Nutrition and Health Implications: Chemical Hazards

Margaret Rita Karagas, MS, PhD
James Squires Professor and Chair
Department of Epidemiology
Geisel School of Medicine at Dartmouth College

Dartmouth

Disclosure Statement

I have no conflicts to disclose.

What do we need to know?

Approaches we can take to learn:

What do people eat?

Are chemical hazards are present in foods people eat?

Are individuals' levels of toxic chemicals associated with the foods they eat?

How do these exposures impact our health?

- When?
- Mechanisms?
- Modifiers?

How does this inform decision making?

What Do People Eat?

Commonly Consumed Seafood Among Women of Childbearing Age and Children

TABLE 3-4 Seafood Species Commonly Consumed, U.S. Women of Childbearing Age, by Percentage of Seafood Meals

Seafood Species	Sample Size (n)	Frequency, Weighted (percent)
1. Shrimp		
2. Tuna		
3. Salmon		
4. Other fish		
5. Crab		
6. Breaded Fish		
7. Catfish		
8. Cod		
9. Scallops		
10. Lobster		

SOURCE: NHANES, 2011–2012 through 2017 frequency questionnaire.

TABLE 3-7 Seafood Species Frequently Consumed, U.S. Children by Percentage of Seafood Meals 2020

	Seafood Species	Sample Size (n)	Frequency, weighted (percent)
1.	Shrimp	7,168	28.7
2.	Tuna	3,466	14.4
3.	Salmon	3,172	12.1
4.	Other fish	2,586	7.8
5.	Breaded fish	1,732	6.7
6.	Crab	1,292	5.2
7.	Catfish	1,344	4.3
8.	Cod	633	2.6
9.	Other unknown	838	2.2

NHANES
- Limited number of pregnant and lactating people, very young children
- One time sample

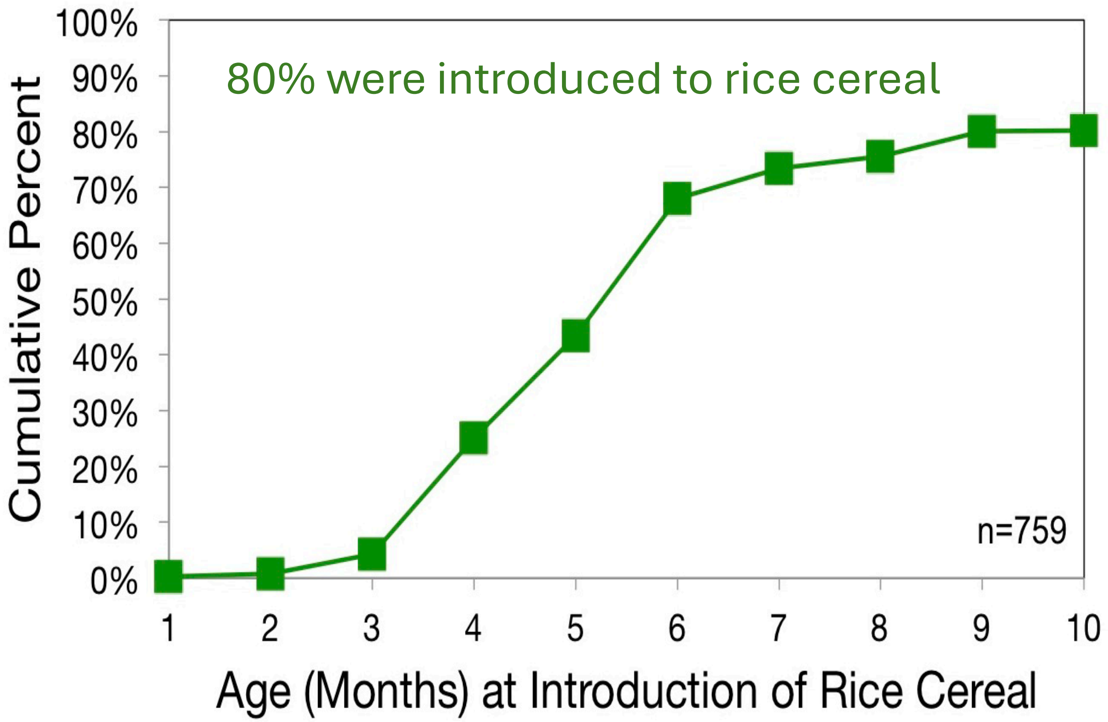
- Children ages 1-2 years ate **<2** seafood meals/month on average
- Children 2-19 years only **6%** ate 2 or more seafood meals/week (DGA)

