



ECHO

Environmental influences
on Child Health Outcomes

A program supported by the NIH

Incorporating Early Life Micronutrient Status in ECHO studies of Neurodevelopment

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Discussant: Nicole Talge, PhD

ECHO DISCOVERY Jan 14, 2026

Site 129: Child Health Advances *from Research with Mothers*

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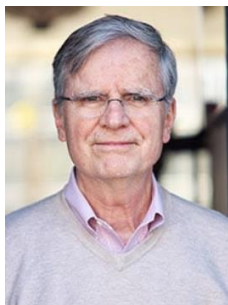
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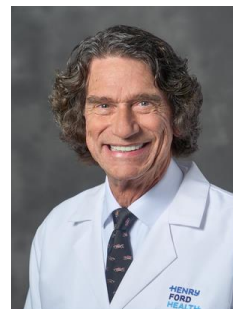
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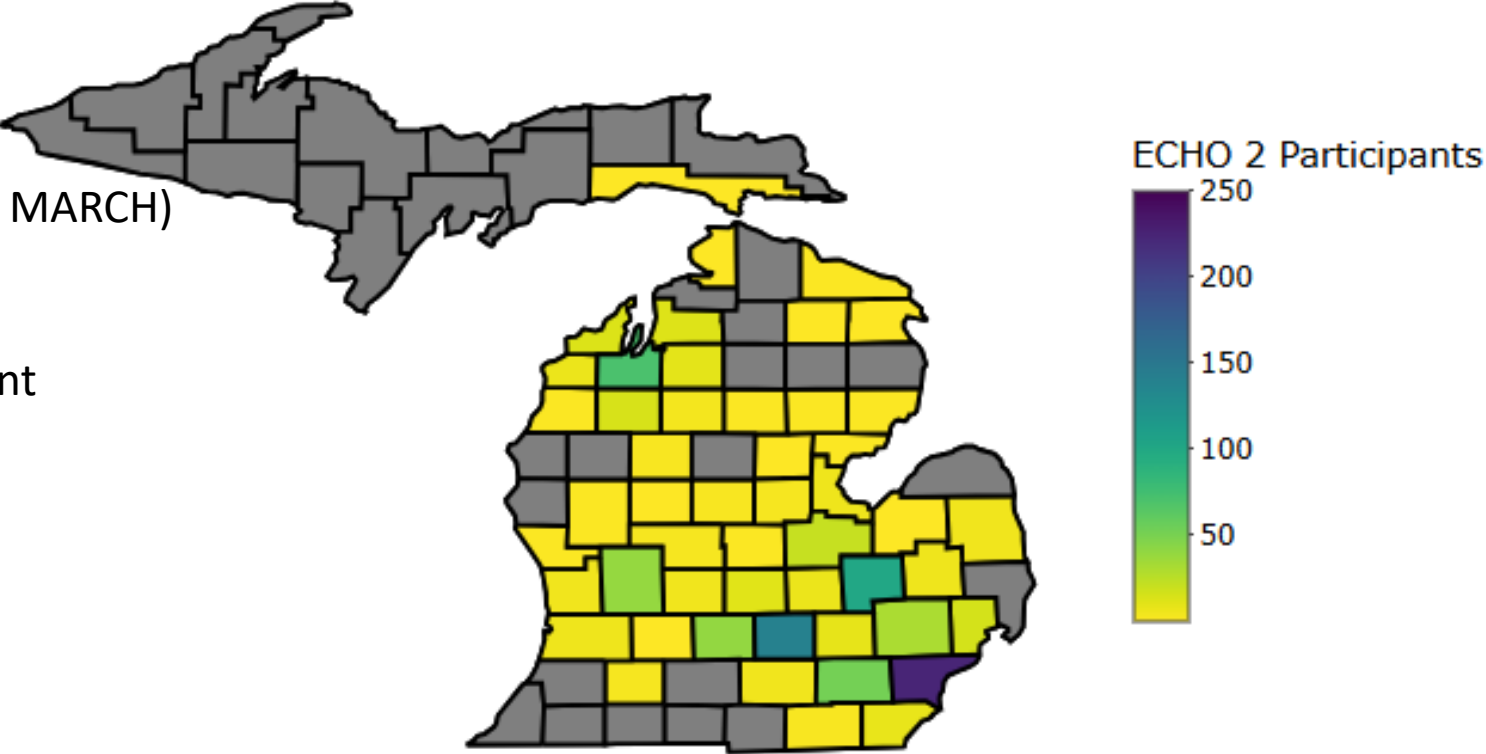
Fichorova
Brigham & Women's



