

# Dr. Susan Carlson

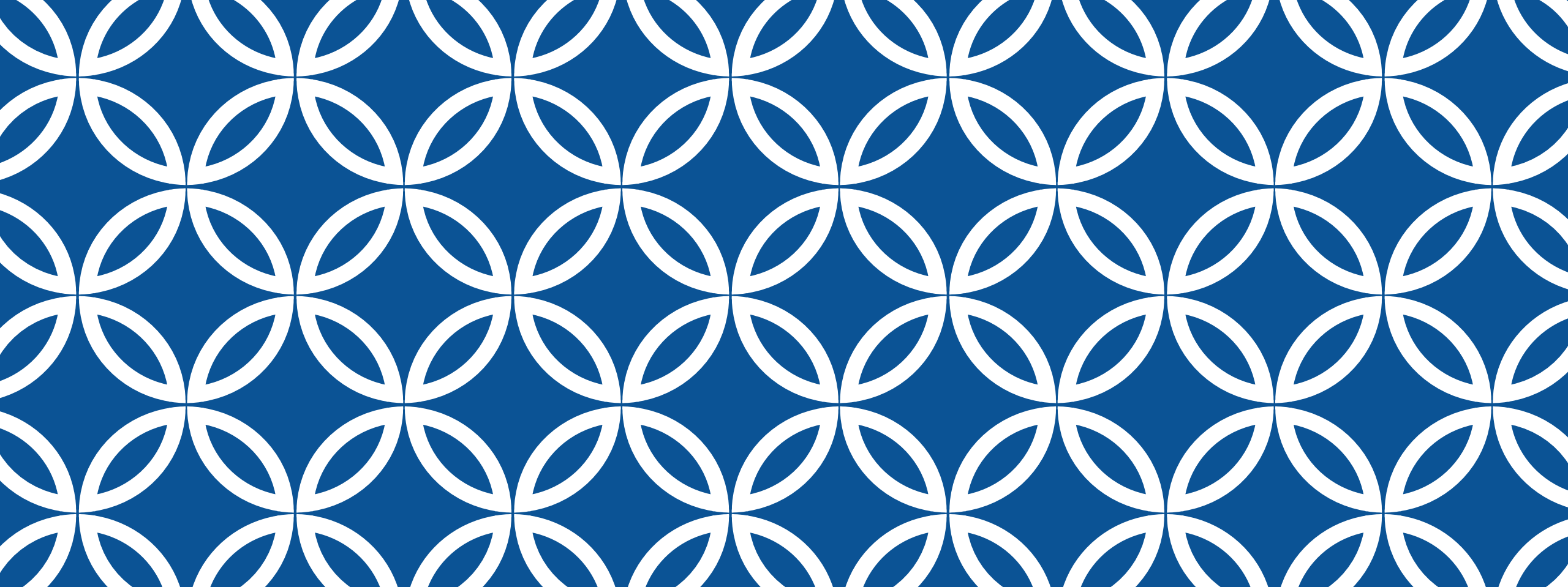
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**A CONSEQUENCE OF THE DHA  
INTAKE GAP IN US PREGNANCIES:**

**Preterm Birth**

# US Dietary DHA Intake Is Low

|                              | <b>Recommended<br/>Daily DHA Intake*</b> | <b>Average Daily<br/>DHA Intake</b> |
|------------------------------|--|-------------------------------------|
| Pregnant/<br>Lactating Women | 300 mg                                   | 54 mg                               |
| Adult Women                  | 220 mg                                   | 61 mg                               |
| Adult Men                    | 220 mg                                   | 78 mg                               |

\*Expert panel convened by NIH/ISSFAL.  
Simopoulos AP, et al. *J Am Coll Nutr.* 1999;18:487-489.  
Benisek D, et al. *J Am Coll Nutr.* 1999;18:543-544.  
Benisek D, et al. *Obstet Gynecol.* 2000;95:77S-78S.

