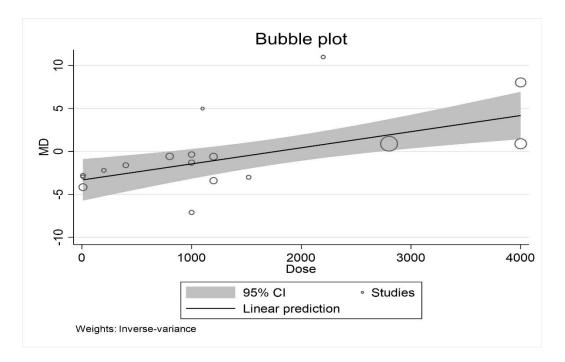


Figure S13. Meta-regression analysis revealed a significant association between P1NP level and dosage of vitamin D supplementation.

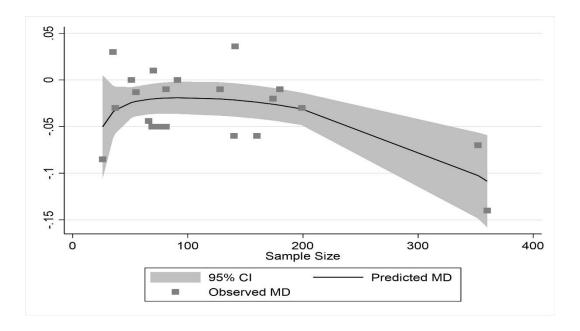


Figure S14. Non-linear meta-regression analysis revealed a significant association between sCTX level and study sample size.

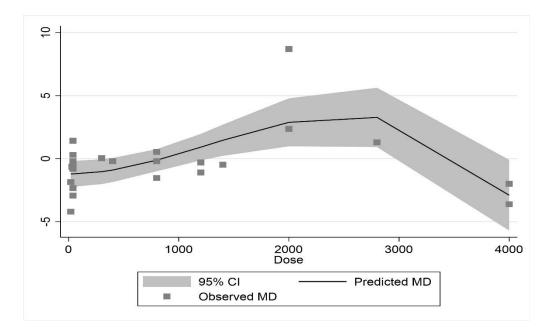


Figure S15. Non-linear meta-regression analysis revealed a significant association between OC level and dosage of vitamin D supplementation.

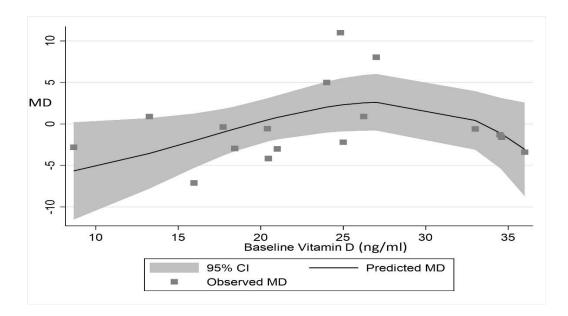


Figure S16. Non-linear meta-regression analysis revealed a significant association between P1NP level and baseline vitamin D level.

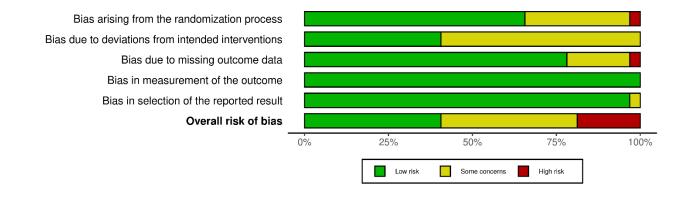


Figure S17a – A summary of risk of bias analysis showing the percentage of studies with "some concerns" or "high risk" of selection, performance, detection, attrition, reporting, or other bias.