Statewide ECHO Child Enrollment

ECHO Enrollment Includes:

- Two extant cohorts (ARCH & MARCH)
- 12 total delivery hospitals
- 22 total prenatal clinics
- ECHO-2 pregnancy enrollment continues in:
 - Rural Traverse City
 - Flint
 - Detroit



Under 1	12-23 Mo	24-35 Mo	3 to 5	6 to 11	11 to 17	Total	Other Than Non-Hispanic White
121	65	62	203	513	241	1217	590

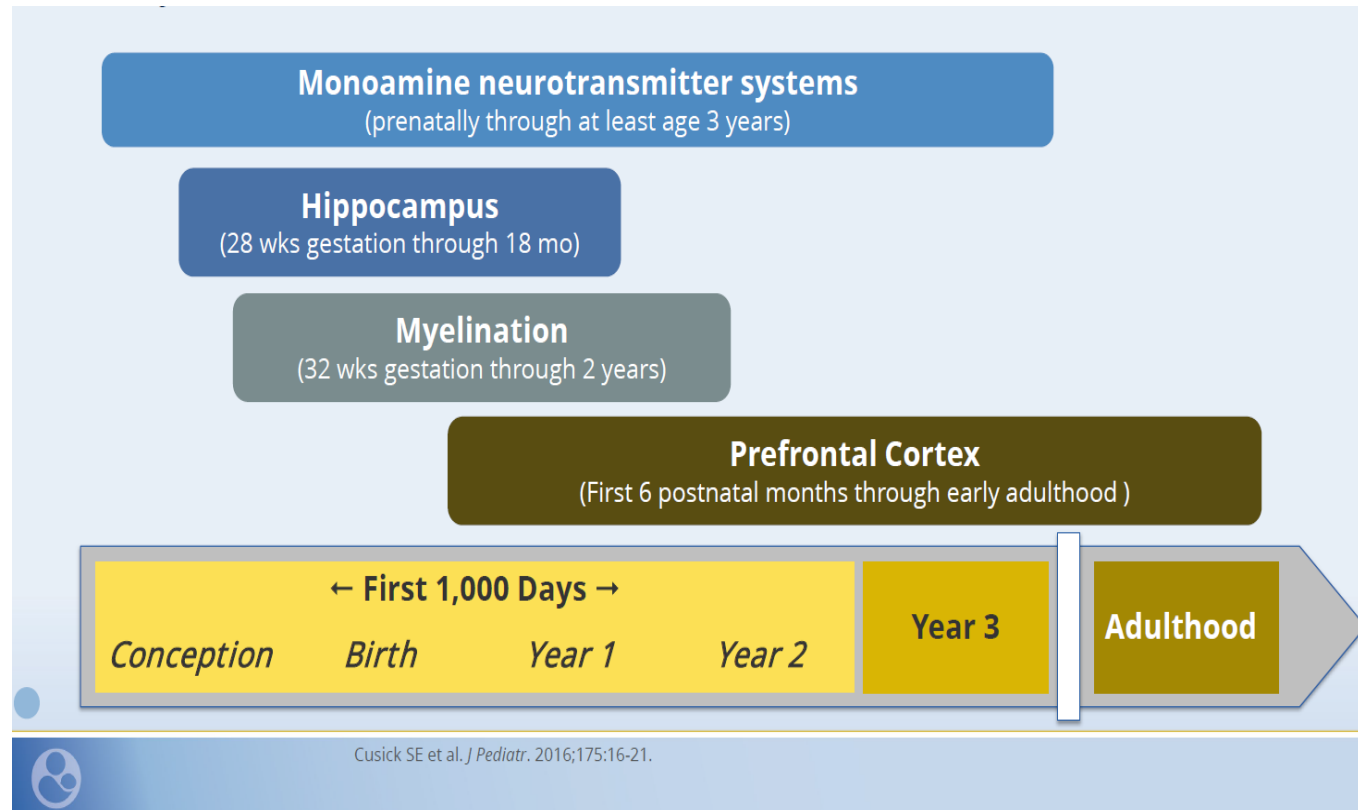


Presentation Goals

List	List nutrients needed for early neurodevelopment in the context of US micronutrient status
Describe	Describe associations between early life micronutrient deficiencies and neurodevelopment, using iodine and iron as examples
Inspire	Inspire nutritional considerations in all ECHO analyses



Early Brain Development



Nutritional Impacts From:

- Maternal Pregnancy Diet/
Nutrient Status
- Infant Feeding Practices
 - Maternal Diet During Lactation
 - Infant Formula Type
 - Complementary Foods
- Child Diet



Macro-Level View of Environmental Factors Impacting Neurodevelopment



Optimal nutrition (first 1,000 days, ~conception thru age 2 y)



Reduction of toxin exposure and toxic stress (all ages)



Strong social support (0-5 y)



Macro-Level View of Early Life Nutrition