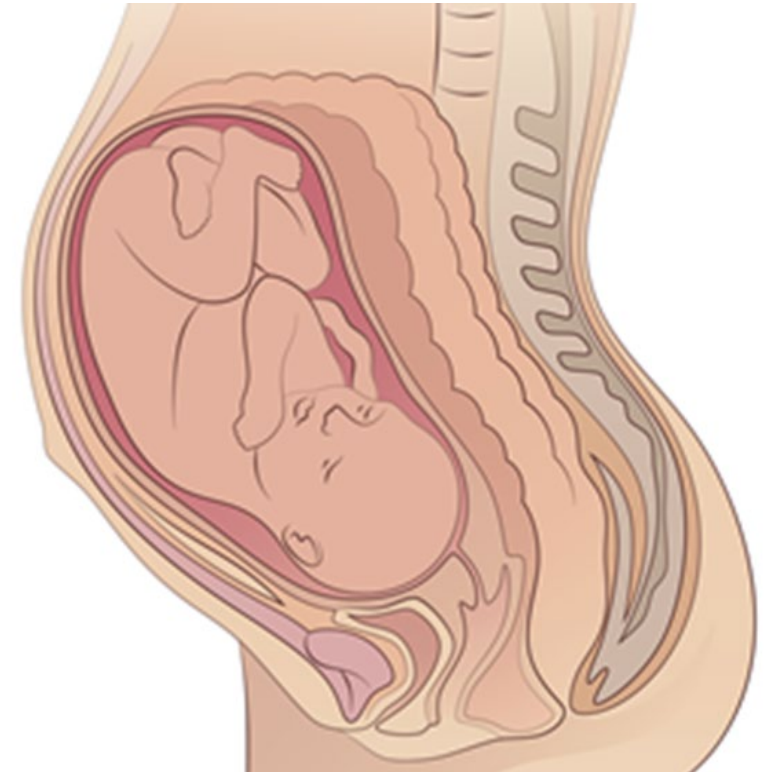
# AAP AND AMA ADVOCACY FOR IMPROVING NUTRITION IN THE FIRST 1000 DAYS TO SUPPORT CHILDHOOD DEVELOPMENT AND ADULT HEALTH

Prenatal maternal nutrition during first 1000 days includes:

- Protein
- Zinc\*
- Iron\*
- Choline\*
- Folate\*
- Copper\*
- Iodine\*
- Vitamins A, D, B<sub>6</sub>, and B<sub>12</sub>
- **Long-chain polyunsaturated fatty acids (DHA)\***

Supported by

- American Medical Association (AMA)
- American Pregnancy Association (APA)
- Academy of Nutrition and Dietetics



<http://americanpregnancy.org/pregnancy-health/prenatal-vitamin-ingredients/>

Schwarzenberg et.al, Pediatrics. 2018 Feb;141(2)

<https://www.ama-assn.org/delivering-care/public-health/ama-backs-global-health-experts-calling-infertility-disease>

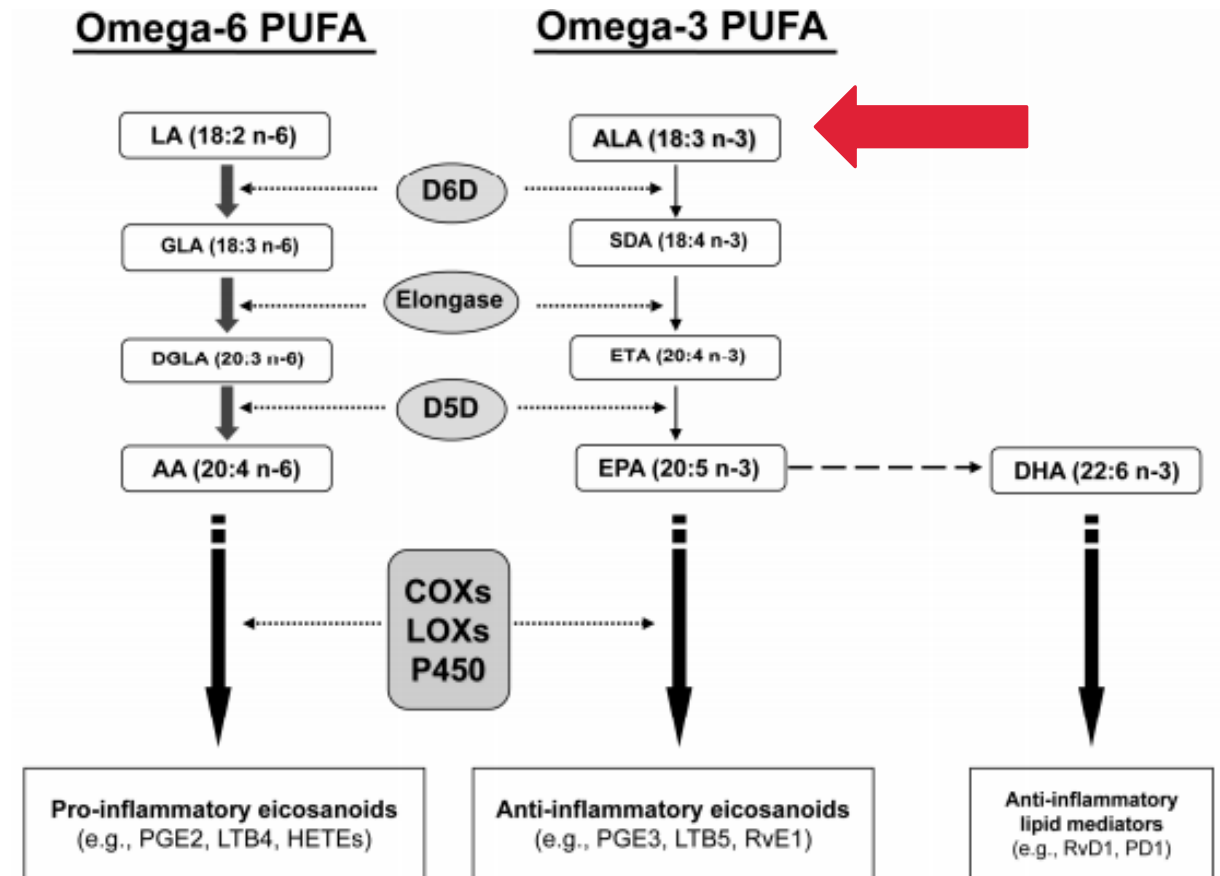
[https://jandonline.org/article/S2212-2672\(14\)00501-2/pdf](https://jandonline.org/article/S2212-2672(14)00501-2/pdf)