What Do People Eat?
Prospective Study of Early Diet

Courtney Carignan, PhD

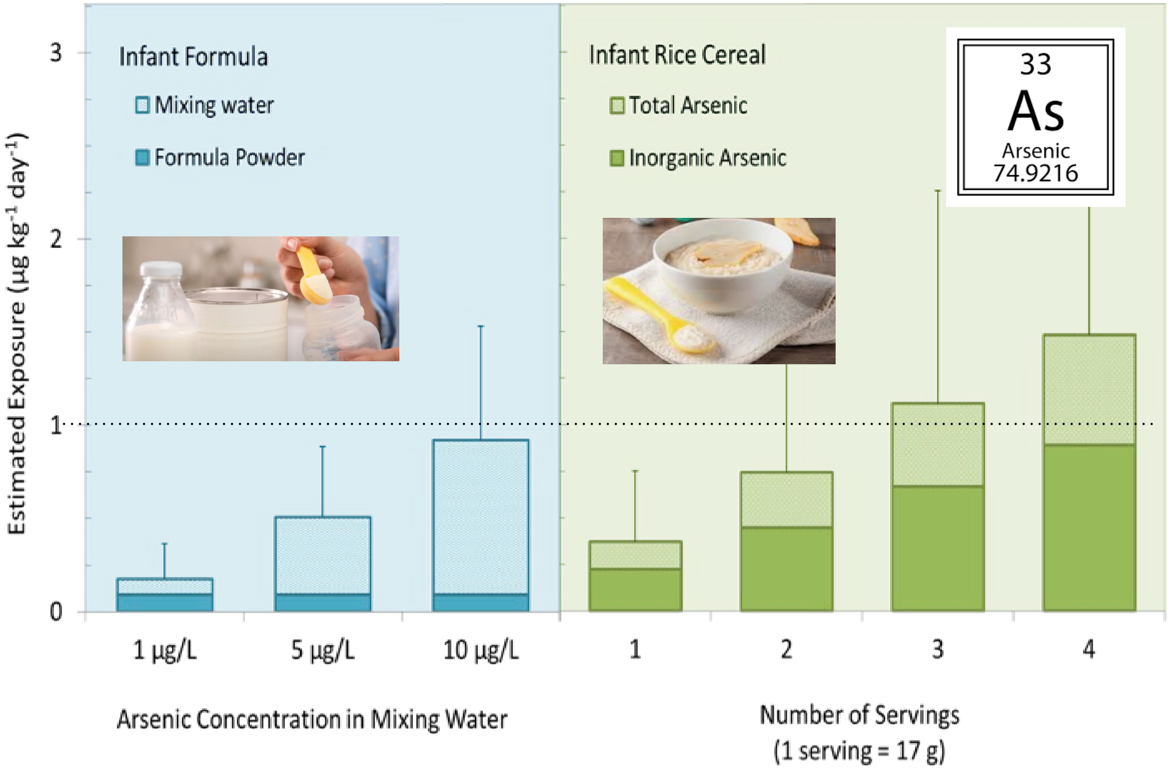
nh birth cohort study

Longitudinal Assessment of the Timing of Introduction of Rice Cereal in the First Year of Life



Karagas et al., 2016

Incorporated Data from the FDA to Estimate Arsenic Exposure from Rice Cereal



Carignan et al., 2016

Are Levels of Toxic Chemicals Related to the Foods People Eat?

