# Using Nutrition Science to Reduce Perinatal Health Disparities

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# Poverty = Stress = Health Disparities

# Chronic Stress

# Unpredictable stress


# Discrimination stress

# Stress effects and health disparities appear early in life

# Prenatal stress effects on the offspring

# Prenatal Programming

# Developmental Origins of Health and Disease

High levels of maternal gluccocortcoids, transported from the maternal compartment to the fetal compartment via the placenta, are believed to be the primary mechanism by which prenatal stress affects the offspring by altering the fetal stress architecture

# Pregnant Black American women living in poverty

- Higher exposure to chronic stress (Evans, 2003)
- Higher rates of adverse birth outcomes (Giscombe & Lobel, 2005)
- Higher risk of poor nutrition (Fowles & Gabrielson, 2005)
- Offspring are more likely to evidence deficits in attention, behavior and emotion regulation

# Nutritional Interventions and brain functioning

- Folic acid supplementation during pregnancy reduces risk of neural tube defects (Locksmith & Duff, 1998)
- Phenylalanine-restricted diet prevents mental retardation in individuals with phenylketonuria (PKU) (National Institutes of Health Consensus Development Panel, 2001)
- Iron supplementation improves cognitive and behavioral functioning prospectively among iron deficient children and adolescents (Lozoff, 2007)

# Omega-3 PUFAs and the brain

- The accumulation of fatty acids in cell membranes is almost entirely dependent on the amount of fatty acids in the diet.
- Fatty acids affect receptor function, neurotransmitter uptake, and signal transmission
- The most prominent omega-3 PUFA in the brain is DHA
- Fish oil is the primary source of DHA

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# Nutrition and Pregnancy Study

NAPS
Nutrition and Pregnancy Study

# Prevention of mental disorders in children

High levels of maternal stress exposure prenatally

Suboptimal modulation of maternal stress response

Pregnancy health

Alterations in fetal stress architecture

Suboptimal modulation of infant stress response

# Impact of omega-3 supplementation during pregnancy on maternal stress and infant outcome

R21 HD 058269

- 66 women recruited at 16-21 weeks gestation
- African American and Medicaid recipient
- <2 servings of sea fish per week
- Randomly assigned to 450 mg DHA or placebo in a 2:1 ratio
- Exclusion criteria: steroid use, gestational diabetes, pre-eclampsia, BMI > 40

*Original Research*

# Association Between Fatty Acid Supplementation and Prenatal Stress in African Americans

## *A Randomized Controlled Trial*

*Kate Keenan, PhD, Alison E. Hipwell, PhD, Jenna Bortner, BA, Amy Hoffmann, BA, and Rose McAloon, BA*

**OBJECTIVE:** To test the association between docosahexaenoic acid (DHA) supplementation and perceived stress and cortisol response to a stressor during pregnancy in a sample of African American women living in low-income environments.

**METHODS:** Sixty-four African American women were enrolled at 16–21 weeks of gestation. Power calculations were computed using published standard deviations for the Perceived Stress Scale and the Trier Social Stress Test. Participants were randomized to either 450 mg per day of DHA (n=43) or placebo (n=21). At baseline and at 24 and 30 weeks of gestation, perceived stress was assessed by self-report. Cortisol response to a controlled stressor, the Trier Social Stress Test was measured from saliva samples collected upon arrival to the laboratory and after the completion of the Trier Social Stress Test.

**RESULTS:** Women in the DHA supplementation group reported lower levels of perceived stress at 30 weeks of gestation, controlling for depression and negative life events (mean 27.4 compared with 29.5, $F$ [3, 47] 5.06, $P$=.029, Cohen's d=0.65). Women in the DHA supplementation had lower cortisol output in response to arriving to the laboratory and a more modulated response to the stressor ($F$ [1.78, 83.85] 6.24, $P$=.004, Cohen's d=0.76).

**CONCLUSION:** Pregnant women living in urban low-income environments who received DHA reported reduced perceived stress and lower levels of stress hormones in the third trimester. Docosahexaenoic acid supplementation may be a method for attenuating the effects of maternal stress during late pregnancy and improving the uterine environment with regard to fetal exposure to glucocorticoids.