Schwarzenberg and Georgieff, Pediatrics 2018; 141/Issue 2

From the American Academy of Pediatrics, Policy Statement

# NO OFFICIAL US REQUIREMENT FOR DHA

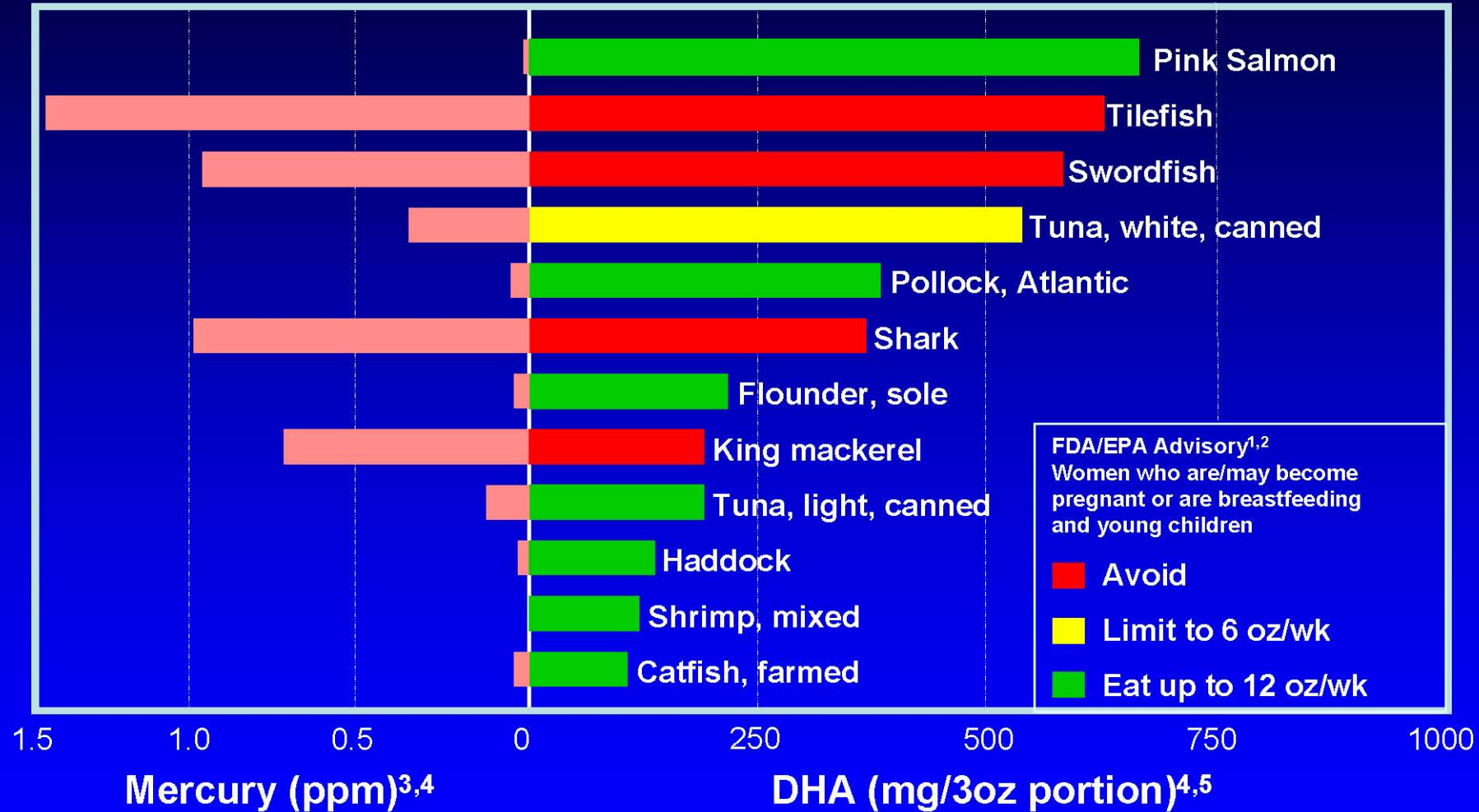
- Biochemical pathway to synthesize
- National Academy of Medicine does not recognize DHA as an essential nutrient at any stage of the life cycle