Directly Measuring Exposure via Biomarkers

OPEN ACCESS Freely available online PLOS | ONE

A Dietary-Wide Association Study (DWAS) of Environmental Metal Exposure in US Children and Adults

CrossMark

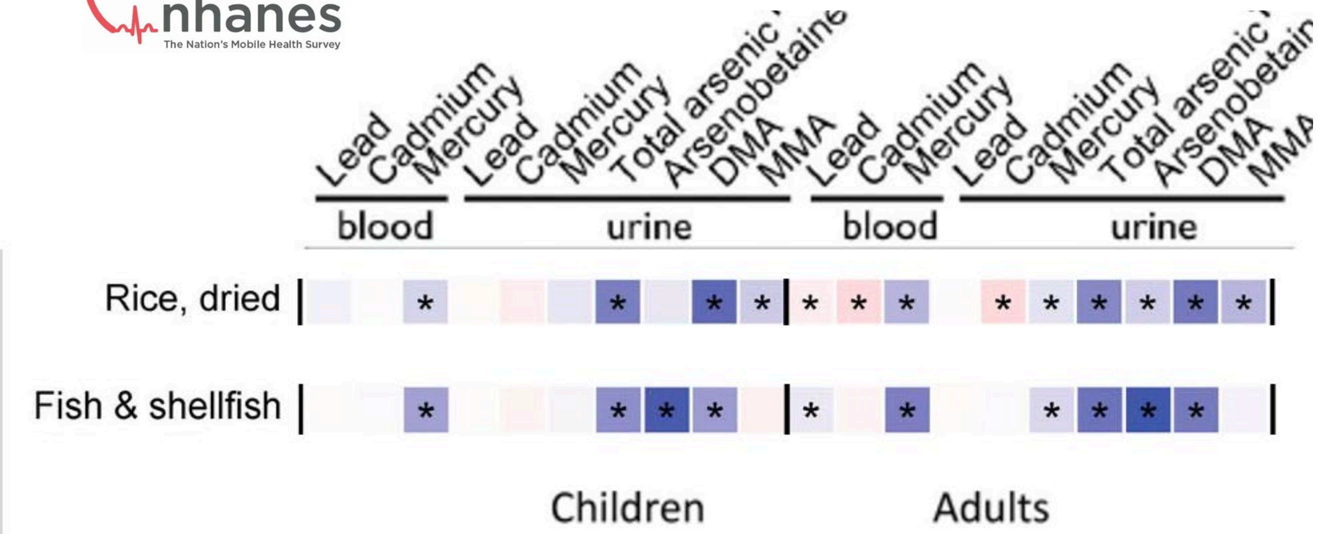
Matthew A. Davis[1,2,3,4]*, Diane Gilbert-Diamond[1,2,4], Margaret R. Karagas[1,2,4], Zhigang Li[1,2,4], Jason H. Moore[1,2,4,5], Scot