**CLINICAL TRIAL REGISTRATION:** ClinicalTrials.gov, www.clinicaltrials.gov, NCT01158976.

(*Obstet Gynecol 2014;124:708–17*)

*DOI: 10.1097/AOG.0000000000000559*

**LEVEL OF EVIDENCE:** I

Consistent with the prenatal programming hypothesis,[1] there is now evidence from multiple studies using a variety of methodologies and across different species that the mother's level of psychosocial stress during pregnancy is significantly associated with suboptimal developmental outcomes in their offspring including disturbances in attention,[2,3] impaired learning and disruption in neurogenesis,[4,5] and increased anxiety-like behaviors.[6] The strength of the causal claim is based on rigorous controlled experiments in which the prenatal effect is distinguished from postnatal effects by using methods such as cross-fostering or nursery rearing. The pattern of findings in humans closely mirrors those from controlled animal studies.[7–9] The strongest candidate for the mechanism by which prenatal stress confers risk to the offspring is the maternal hypothalamic–pituitary–adrenal axis. Prenatal stress causes long-term alterations in the functioning of the offspring's hypothalamic–pituitary–adrenal axis,[10,11] and each of the phenotypic outcomes identified can be linked

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***Financial Disclosure***

*The authors did not report any potential conflicts of interest.*



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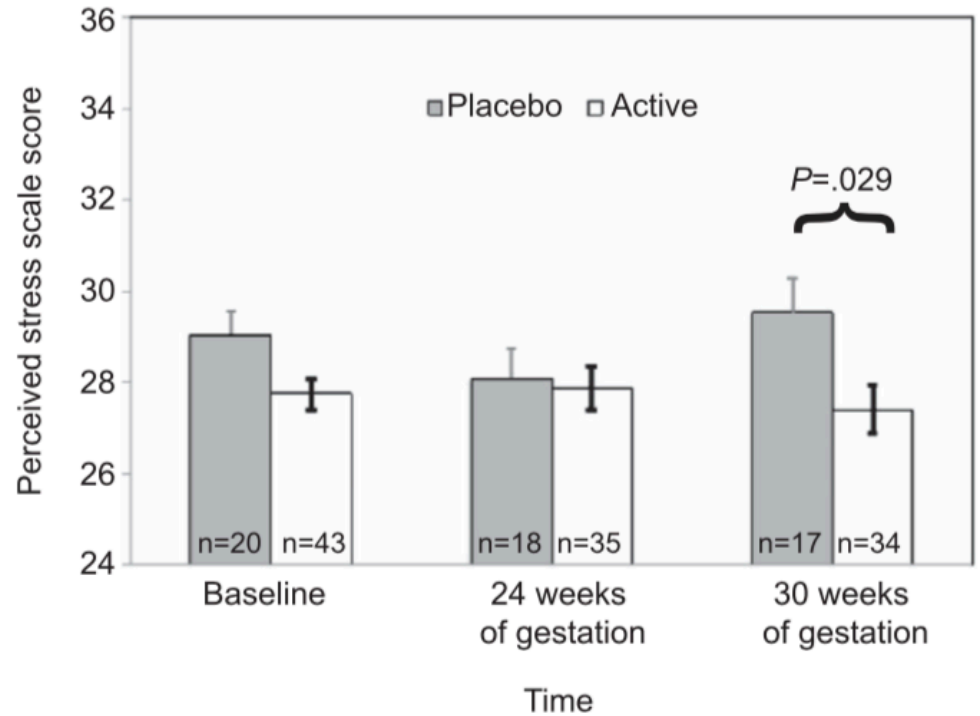



**Fig. 2.** Effect of omega-3 supplementation on perceived stress score, controlling for negative life events and depression scores.

