



## Q/What is the best age to start vitamin D supplementation to prevent rickets in breastfed newborns?

### EVIDENCE-BASED ANSWER

**A** | IT'S UNCLEAR what age is best to start vitamin D supplementation because no comparison studies exist. That said, breastfed infants who take vitamin D beginning at 3 to 5 days of life don't develop rickets (strength of recom-

mendation [SOR]: **B**, randomized trial).

Starting infants on vitamin D supplementation at one to 36 months of age reduces the risk of rickets (SOR: **B**, a controlled and a randomized controlled trial).

### Evidence summary

A Cochrane review of interventions for preventing rickets in children born at term found 2 studies, a controlled clinical trial and a cluster-randomized controlled trial, that included 905 breastfed infants.<sup>1</sup> In these trials, oral vitamin D (300 or 400 IU per day) starting between one and 36 months of age reduced the risk of rickets when compared with no supplementation (TABLE). The authors concluded that it was reasonable to offer preventive measures (vitamin D or calcium) to all children 2 years or younger.

### 400 IU of vitamin D daily increases blood levels the most

A study done in north and south China investigated vitamin D dose by randomizing 312 infants to receive supplements of 100, 200, or 400 IU daily.<sup>2</sup> Although no infant developed rickets, a dose of 400 IU per day achieved higher serum levels of 25-hydroxy vitamin D (25[OH]-D) than the lower doses.

In the northern location, doses of 100, 200, or 400 IU daily increased 25(OH)-D levels from 5 ng/mL at birth to an

average of 12, 15, and 25 ng/mL, respectively, at 6 months. In the southern location, 25(OH)-D levels increased from 14 ng/mL at birth to 20, 22, and 25 ng/mL at 6 months for the 100, 200, and 400 IU per day doses, respectively.

### Recommendations

The guidelines from the American Academy of Pediatrics (AAP) on preventing rickets and vitamin D deficiency in infants, children, and adolescents recommends that exclusively breastfed neonates receive 400 IU of vitamin D daily, starting in the first days of life—a revision of the previous recommendation of 200 IU daily beginning at 2 months. The AAP doesn't recommend giving vitamin D supplements to formula-fed infants because formula contains 400 IU/L of vitamin D; infants who don't drink at least 1 liter of formula per day should receive supplementation. The AAP advocates a serum 25(OH)-D level of at least 20 ng/mL.<sup>3</sup>

The Pediatric Endocrine Society (PES) defines vitamin D deficiency as a serum 25(OH)-D level below 15 ng/mL and recom-

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TABLE

Vitamin D supplementation and rickets: How the studies stack up

Study Type	Participants, (N)	Age at inclusion	Follow-up (mo)	Intervention (N)	Outcome	Location
CT <sup>1</sup>	676	3-36 mo	12	Oral vitamin D 400 IU/d (302) vs placebo (374)	RR for developing rickets=0.04 (95% CI, 0-0.71); ARR=3.7%	Rural Turkey
RCT <sup>1</sup>	229	1 mo	6-30	Oral vitamin D 300 IU/d (183) vs placebo (46)	RR for developing rickets=0.76 (95% CI, 0.61-0.95); ARR=17.1%	Rural China
RT <sup>2</sup>	312	3-5 days	6	Oral vitamin D 100 IU/d (104) Oral vitamin D 200 IU/d (104) Oral vitamin D 400 IU/d (104)	No evidence of rickets in any subject	Rural China

ARR, absolute risk reduction; CI, confidence interval; CT, controlled trial (not randomized); RCT, randomized controlled trial; RR, relative risk; RT, randomized trial (no control group).

mends maintaining the level above 20 ng/mL to prevent rickets. The PES also recommends

that breastfed infants receive 400 IU of vitamin D daily starting at birth.<sup>4</sup>

JFP

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