nhanes The Nation's Mobile Health Survey

24-hour dietary recall + bioassays of As, Pb, Cd, Hg

Matthew Davis, MPH, PhD

H. Robert Frost, PhD



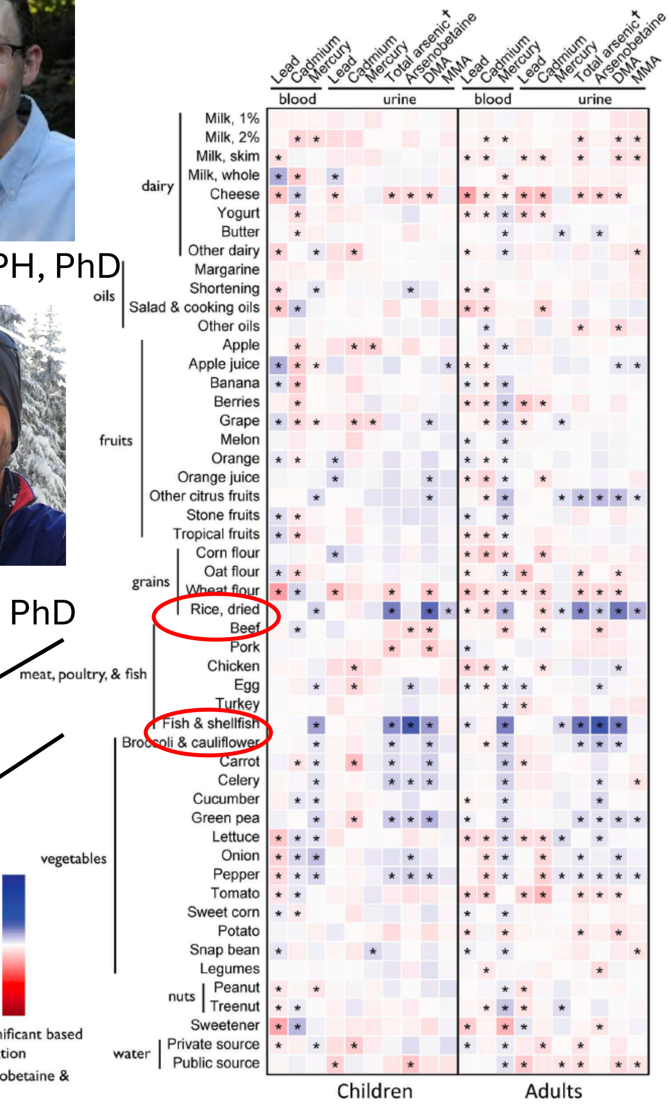


Figure 2. Spearman correlation coefficients between grams of food per day and lead cadmium, mercury, and arsenic biomarker concentrations among children versus adults. Abbreviations: DMA, dimethylarsinic acid; MMA, monomethylarsonic acid; FDR, false discovery rate.

Do Levels of Toxic Chemicals Relate to Foods People Eat?

Prospective Study of Emerging Dietary Exposures During Pregnancy and Lactation

ELSEVIER

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Association of diet with per- and polyfluoroalkyl substances in plasma and human milk in the New Hampshire Birth Cohort Study

Yuting Wang[a,*,1], Jiang Gui[b], Caitlin G. Howe[a], Jennifer A. Emond[b], Rachel L. Criswell[a,c], Lisa G. Gallagher[a], Carin A. Huset[d], Lisa A. Peterson[e,f], Julianne Cook Botelho[g], Antonia M. Calafat[g], Brock Christensen[a], Margaret R. Karagas[a], Megan E. Romano[a]