- Obesity can be a form of “malnutrition” affecting neurodevelopment¹
 - Maternal obesity during pregnancy
 - Childhood obesity
- Microbiota-Gut-Brain Axis
 - Affected by delivery mode, early feeding
 - Impacts of obesity (maternal microbiome, delivery mode, early feeding)
- Nutritional Status
 - Dietary Intake
 - **Nutrient Biomarkers (today’s focus)**

¹Mehta SH, Kerver JM, et al. Maternal obesity and neurodevelopmental outcomes. *J Pediatr.* 2014 Nov;165(5):891-6.



Nutrients Required for Early Brain Development

Macronutrients

- Protein*
- Fat (e.g., LC-PUFA)*
- Carbohydrate (Glucose)

Micronutrients

- Vitamins
 - Folate*
 - Other B vitamins (B6, B12)
 - Choline*
 - Vitamins A and D
- Minerals/Trace Elements
 - **Iodine* (today's focus)**
 - **Iron* (today's focus)**
 - Copper*
 - Zinc*
 - Selenium

*Nutrients that impact critical (must have) or sensitive (best time) windows of opportunity



Estimating Iodine Intake

- Iodine status is assessed using urinary iodine, which reflects very recent iodine intake (not usually assessed clinically or individually)
- Median urinary iodine concentrations (**UIC**) from spot samples collected from large groups, are used to characterize the iodine status of populations