## DHA Dietary Sources: Fatty Fish, Meat, Eggs

| Food                                  | DHA (mg) |
|---------------------------------------|----------|
| 3 oz pink salmon filet, baked/broiled | 638      |
| 3 oz white tuna, canned in water      | 535      |
| 3 oz smoked salmon (lox)              | 227      |
| 3 oz crab, steamed                    | 196      |
| 12 large shrimp, steamed              | 96       |
| 3 oz tuna salad                       | 47       |
| 2 pieces chicken, fried               | 37       |
| 1 large egg, hard-boiled              | 19       |

# DHA and Mercury Levels in Selected Fish and Shellfish



1. <http://fda.gov/bbs/topics/NEWS/2006/NEW01382.html>. Accessed May 8, 2007; 2. <http://www.cfsan.fda.gov/~dms/admehg3.html>. Accessed May 8, 2007; 3. EPA Mercury Levels in Commercial Fish and Shellfish. [www.cfsan.fda.gov/~frf/sea-mehg.html](http://www.cfsan.fda.gov/~frf/sea-mehg.html). Accessed February 28, 2007; 4. Institute of Medicine. <http://www.iom.edu/CMS/3788/23788/37679/37686.aspx>. Accessed February 20, 2007; 5. USDA National Nutrient Database. [www.ars.usda.gov/ba/bhnrc/ndl](http://www.ars.usda.gov/ba/bhnrc/ndl). Accessed February 28, 2007.

## First Studies to Suggest Omega-3 LCPUFA Reduce Early Preterm Birth (<34 weeks gestation)

| Trial                 | N    | DHA / EPA (g) | Subject selection  | Delivery < 34 wks (Cont vs. Supp) |
|-----------------------|------|---------------|--|-----------------------------------|
| Bulstra-Ramakers 1994 | 64   | 0 / 3.0       | IUGR +/- PIH in a previous pregnancy                       | 19.3 vs. 9.4                      |
| Olsen 2000            | 797  | 0.9 / 1.3     | Twins, preterm delivery, IUGR, PIH in a previous pregnancy | 14.9 vs. 10.6                     |
| Makrides 2010         | 2399 | 0.8 / 0.1     | Healthy women carrying singleton                           | 2.25 vs. 1.09                     |
| Carlson 2013          | 301  | 0.6 / 0       | Healthy women carrying singleton                           | 4.8 vs. 0.6                       |



