

ALLERGY, VITAMINS

# REFUTATION OF THE VITAMIN D HYPOTHESIS?

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A new epidemiological study arguments against vitamin D inducing later allergy (Parr et al., Vitamin A and D intake in pregnancy, infant supplementation, and asthma development: the Norwegian Mother and Child Cohort, *Am J Clin Nutr* 2018;107:789-798). Table 5 in the most recent paper shows no effect when correlating first year of life supplementation and later asthma.

**TABLE 5**  
Infant supplement use in the first 6 mo and crude and adjusted RR estimates (95% CIs) for current asthma at age 7 y<sup>1</sup>

	Cases/total <i>n</i>	Prevalence, %	Crude RR <sup>2</sup>	Crude RR <sup>3</sup>	Adjusted RR <sup>3,4</sup>
Cod liver oil					
No	1095/25,365	4.3	1 (ref)	1 (ref)	1 (ref)
Sometimes	428/11,579	3.7	0.86 (0.77, 0.96)	0.86 (0.77, 0.97)	0.91 (0.81, 1.02)
Daily	721/18,198	4.0	0.92 (0.84, 1.01)	0.92 (0.84, 1.01)	0.97 (0.87, 1.09)
Vitamin D only					
No	1617/39,343	4.1	1 (ref)	1 (ref)	1 (ref)
Sometimes	152/3746	4.1	0.99 (0.84, 1.16)	1.02 (0.87, 1.19)	1.05 (0.89, 1.23)
Daily	475/12,053	3.9	0.96 (0.87, 1.06)	0.99 (0.90, 1.10)	0.97 (0.86, 1.09)
Multivitamins					
No	2008/50,363	4.0	1 (ref)	1 (ref)	1 (ref)
Sometimes	81/2129	3.8	0.95 (0.77, 1.19)	0.97 (0.78, 1.21)	0.88 (0.71, 1.10)
Daily	155/2650	5.9	1.47 (1.25, 1.72)	1.45 (1.24, 1.70)	1.19 (1.01, 1.41)
Combined use (sometimes/daily)					
Neither category	410/9397	4.3	1 (ref)	1 (ref)	1 (ref)
Cod liver oil only	936/24,545	3.8	0.89 (0.80, 1.00)	0.90 (0.80, 1.01)	0.97 (0.86, 1.09)
Vitamin D only	524/12,978	4.0	0.95 (0.83, 1.08)	0.97 (0.85, 1.10)	1.00 (0.88, 1.15)
Multivitamin only	149/2493	6.0	1.40 (1.16, 1.69)	1.39 (1.15, 1.67)	1.19 (0.98, 1.43)
Any vitamin D supplement and multivitamin	108/2541	4.3	1.00 (0.81, 1.23)	1.03 (0.84, 1.27)	0.94 (0.76, 1.15)
Multiple vitamin D supplements	126/3188	4.0	0.93 (0.76, 1.13)	0.99 (0.81, 1.21)	1.02 (0.83, 1.26)

But why did they authors not even cite our study from 2004 (Hyppönen et al. Infant Vitamin D Supplementation and Allergic Conditions in Adulthood Northern Finland Birth Cohort 1966. *Ann. N.Y. Acad. Sci.* 1037: 84-95) ??

**TABLE 2. Prevalence of allergy and asthma at age 31 by the use of vitamin D supplements and suspected rickets in infancy**

	Number of participants with information on atopy/allergic rhinitis and asthma <sup>a</sup>	Atopy Cases (%)	Allergic rhinitis Cases (%)	Asthma Cases (%)
Use of vitamin D				
None	9/20	3 (33)	3 (15)	0 (0)
Irregularly	576/880	129 (22)	198 (22)	47 (5.2)
Regularly	4422/6748	1407 (32)	1974 (29)	470 (7.0)
Dose of Vitamin D <sup>b</sup>				
<2000 IU	29/55	9 (31)	13 (24)	1 (1.8)
2000 IU	4174/6350	1340 (32)	1847 (29)	444 (7.0)
>2000 IU	197 /317	49 (25)	102 (32)	23 (7.3)
Suspected rickets				
No	4921/7505	1518 (31)	2141 (29)	509 (6.8)
Yes	86/143	18 (21)	31 (22)	8 (5.6)

<sup>a</sup>Information on atopy available from the subsample invited to the clinical examination; data on allergic rhinitis and asthma obtained from questionnaire survey addressed to the whole cohort.

<sup>b</sup>Restricted to children receiving vitamin D supplementation regularly.

Although our interest was more with allergy there have been clear effects on asthma that have been confirmed now two dozen times. Why did the authors miss that effect?

- The cohort consists of 115,000 children but only 55,000 are analyzed. So selection bias is omnipresent.
- A key issue is the definition of “asthma” as “having  $\geq 2$  pharmacy dispensations of asthma medication within a 12-month interval, which is more a “last resort” option than a correct diagnosis. “We cannot rule out some misclassification in our asthma outcome cation in our asthma outcome”. I agree.
- Another issue is the unrecorded vitamin supply by standard baby food in the range of 500-1000 IU/daily. Does it make any sense to test for excess supplements in a population that is already heavily exposed to >90%? “A limitation of this study is that we did not have data on nutrient intake from supplements in infant”. I agree, it makes the study worthless.
- The supplementation with cod liver oil, vitamin D and multivitamins is chaotic as been shown in the last row of table 5. In real life or just in this paper? Numbers are contradicting “Vitamin D only, sometimes” and “daily” do not add to the number given for “vitamin D only” in the “combined use” section.
- Supplementation at month 6 is even a late event if we believe that the first allergen contact under vitamin D exposure is being important.

So, still not need to drop the vitamin D hypothesis.