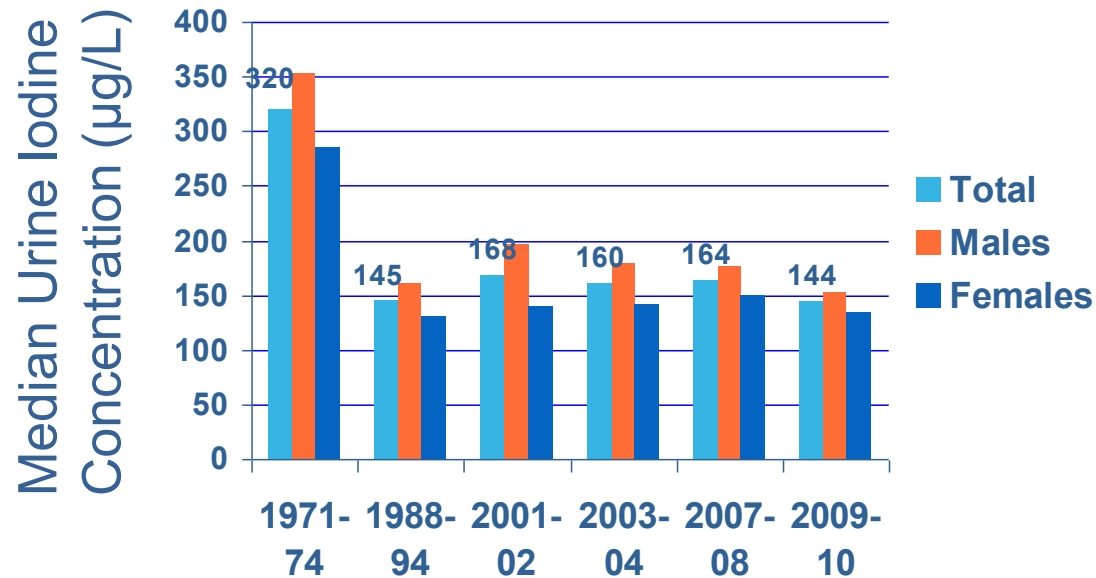


Median US Urinary Iodine Concentrations, NHANES

WHO cutoff for population pregnancy adequacy = 150 mcg/L (500 mcg/L for excessive iodine)

US Estimated Average Requirement (EAR) for pregnancy = 160 mcg/d

US Tolerable Upper Intake Level (UL) for pregnancy = 1100 mcg/d



NHANES Pregnant Participants (mUIC)

- 2001-2006 = 153 mcg/L
- 2005-2010 = 129 mcg/L
- 2007-2014 = 144 mcg/L

Groups at Risk of Iodine Inadequacy

- People living in regions with iodine-deficient soil
- People who do not use iodized salt
- Vegans and people who eat few/no dairy, seafood, eggs
- Pregnant women

- NHANES is used to monitor US iodine status
- Generally stable since the sharp drop between 1974-88
- Drop due to food processing changes in bread and milk

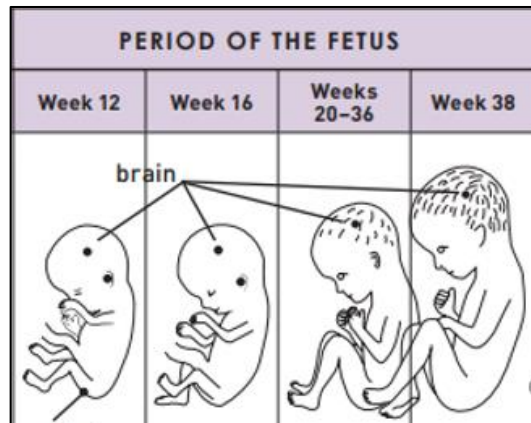


Why Pregnancy Iodine Matters

Increased demand for thyroid hormone (\uparrow 50%)



Iodine must be transferred to the fetus in late pregnancy



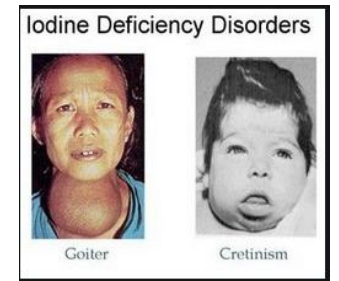
World Health Organization

Iodine deficiency, through its effects on the developing brain... is the single most preventable cause of brain damage.