*KUDOS: Very Low Birth Weight & Hospitalization*  
(Placebo, n=147; DHA, n=154)

|  | Placebo | DHA<br>600 mg | P-value |
|--|---------|---------------|---------|
| Early preterm birth (<34 wks)*         | 4.8 %   | 0.6 %         | P=0.025 |
| Birth weight <1500 g*                  | 3.4 %   | 0 %           | P=0.026 |
| Neonatal Intensive Care Unit admission | 8.3%    | 10.4%         | NS      |
| Days hospitalized (mean #)**           | 40.8    | 8.9           | P=0.026 |

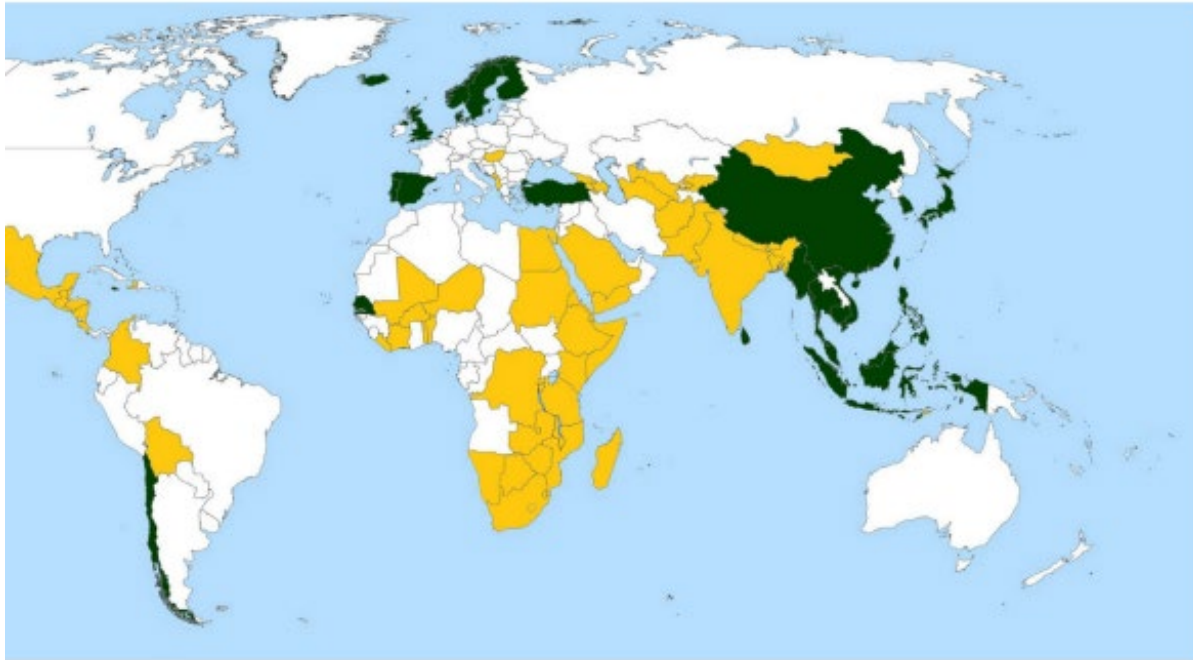
\*One tailed *P* values at  $\alpha=0.05$ ; \*\*if born <37 wks  
*Carlson et al., AJCN 2013*

## Public Health Significance

Evidence from KUDOS Trial (600 mg/d DHA)

- Savings of \$1,652 / dyad with DHA supplementation
- Possible savings to US of up to \$6 billion for hospitalization costs alone with universal supplementation

