Subgroup analysis by neonatal risk status (high risk or low risk)

Source: Tan ML, Abrams SA, Osborn DA. Vitamin D supplementation for term breastfed infants to prevent vitamin D deficiency and improve bone health. Cochrane Database Syst Rev. 2020;(12):CD013046.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin D	Placebo or no supplementation	Relative (95% CI)	Absolute (95% CI)		
Vitamin D insufficiency (25(OH) vitamin D < 50 nmol/L) – high-risk infants												
3	randomized trials	serious [a]	not serious	not serious	serious [c]	none	25/64 (39.1%)	42/70 (60.0%)	**RR 0.65** (0.46 to 0.94)	**210 fewer per 1000** (from 324 fewer to 36 fewer)	⊕⊕◯◯ LOW	CRITICAL
Serum 25(OH) vitamin D level at latest time reported to 6 months of age – high-risk infants												
3	randomized trials	serious [a]	not serious	not serious	serious [c]	none	64	70	-	MD **18.24 higher** (9.39 higher to 27.09 higher)	⊕⊕◯◯ LOW	CRITICAL
Vitamin D deficiency (25(OH) vitamin D < 30 nmol/L) – high-risk infants												
2	randomized trials	serious [a]	not serious	not serious	very serious [b,d,e]	none	5/58 (8.6%)	14/64 (21.9%)	**RR 0.41** (0.16 to 1.05)	**129 fewer per 1000** (from 184 fewer to 11 more)	⊕◯◯◯ VERY LOW	CRITICAL
Nutritional rickets: biochemical – high risk infants: D2 400 IU/day from birth to 6 months of age; all seasons												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,f]	none	0/9 (0.0%)	0/9 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Vitamin D insufficiency (25(OH) vitamin D < 50 nmol/L) – low risk infants												
1	randomized trials	serious [a]	not serious	not serious	serious [c]	none	4/68 (5.9%)	22/72 (30.6%)	**RR 0.19** (0.07 to 0.53)	**248 fewer per 1000** (from 284 fewer to 144 fewer)	⊕⊕◯◯ LOW	CRITICAL
Serum 25(OH) vitamin D level at latest time reported to 6 months of age – low risk infants												
3	randomized trials	serious [a]	not serious	not serious	serious [c]	none	95	105	-	MD **25.53 higher** (18.34 higher to 32.72 higher)	⊕⊕◯◯ LOW	CRITICAL
Nutritional rickets: biochemical – low-risk infants: D2 400 IU/day from birth to 6 months of age												
1	randomized trials	very serious [g]	not serious	not serious	very serious [b,f]	none	0/8 (0.0%)	0/8 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin D	Placebo or no supplementation	Relative (95% CI)	Absolute (95% CI)		
Bone mineral content at the end of intervention – low-risk infants; D2 400 IU/day from birth to 3 months of age												
1	randomized trials	serious [a]	not serious	not serious	serious [c]	none	9	9	-	MD **15 higher** (6.68 higher to 23.32 higher)	⨁⨁◯◯ LOW	CRITICAL
Bone mineral content at the end of intervention – low-risk infants; D2 400 IU/day from birth to 6 months of age												
1	randomized trials	serious [a]	not serious	not serious	serious [c]	none	19	19	-	MD **11.5 lower** (21.32 lower to 1.68 lower)	⨁⨁◯◯ LOW	CRITICAL

CI: confidence interval; MD: mean difference; RR: risk ratio.
a. The pooled effect provided by studies “B”.
b. Less than 300 babies.
c. Less than 400 babies.
d. Less than 30 events.
e. Wide confidence interval crossing the line of no effect.
f. No events.
g. The pooled effect provided by studies “C”.