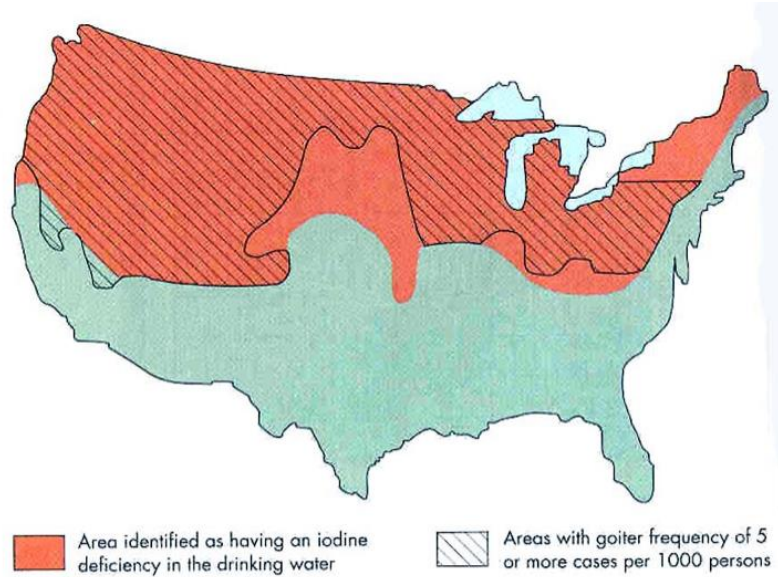
Nearly 2B people worldwide with iodine deficiency.



This is Preventable



US Goiter Belt (pre-1920s) Because Soil Iodine (and everything grown in soil) Varies Widely



1920's: US adopted voluntary iodine fortification of salt

1924: The first iodized salt available in grocery stores was in Michigan

Sodium & Salt in the Current US Diet

77% of sodium in US diet is from restaurant/processed food, usually not iodized

53% of table salt sold in the U.S. is iodized, but only 11% of table salt added at the table or in cooking is iodized

50% of reproductive age women never/rarely use table salt



Best Sources of Iodine in the US Diet

Iodine Rich Foods



- Dairy products
- Grains
- Eggs
- Ocean fish are high in iodine but not consumed in large amounts in US diets



- Prenatal Supplements?
- 58% of prenatal supplements contain iodine
- **Only 20% of US pregnant women take prenatal supplements with iodine**



Estimating Iodine Intake in a Single Cohort

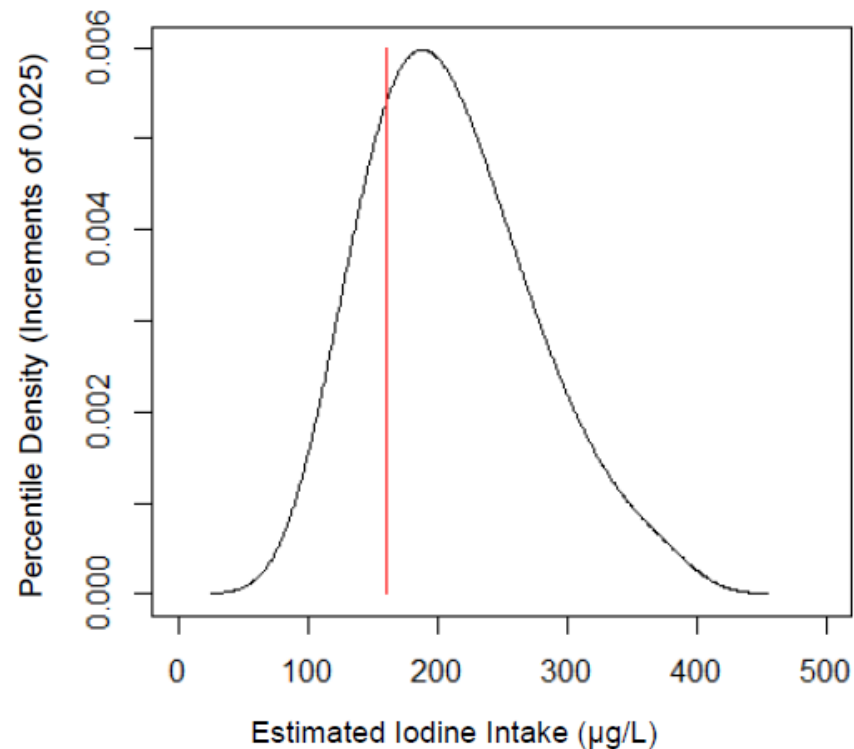


Figure: Smoothed Density Plot of Estimated Iodine Intake (µg/L) using Percentile Increments from 0.025 to 0.975

Study Design: Pregnancy cohort in Lansing, MI (n=464)