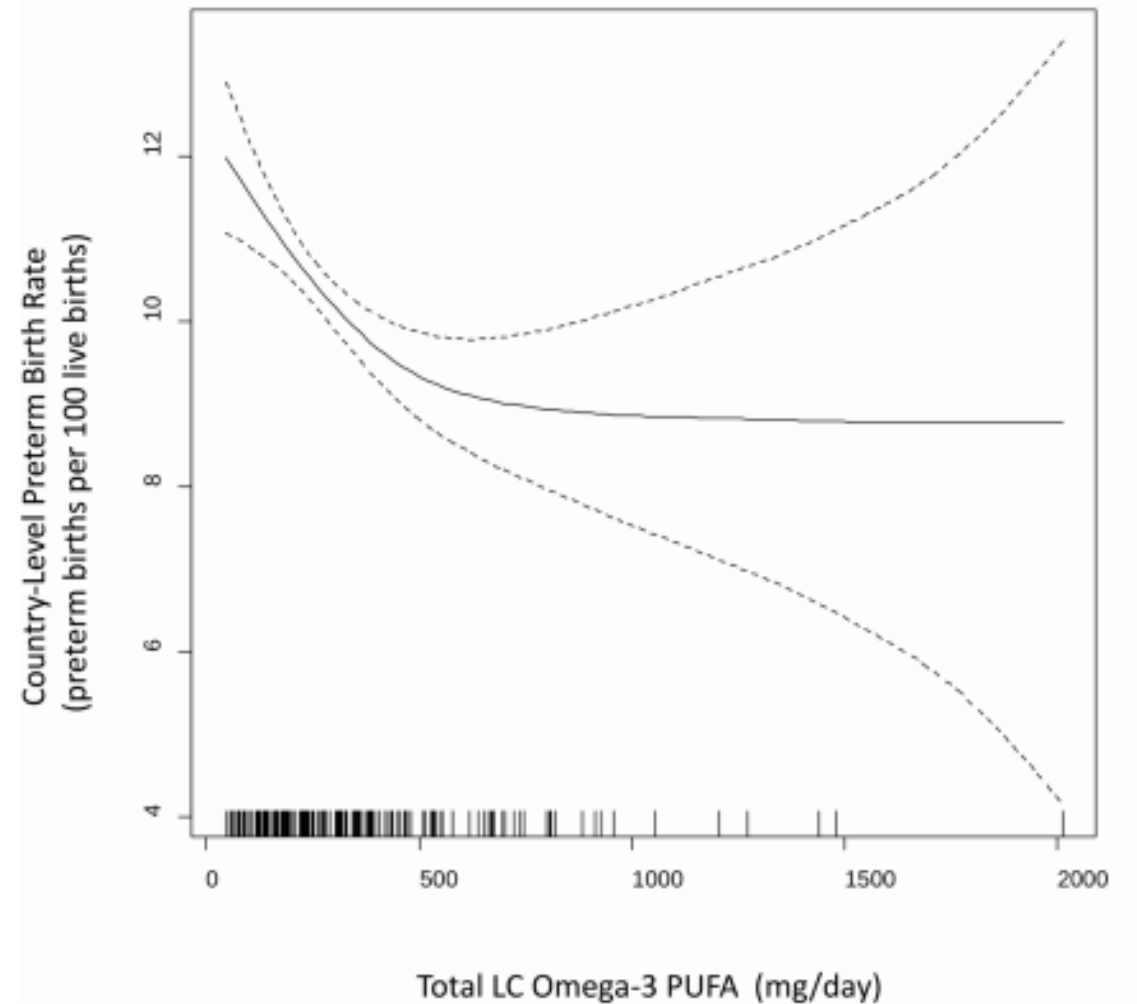
# Correlation of Female Omega-3 LCPUFA Intake and Preterm Birth in 184 Countries: Benefits Found Up to 600 mg/d