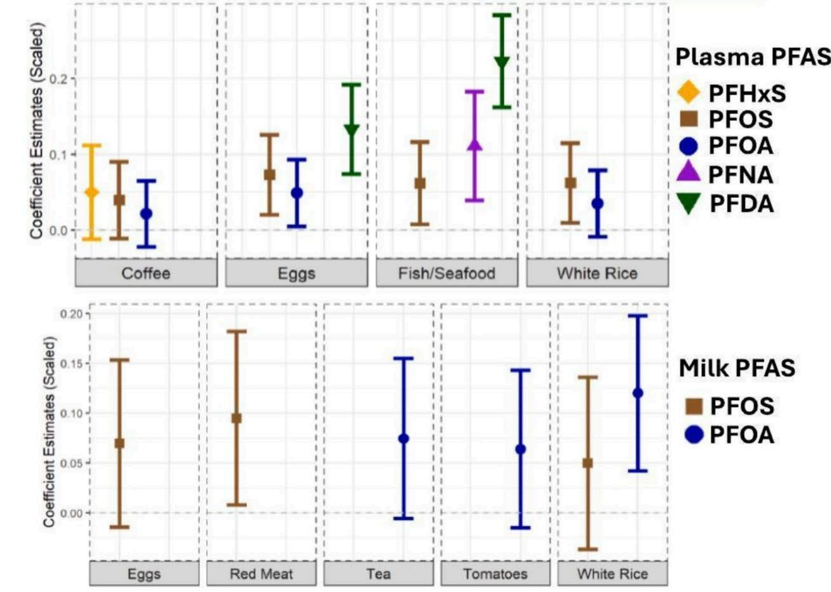
Yuting Wang, PhD

adaptive elastic net variable selection of prenatal diet & PFAS

nh birth cohort study

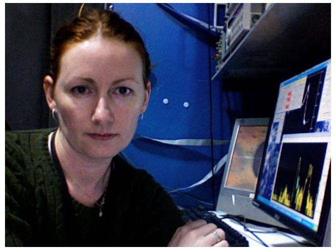
Dietary Factors During Pregnancy → PFAS Concentrations
- Maternal Plasma
- Human Milk

- Higher gestational **Plasma** PFAS associated with Coffee, Eggs, Fish/Seafood & Rice
- Higher **Human Milk** PFAS during lactation related to Eggs, Meat, Tea, Tomatoes and Rice



Do Levels of Toxic Chemicals Relate to Foods People Eat?

Pinpointing the timing of dietary exposures using novel biomarkers



Tracy Punshon, PhD

Julia Bauer, PhD

ELSEVIER

Contents lists available at ScienceDirect

Environmental Research

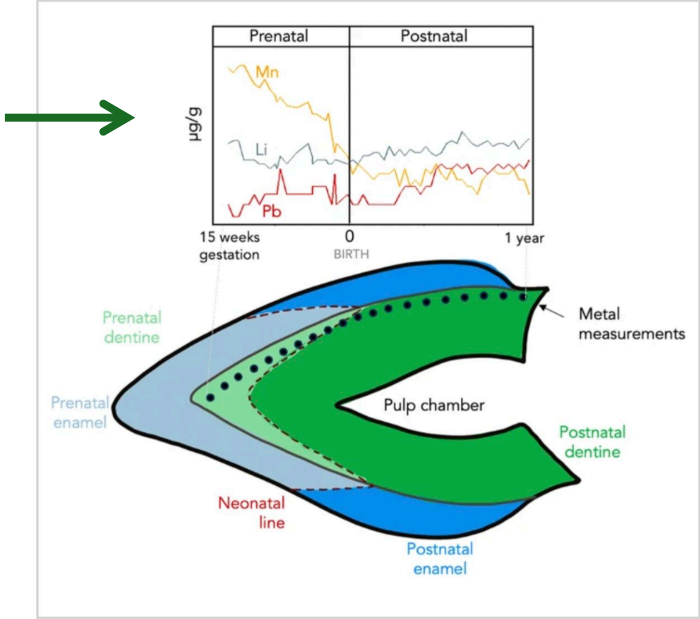
journal homepage: www.elsevier.com/locate/envres

