

3 Higher dose vitamin D supplementation compared to lower dose vitamin D supplementation in preterm infants for prevention of vitamin D deficiency

Patient or population: preterm infants Settings: Newborn intensive care Intervention: Higher dose vitamin D supplementation Comparison: lower dose vitamin D supplementation						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk Lower dose vitamin D supplementation	Corresponding risk Higher dose vitamin D supplementation				
Vitamin D deficiency Follow-up: discharge / term corrected age	142 per 1000	18 per 1000 (7 to 44)	RR 0.13 (0.05 to 0.31)	554 (9 studies)	⊕⊕⊕⊖ moderate ¹	RD -0.13, 95% CI -0.17 to -0.08; NNTB 7.7, 95% CI 5.9 to 12.5 No significant difference found across dose subgroups or gestation / birth weight subgroups.
Vitamin D insufficiency or deficiency Follow-up: discharge / term corrected age	343 per 1000	96 per 1000 (69 to 141)	RR 0.28 (0.20 to 0.41)	565 (9 studies)	⊕⊕⊕⊖ moderate ²	RD -0.24, 95% CI -0.30 to -0.19; NNTB 4.2, 95% CI 3.3 to 5.3 Significant difference found across dose subgroups. No significant difference

						across gestation / birth weight subgroups.
Vitamin D excess Follow-up: discharge / term corrected age	0 per 1000	45 per 1000 (10 to 90)	RR 5.76 (1.09 to 30.3)	357 (4 studies)	⊕⊕⊕⊖ moderate ³	RD 0.05, 95% CI 0.01 to 0.09; NNTH 20, 95% CI 11.1 to 100 No significant difference found across dose subgroups. Insufficient data to test for subgroup differences by gestation / birth weight.
Radiological evidence of osteopenia of prematurity Follow-up: four weeks to discharge / term corrected age	96 per 1000	88 per 1000 (46 to 169)	RR 0.92 (0.48 to 1.76)	339 (6 studies)	⊕⊕⊖⊖ low ^{4,5}	
Bone mineral content Follow-up: discharge / term corrected age	The mean bone mineral content in the intervention groups was 0.39 mean standard deviations higher (0.3 to 0.75 higher)		SMD 0.39 (0.03 to 0.75)	124 (4 studies)	⊕⊕⊖⊖ low ^{4,5}	
Secondary hyperparathyroidism	304 per 1000	140 per 1000 (94 to 204)	RR 0.46 (0.31 to 0.67)	409 (6 studies)	⊕⊕⊕⊖ moderate ¹	RD -0.17, 95% CI -0.25 to -0.09; NNTB 5.9, 95% CI 4 to 11.1

Follow-up: discharge / term corrected age						Significant difference found across dose subgroups.
Hypercalcaemia Follow-up: discharge / term corrected age	11 per 1000	12 per 1000 (2 to 79)	RR 1.10 (0.16 to 7.45)	418 (6 studies)	⊕⊖⊖⊖ very low ^{1,6}	

*The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **RD:** risk difference; **NNTB:** number needed to treat for an additional beneficial outcome; **NNTH:** number needed to treat for an additional harmful outcome; **SMD:** standard mean difference

GRADE Working Group grades of evidence

High certainty: further research is very unlikely to change our confidence in the estimate of effect.

1. **Moderate certainty:** further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
2. **Low certainty:** further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
3. **Very low certainty:** we are very uncertain about the estimate.

Footnotes

¹ Downgraded one level for risk of bias as only two small trials assessed as low risk of bias.

² Downgraded one level for inconsistency as moderate heterogeneity found between studies.

³ Downgraded one level of imprecision as sensitivity analysis estimate of effect included null (RR 7.94, 95% CI 1.00 to 62.96).

⁴ Downgraded one level for risk of bias as all trials assessed as high risk of bias.

⁵ Downgraded one level for imprecision due to wide confidence intervals.

⁶ Downgraded two levels for imprecision as few events and small number of participants result in very wide confidence intervals.