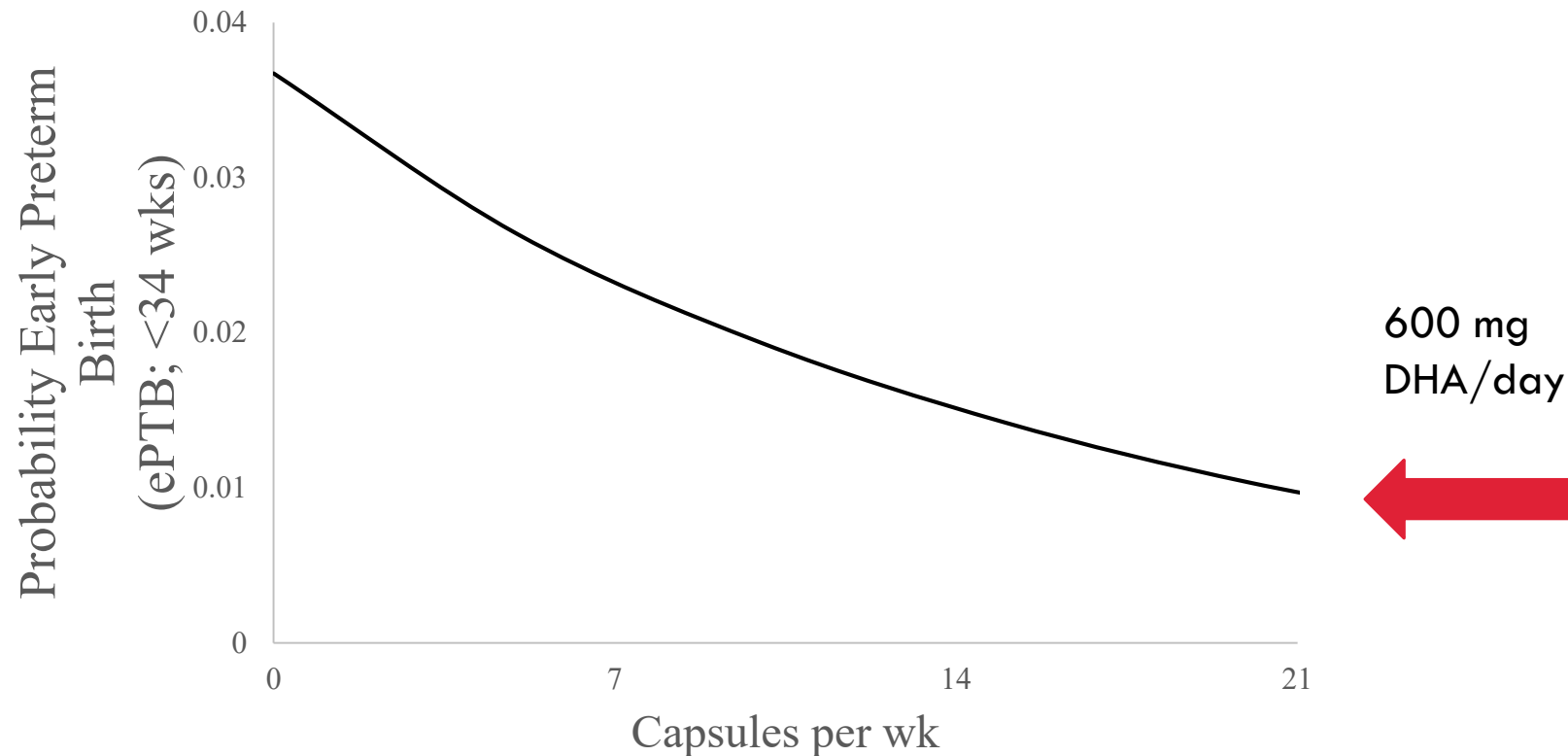
Green: >600 mg/d omega-3 LCPUFA

Gold: <217 mg/d

White: 217-600 mg/d



## How Much Omega-3 Supplementation is Needed to Reduce Early Preterm Birth? Weekly Capsule Intake (200 mg DHA/capsule)



# OMEGA-3 FATTY ACIDS SUPPLEMENTATION DURING PREGNANCY: WHAT IS THE EVIDENCE FOR BENEFIT?

State of the art evidence from the November 2018 Cochrane Review

70 RCTs involving 19,927 women

Compared omega-3 interventions (supplements or food)  
with placebo

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018

# PRETERM BIRTH: OMEGA-3 VS NONE

<37 weeks: 27 RCTs, 10,304 participants

*High quality evidence for an 11% reduction\**

<34 weeks: 9 RCTs, 5204 participants

*High quality evidence for a 42% reduction*

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018

# OTHER EFFECTS OF OMEGA-3 FATTY ACID INTAKE ON PREGNANCY OUTCOME

## Low birth weight (<2500 g)

- 15 RCT, 8449 participants
- *High quality evidence* for a 10% reduction

Makrides 2018: ORIP (n=5544), NEJM Sept 2019

Carlson 2018: Recruiting for ADORE 200 vs 1000 mg (n=950 of 1250)