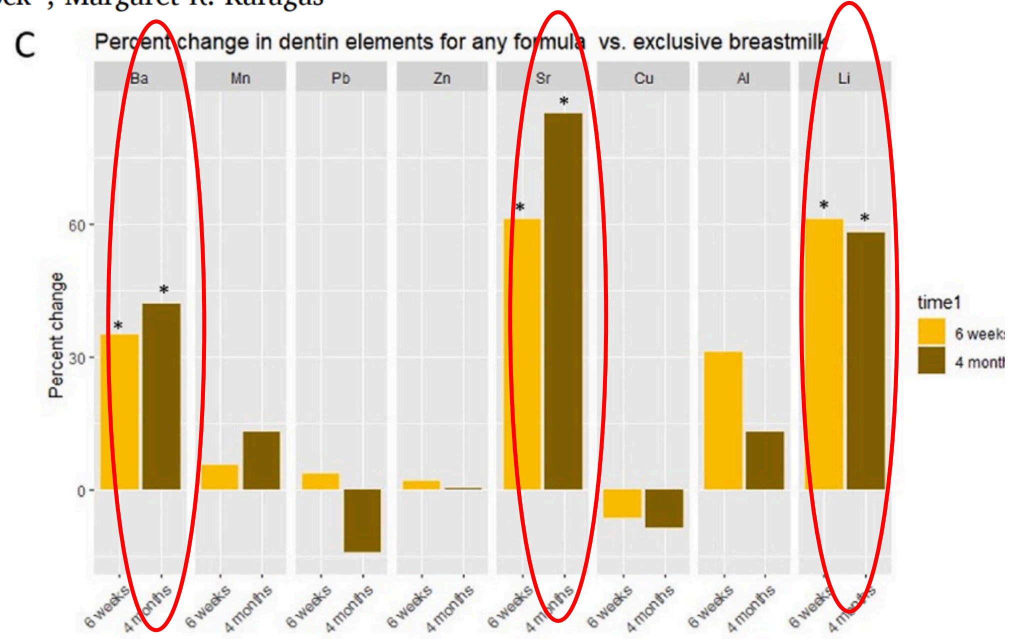
Check for updates

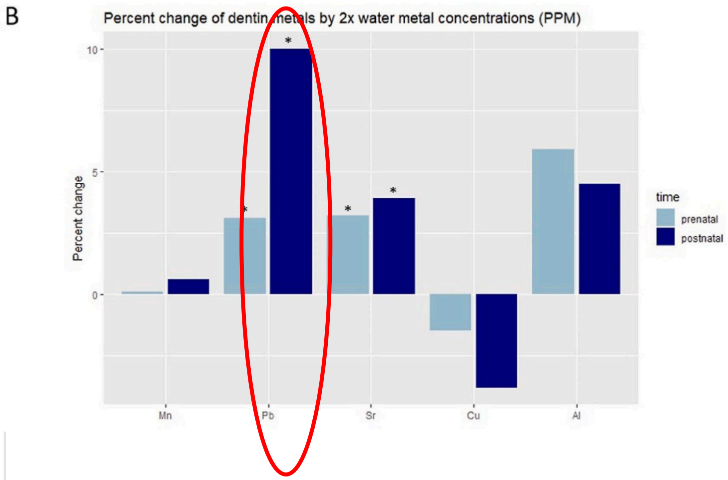
Deciduous teeth from the New Hampshire birth cohort study: Early life environmental and dietary predictors of dentin elements

Julia A. Bauer[a,b,*], Tracy Punshon[c], Matthew N. Barr[d], Brian P. Jackson[d], Marc G. Weisskopf[e], Felicitas B. Bidlack[f], Modupe O. Coker[a,g], Janet L. Peacock[a], Margaret R. Karagas[a]

nh birth cohort study







Do Levels of Toxic Chemicals Relate to Foods People Eat?