Methods: Used multiple urine samples for more precise prevalence estimates

- Estimated Average Requirement (EAR) <160 µg/d
- Tolerable Upper Limit (UL) ≥ 1100 µg/d

Results:

- Prevalence of inadequate iodine intake was 23%
- Prevalence of excessive iodine intake was < 1%



Estimating Iodine Intake in ECHO (EC0733)

- Data are from the subset of ECHO participants who had urinary iodine data. This includes 10 ECHO Award Sites Across 4 US Regions
 - **East (New York, Rhode Island)**
 - **Midwest (Illinois, Michigan)**
 - **South (Georgia, Tennessee)**
 - **West (No. California, So. California, New Mexico, Utah)**
- All participants with urinary iodine concentrations from at least two time points during pregnancy were included (**n=3,027 urine specimens; n=1,444 participants**)
- Biomarker data were from EQUIP Labs (HHEAR, CDC, Pearce)



Characteristics of the ECHO Iodine Sample (in preparation for publication)

Maternal Characteristics (n=1,444)	Percent (n)
Year of Delivery/Birth (n=32 missing)	
2005-2009	5.1 (72)
2010-2014	28.2 (398)
2015-2019	62.7 (885)
2020-2022	4.0 (57)
Highest level of education (n=122 missing)	
< High School	11.8% (156)
High School Degree, GED/Equivalent	24.0% (317)
Some College	27.4% (362)
Bachelor's Degree and Above	36.8% (487)
Race and Ethnicity (n=7 missing)	
Hispanic	16.6% (238)
NH White	38.0% (546)
NH Black	19.5% (280)
NH American Indian or Alaska Native	20.4% (293)
NH Other or Multiple Race	5.6% (80)



Overall Iodine Results Using Two Methods

1. Median UIC (WHO cutoff for population adequacy = 150 mcg/L)
 - 125.2 mcg/L
2. Using multiple urine samples per woman to estimate prevalence
 - Inadequate iodine = 0.48 (almost half the population studied)
 - Excessive iodine < 0.01 (only 1 person)



Prevalence of Inadequate Iodine by Two Methods by Maternal Characteristics

Group	Maternal N	Median UIC (ug/L)	Prevalence of Inadequate Iodine % (SE)
Overall	1,444	125.2	0.48 (0.0181)
Highest level of education			
< High School	156	126.2	0.53 (0.0528)
High School Degree/GED	317	126.8	0.38 (0.0495)
Some College	262	120.9	0.50 (0.0341)
≥ Bachelor's Degree	487	138.5	0.40 (0.0360)
Maternal Race and Ethnicity			
Hispanic	238	138.6	0.37 (0.0532)
NH White	546	149.8	0.36 (0.0352)
NH Black	280	131.8	0.36 (0.0542)
NH American Indian or Alaska Native	293	73.0	0.80 (0.0642)
NH Other or Multiple Race	80	139.6	0.47 (0.0692)



Iodine Status Conclusions and Next Steps

Many pregnant women in the US are not consuming enough iodine, a nutrient required for brain development

Preliminary results indicate the lowest levels among those in the NH American Indian or Alaska Native race category (due to geography, soil content, food access)

Using median iodine values to assess population adequacy for an area as large as the US is not appropriate for preventing iodine deficiency

In ECHO, we will estimate individual level iodine intake in association with child neurodevelopmental outcomes (e.g., cognition, autism traits, ADHD symptomology)

