## VITAMIN A SUPPLEMENTATION FOR PREVENTION OF BRONCHOPULMONARY DYSPLASIA

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# Vitamin A

- Involved in the regulation of lung development and injury repair.
- Low levels associated with increased BPD.



Shenai, Jayant P., Frank Chytil, Mildred T. Stahlman. "Vitamin A status of neonates with bronchopulmonary dysplasia." Pediatric research 19.2 (1985)
Tyson, Jon E., et al. "Vitamin A supplementation for extremely-low-birth-weight infants." New England journal of medicine 340.25 (1999): 1962-1968.

### Vitamin A supplementation to prevent mortality and shortand long-term morbidity in very low birthweight infants (Review)

Darlow BA, Graham PJ



Darlow, Brian A., and P. J. Graham. "Vitamin A supplementation to prevent mortality and short-and long-term morbidity in very low birthweight infants." *The Cochrane Library* (2011).

## Analysis I.2. Comparison I Supplemental vitamin A vs no supplementation, Outcome 2 Chronic lung disease (oxygen use at 1 month in survivors).



# Analysis 1.5. Comparison I Supplemental vitamin A vs no supplementation, Outcome 5 Chronic lung disease (oxygen use at 36 weeks' postmenstrual age in survivors).

Study or subgroup	Vitamin A	Control		Risk	Ratio	Weight	Risk Ratio
	n/N	n/N		M-H,Fixed,9	95% CI	1.0000000 Broot	M-H,Fixed,95% CI
I Supplementation via intramu	scular injection						
Ravishankar 2003	4/17	5/14	+			2.3 %	0.66 [ 0.22, 2.00 ]
Tyson 1999	163/346	193/347				81.4 %	0.85 [ 0.73, 0.98 ]
Subtotal (95% CI)	363	361		-		83.7 %	0.84 [ 0.73, 0.97 ]
Total events: 167 (Vitamin A),	198 (Control)						
Heterogeneity: Chi <sup>2</sup> = 0.19, df	= I (P = 0.66); I <sup>2</sup> = 0	0.0%					
Test for overall effect: $Z = 2.33$	3 (P = 0.020)						
2 Supplementation via oral rou	ıte						
Wardle 2001	40/52	37/48		× •	-	16.3 %	1.00 [ 0.81, 1.24 ]
Subtotal (95% CI)	52	48		-		16.3 %	1.00 [ 0.81, 1.24 ]
Total events: 40 (Vitamin A), 3	7 (Control)						
Heterogeneity: not applicable							
Test for overall effect: $Z = 0.02$	2 (P = 0.98)						
Total (95% CI)	415	409		-		100.0 %	0.87 [ 0.77, 0.98 ]
Total events: 207 (Vitamin A),	235 (Control)						
Heterogeneity: Chi <sup>2</sup> = 1.98, df	= 2 (P = 0.37); I <sup>2</sup> = 0	).0%					
Test for overall effect: $Z = 2.23$	3 (P = 0.026)						
Test for subgroup differences: (	$Chi^2 = 1.66, df = 1$ (F	P = 0.20), I <sup>2</sup> =40%					
	-		Т		D 34		
			0.5	0.7 1	1.5 2		
			Favours \	Vitamin A	Favours control		

### Vitamin A Supplementation for Extremely Low Birth Weight Infants: Outcome at 18 to 22 Months

Outcome*	Vitamin A Group	Control Group	Adjusted RR Vitamin A Versus Control (95% CI)†	P Value‡
Death, $n/N$ (%)	73/405 (18)	76/402 (19)	0.95 (0.69-1.28)	.8
NDI in survivors, $n/N$ (%)	117/272 (43)	128/266 (48)	0.90 (0.73-1.08)	.3
NDI/death, n/N (%)	190/345 (55)	204/342 (60)	0.94 (0.80-1.07)	.3

TABLE 2. NDI or Death Among Vitamin A Trial Participants by Treatment Group

→ Long-term follow-up of infants at 18–22 months could not demonstrate any improvement in mortality, neurodevelopmental impairment, or respiratory outcomes from treatment with Vitamin A.

## Vitamin A supplementation to prevent mortality and shortand long-term morbidity in very low birthweight infants (Review)

**Conclusion**: Whether clinicians decide to utilize repeat intramuscular doses of vitamin A to prevent chronic lung disease may depend upon the local incidence of this outcome and the value attached to achieving a modest reduction in this outcome, balanced against the lack of other proven benefits and the acceptability of treatment. Information on long-term neurodevelopmental status suggests no evidence of either benefit or harm from the intervention.

#### Vitamin A Status After Prophylactic Intramuscular Vitamin A Supplementation in Extremely Low Birth Weight Infants

Table 2. Clinical Outcome of Extremely Low Birth Weight Infants in the Vitamin A–Supplemented (VAS) and Unsupplemented (No-VAS) Groups.

Characteristics	VAS	No-VAS	P Value
BPD, No. (%)	15 (42.8)	15 (46.8)	.80
Died <36 wk GA, No. (%)	1 (2.8)	2 (6.2)	.60
Died at any time, No. (%)	2 (5.7)	3 (9.3)	.30

## The Effect of the National Shortage of Vitamin A on Death or Chronic Lung Disease in Extremely Low-Birth-Weight Infants

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective cohort study of 7925 infants with birth weights between 401 and 1000 g who were cared for in US neonatal intensive care units managed by the Pediatrix Medical Group. Infants were discharged between January 1, 2010,



Tolia, Veeral N., et al. "The effect of the national shortage of vitamin A on death or chronic lung disease in extremely low-birth-weight infants." *JAMA pediatrics* 168.11 (2014): 1039-1044.

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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**CONCLUSIONS AND RELEVANCE** The occurrence of death or chronic lung disease appears unaffected by the recent shortage of vitamin A. However, the center of birth appears to be an important risk factor for these infants' outcomes.

Tolia, Veeral N., et al. "The effect of the national shortage of vitamin A on death or chronic lung disease in extremely low-birth-weight infants." *JAMA pediatrics* 168.11 (2014): 1039-1044.

## Vitamin A Supplementation for Prevention of Bronchopulmonary Dysplasia: Cornerstone of Care or Futile Therapy?

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### Catherine A. Gawronski, PharmD Candidate<sup>1</sup>, and Kristen M. Gawronski, PharmD<sup>2</sup>

This large observational evaluation calls into question the place of vitamin A in BPD prevention. **Conclusions:** VAS has been identified as a strategy to decrease the incidence of BPD. Initial large-scale prospective evaluations have shown clear benefit of VAS in reducing the incidence of CLD or death. However, changing definitions of BPD and implementation of noninvasive

Gawronski, Catherine A., and Kristen M. Gawronski. "Vitamin A Supplementation for Prevention of Bronchopulmonary Dysplasia Cornerstone of Care or Futile Therapy?." *Annals of Pharmacotherapy* (2016): 1060028016647066.

# Route & dosage

- Mostly IM.
- 2000 IU IM every other day for 28 days.
- 5000 IU IM 3 times weekly for 4 weeks.

Gawronski, Catherine A., and Kristen M. Gawronski. "Vitamin A Supplementation for Prevention of Bronchopulmonary Dysplasia Cornerstone of Care or Futile Therapy?." *Annals of Pharmacotherapy* (2016): 1060028016647066.

# Conclusions

- BPD still remains a very important complication of neonatal intensive care.
- Vitamin A have been shown to reduce the incidence of BPD.
- Little is known about the optimal intake or the mode of VA delivery in preterm infants, especially in ELBW babies.