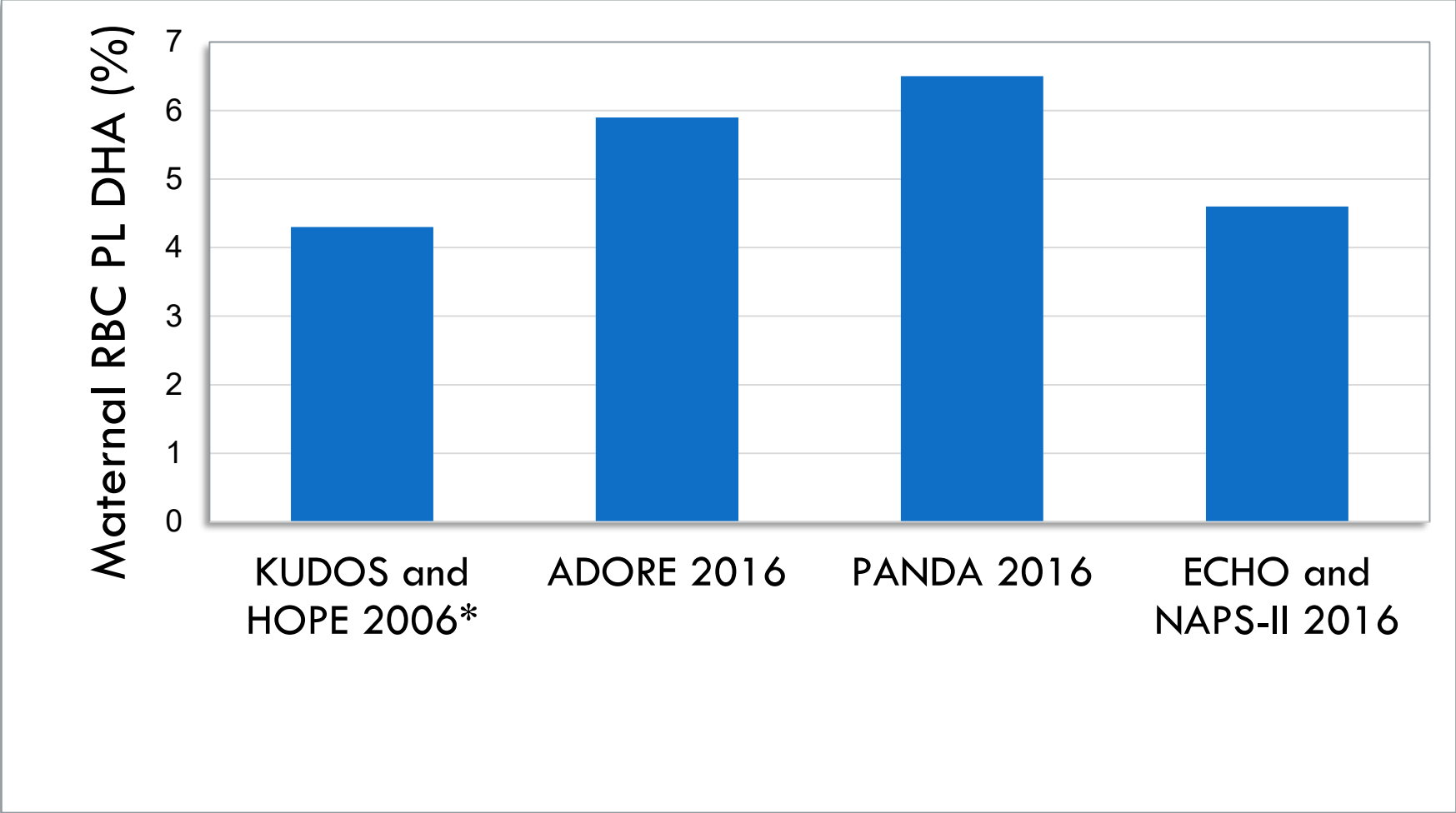
- 10 RCTs, 7026 participants
- *Moderate quality evidence* for a 25% reduction

## NICU admissions:

- 9 RCTs, 6920 participants.
- *Moderate quality evidence* for an 8% reduction

Middleton et al., Omega-3 fatty acid supplementation during pregnancy, Cochrane Review 2018

# Pregnancy RBC PL DHA at Baseline



\*Gustafson KM et al., PLEFA 2013; 88: 331; Carlson SE et al., AJCN 2013; 97:808



# SUMMARY

- Very low DHA intakes are associated with an increased risk of the most costly and devastating early births – those before 34 weeks gestation
- The 2018 Cochrane Review demonstrates strong evidence for increasing DHA intake to reduce preterm birth with most benefit for births before 34 weeks gestation
- The authors suggest a need for >500 mg/day based on their analysis of the literature
- A trial reported last week in NEJM found a 16% decrease in preterm birth (<37 weeks), but no decrease in birth before 34 weeks
- Does not refute the Cochrane Review finding that DHA can reduce early preterm and preterm birth
- DHA is a nutrient, and prenatal supplements containing DHA are now widely used in both the US and Australis such that women may be entering pregnancy with improved DHA status compared to 2006