			Ri	sk of bia	s doma	ins	
		D1	D2	D3	D4	D5	Overall
	Bin Lee et al.2022	+	-	+	+	+	-
	Rodziewicz- Flis et al.2022	+	-	+	+	+	-
	Zhang et al.2020	-	-	+	+	+	-
	Gronborg et al.2019	+	+	+	+	+	+
	Bislev et al.2019	+	+	+	+	+	+
	Uenishi et al.2018	+	+	+	+	+	+
	Nahas-Neto et al.2018	+	+	+	+	+	+
	Cheng et al.2018	+	+	+	+	+	+
	Välimäki et al.2016	-	-	+	+	+	-
	Gao et al.2015	X	-	+	+	-	×
	Cho et al.2015	+	+	+	+	+	+
	Toxqui et al.2014	+	+	+	+	+	+
	Macdonald et al.2013	+	+	+	+	+	+
	Chung et al.2013	+	+	+	+	+	+
	Aloia et al.2013	-	-	+	+	+	-
dy	Gorai et al.2012	+	-	+	+	+	-
Study	Olmos et al.2012	+	-	+	+	+	-
	von Hurst et al.2010	+	+	+	+	+	+
	Manios et al.2009	+	-	+	+	+	-
	Majima et al.2008	-	-	×	+	+	×
	Zhu et al.2008	+	+	+	+	+	+
	Shiraki et al.2004	-	-	-	+	+	X
	Cooper et al.2003	+	+	+	+	+	+
	Ushiroyama et al.2002	-	-	-	+	+	X
	Ushiroyama et al.2001	-	-	-	+	+	X
	Son et al.2001	-	-	+	+	+	-
	Pfeifer et al.2000	-	-	+	+	+	-
	Hunter et al.2000	+	+	+	+	+	+
	Gorai et al.1999	+	-	+	+	+	-
	Shiraki et al.1996	+	<u> </u>	<u> </u>	+	+	-
	Ushiroyama et al.1995	<u> </u>	•	-	+	+	X
	Ooms et al.1995	+	<u> </u>	<u> </u>	+	+	-
		D3: Bias D4: Bias	arising fr due to de due to m in measu	om the rar eviations fr issing out irement of on of the r	come data the outco	a. – Som ome.	nt s. ention. e concerns

Figure S17b – Risk of bias analysis of all studies included in the meta-analysis.

- (+) Circles filled in green = Low risk of bias
- (-) Circles filled in yellow = Some concerns
- (×) Circles filled in red = High risk of bias

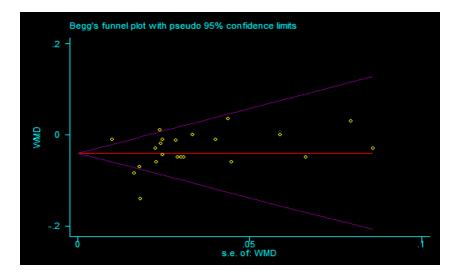


Figure S18. Funnel plot showing results of all studies testing the effects of vitamin D supplementation on sCTX.

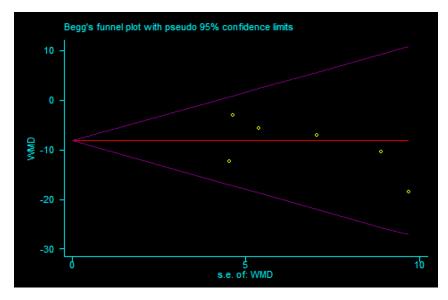


Figure S19. Funnel plot showing results of all studies testing the effects of vitamin D supplementation on uNTX.

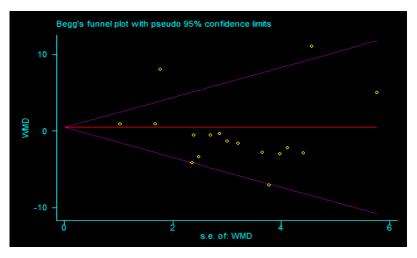


Figure S20. Funnel plot showing results of all studies testing the effects of vitamin D supplementation on OC.

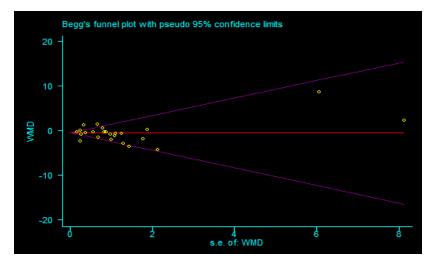


Figure S21. Funnel plot showing results of all studies testing the effects of vitamin D supplementation on P1NP.

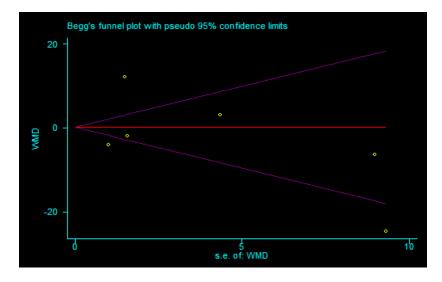


Figure S22. Funnel plot showing results of all studies testing the effects of vitamin D supplementation on BALP.