*Keenan. Effects of DHA Supplementation on Prenatal Stress. Obstet Gynecol 2014.*

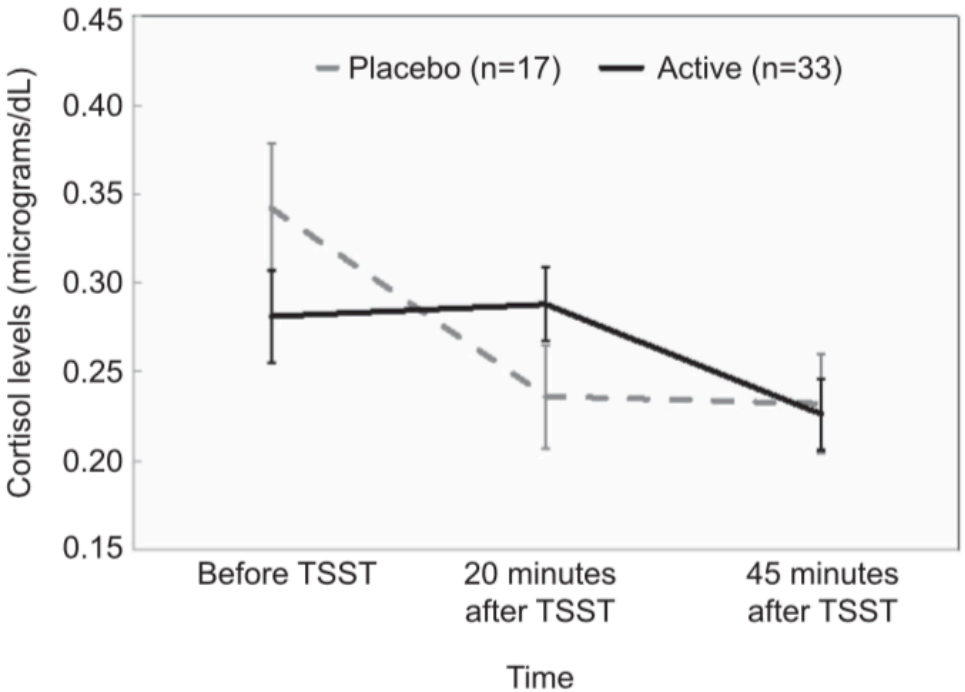



**Fig. 3.** Cortisol levels before and after the Trier Social Stress Test (TSST) at 30 weeks of gestation ($F$ [1.78, 83.85] 6.24, $P$=.004; Cohen's d=0.76); error bars indicate standard error at each time point within each group.

*Keenan. Effects of DHA Supplementation on Prenatal Stress. Obstet Gynecol 2014.*

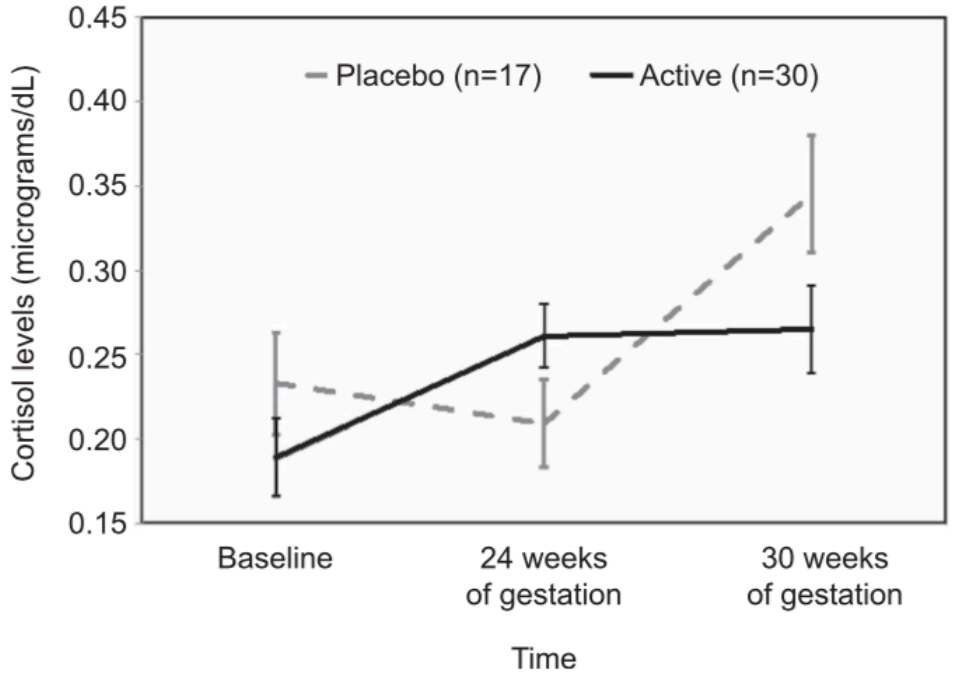
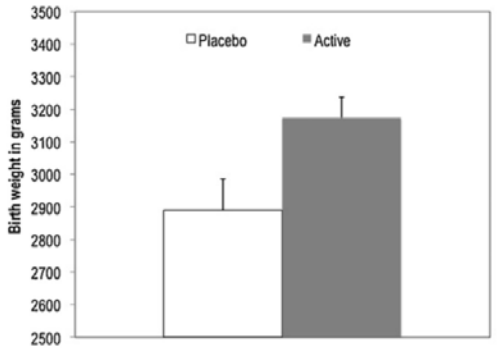