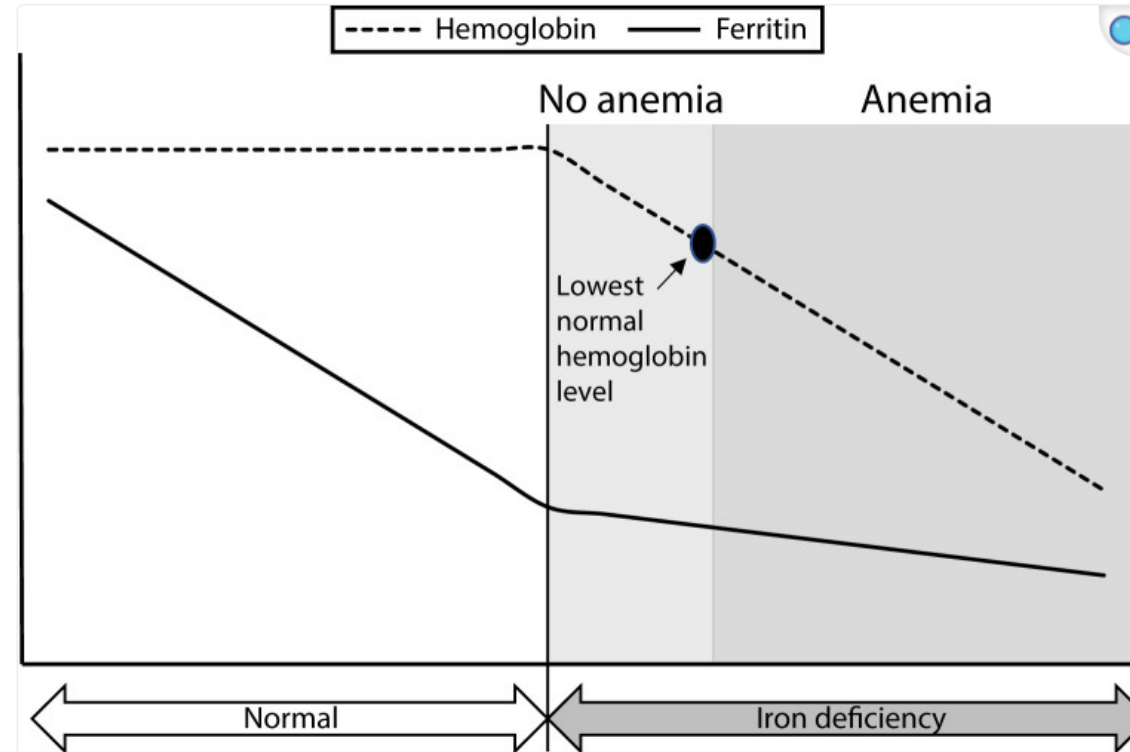


Iron Deficiency and Iron Deficiency Anemia

© American Public Health Association 2022 **FIGURE 1—**

Am J Public Health. 2022 Oct;112(Suppl 8):S826–S835.

- Anemia (low Hgb)
- Iron Deficiency (low Ferritin)
- Ferritin increases in the presence of inflammation



Relationship Between Ferritin and Hemoglobin

Source. Adapted from Guthrie and Picciano.¹⁶



Iron Deficiency and Iron Deficiency Anemia

Prenatal care providers routinely screen for anemia (low Hgb), but not the less severe form of iron deficiency (low ferritin)

“Surveillance data for iron deficiency are sparse at all levels, with critical gaps for pregnant women and younger children.”

- >70% of iron deficiency in pregnancy is missed by relying on Hgb
- >80% of iron deficiency in young children



Conflicting Conclusions = ECHO Opportunity

“Widely Known”

- Both iron deficiency and iron deficiency anemia impair brain development
- Oral iron supplementation is a safe and effective treatment for iron deficiency and iron deficiency anemia

2024 USPSTF Recommendations

- Not enough evidence for routine **screening** for iron deficiency during pregnancy
- Not enough evidence for routine iron **supplementation** during pregnancy



ECHO Pregnancy Iron and Child Development (EC0671)

Early stage of the analysis proposal

- n~1100 pregnant women with ferritin biomarker data
- Of those:
 - N=206 have Ages and Stages data
 - **N=99 have NIH toolbox data**
 - N=377 have CBCL data



ECHO Biospecimen Assay Task Force (BATF)

Biochemical assays recommended for pregnancy samples:

- Chemical exposures: targeted analysis for Per- and polyfluoroalkyl Substances (PFAS) in plasma ideally. Approaches will also yield untargeted data, retaining the ability to re-analyze the comprehensive datasets in subsequent years for other chemicals.
- Immune and inflammatory biomarkers: Blood plasma will be analyzed for 11 cytokines using Meso Scale Discovery, an established validated immunoassay multiplex platform. Specifically, IFN- γ , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, IL-17A and TNF- α . In addition, hs-CRP will be measured as part of the clinical assay panel.
- Multiplexed clinical assays: The proposed pregnancy panel includes liver function (ALT and AST), immune and immunoglobulin (hs-CRP, CMV IgG, and CMV IgM), thyroid (TSH, free T3 and Free T4), **nutrition (ferritin, folate, vitamin B12, Total 25-OH Vit D)** and albumin. Other clinical markers are included in the NMR panel.



ECHO Micronutrient Diet and Biomarker Data

Current Developments in Nutrition 7 (2023) 102019



journal homepage: <https://cdn.nutrition.org/>



Opportunities for Examining Child Health Impacts of Early-Life Nutrition in the ECHO Program: Maternal and Child Dietary Intake Data from Pregnancy to Adolescence

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ECHO Micronutrient Diet and Biomarker Data

TABLE 7

Number of ECHO cohort study sites (and individual participants) with publicly available dietary intake data as of August 31, 2022 who also have nutrient biomarkers measured

Nutrient	Matrix	Total ¹	Pregnancies (prenatal only)	Children			
				Delivery/infancy	Early childhood	Middle childhood	Adolescence
Number of cohort study sites (number of individuals)							
Carotenoid	Blood	8 (948)	2 (428)	0 (0)	7 (512)	1 (8)	0 (0)
Fatty acid	Blood	8 (948)	2 (428)	0 (0)	7 (512)	1 (8)	0 (0)
Folate	Blood	9 (593)	4 (461)	0 (0)	0 (0)	5 (92)	3 (40)
Iodine	Urine	10 (682)	10 (682)	0 (0)	0 (0)	0 (0)	0 (0)
Iron	Blood	9 (594)	4 (461)	0 (0)	0 (0)	5 (93)	3 (40)
Trace metals	Blood	5 (1669)	5 (1669)	0 (0)	0 (0)	0 (0)	0 (0)
	Cord blood	1 (23)	0 (0)	1 (23)	0 (0)	0 (0)	0 (0)
	Cord tissue	1 (198)	0 (0)	1 (198)	0 (0)	0 (0)	0 (0)
	Hair	1 (120)	1 (120)	0 (0)	0 (0)	0 (0)	0 (0)
	Tooth	4 (255)	0 (0)	0 (0)	0 (0)	4 (255)	0 (0)
Vitamin D	Urine	12 (2940)	8 (2036)	1 (<5)	2 (729)	0 (0)	1 (171)
	Blood	20 (4464)	10 (2793)	1 (149)	11 (1443)	8 (477)	3 (40)
	Cord blood	5 (2253)	0 (0)	5 (2253)	0 (0)	0 (0)	0 (0)
Zinc	Blood	5 (1642)	5 (1642)	0 (0)	0 (0)	0 (0)	0 (0)
	Cord tissue	1 (198)	0 (0)	1 (198)	0 (0)	0 (0)	0 (0)
	Hair	1 (120)	1 (120)	0 (0)	0 (0)	0 (0)	0 (0)
	Urine	8 (2058)	4 (1154)	1 (<5)	2 (729)	0 (0)	1 (171)

ECHO, Environmental influences on Child Health Outcomes.

¹ For the “Total” column, participants are counted once per nutrient biomarker. For the columns describing stages of childhood, participants are only counted once per life stage but may be included in several life stages.



ECHO Micronutrient-Related Potential

- Main Exposure
- Toxicant Mitigator
- Epigenetics
- Metabolomics

All studies with neurodevelopmental outcomes should consider including iron status (and possibly other micronutrients) as a confounder or at least noting in the limitation section that unmeasured micronutrient status is a potential confounder, known to affect neurodevelopment.





ECHO

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A program supported by the NIH

Interested? Contact me!

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