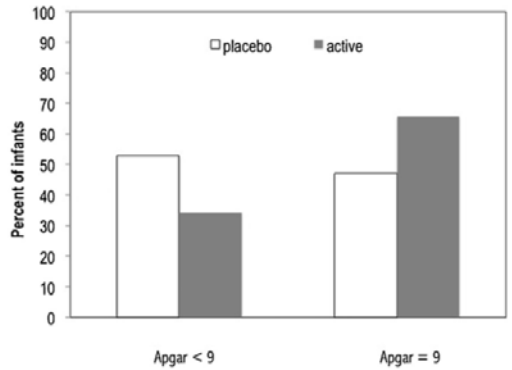

**Fig. 4.** Cortisol levels 20 minutes after arrival to the laboratory at baseline, at 24 weeks of gestation, and at 30 weeks of gestation ($F$ [1.74, 74.63], $P$=.041; Cohen's d=0.56); error bars indicate standard error at each time point within each group.

*Keenan. Effects of DHA Supplementation on Prenatal Stress. Obstet Gynecol 2014.*




*F* (1,40) = 6.09, *p* = .018, cohen's *d* = .77, controlling for gestational age; n for placebo = 13; n for active =30; error bars represent standard error for the mean within each group

**Fig. 2.** *F* (1.40) = 6.09, *p* = 0.018, cohen's *d* = 0.77, controlling for gestational age; n for placebo = 13; n for active = 30; error bars represent standard error for the mean within each group.




*Odds ratio* = 5.99 (95% *CI* = 1.25 – 28.75), *p* = .025, controlling for birth weight and gestational age; n for placebo = 13; n for active = 30

**Fig. 3.** *Odds ratio* = 5.99 (95% *CI* = 1.25–28.75), *p* = 0.025, controlling for birth weight and gestational age; n for placebo = 13; n for active = 30.

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# The effect of prenatal docosahexaenoic acid supplementation on infant outcomes in African American women living in low-income environments: A randomized, controlled trial

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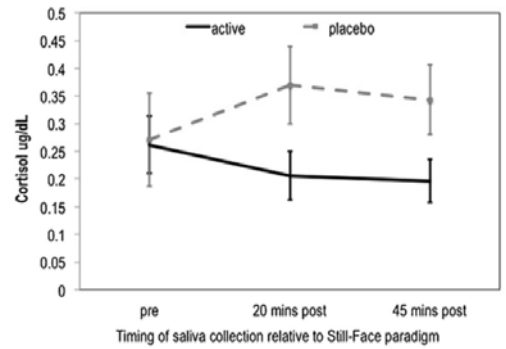


*F* (1, 32) = 5.36, *p* = .027, cohen's *d* = .82, Controlling for time of collection and pre-stressor cortisol levels; error bars represent standard error for the mean within each group at each time point

**Fig. 4.** *F* (1, 32) = 5.36, *p* = 0.027, cohen's *d* = 0.82, Controlling for time of collection and pre-stressor cortisol levels; error bars represent standard error for the mean within each group at each time point.

# Goal: Reduce Perinatal Health Disparities

## Test

- Test differential effects of stress exposure

## Specify

- Specify systems that are impacted

## Characterize

- Characterize patterns of response associated with suboptimal health

## Deploy

- Deploy preventive interventions to modify patterns of response

## Explore

- Explore for whom and in which context