Investigating Dietary Patterns & Elemental Mixtures

Leyre Notario-Barandiaran, PhD

Contents lists available at ScienceDirect

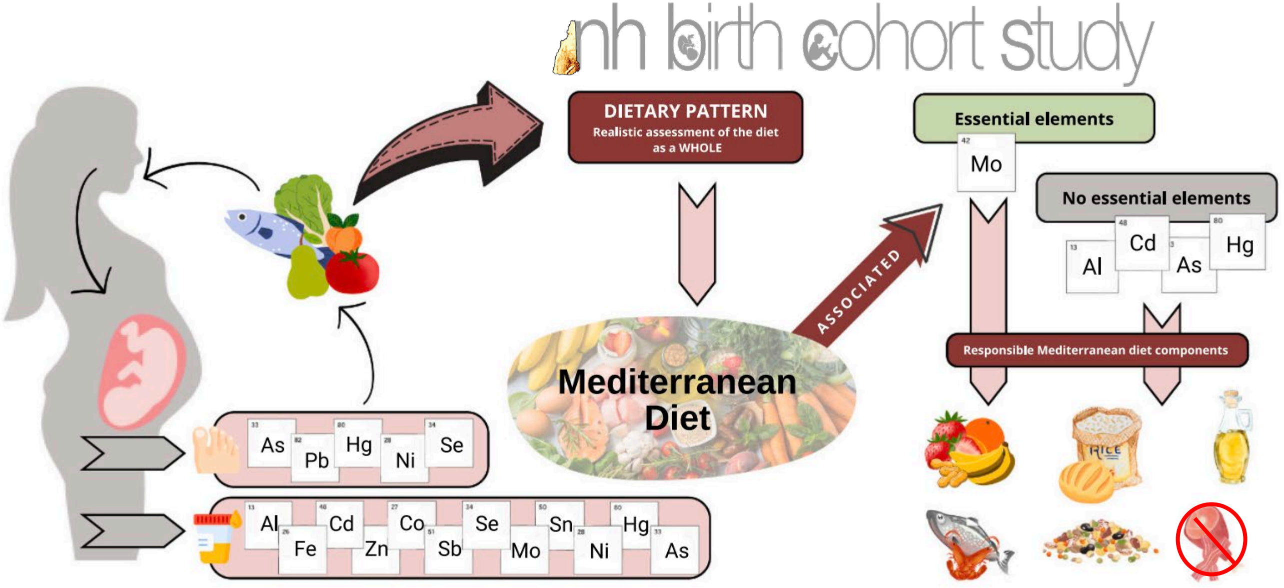
Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Association between Mediterranean diet and metal mixtures concentrations in pregnant people from the New Hampshire Birth Cohort Study

L. Notario-Barandiaran [a,*], A.J. Signes-Pastor [a,b,c,d], H.E. Laue [a], A. Abuawad [a], B.P. Jackson [e], J.C. Madan [a,f], M.R. Karagas [a]

WQS



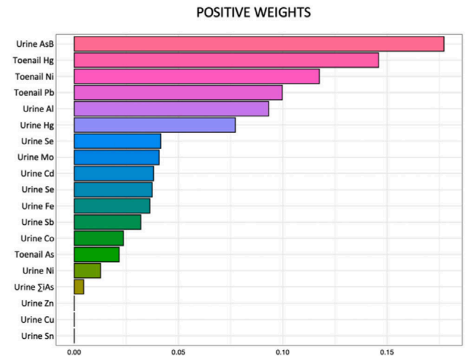


Fig. 3. Metal mixtures exposure and rMED score among pregnant people from the NHBCS ($n = 907$). WQS regression models. rMED, relative Mediterranean diet score; NHBCS, New Hampshire Birth Cohort Study; WQS, Weighted Quantile Sum. Models were adjusted by age, pre-pregnancy BMI, pregnant person's education

Adherence to the MD associated with

- Higher AsB, Hg, Ni, Pb, Al, Cd
- Lower Cu & Sn

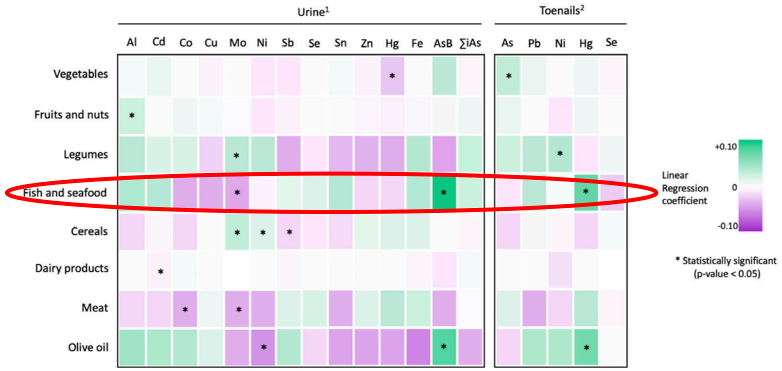


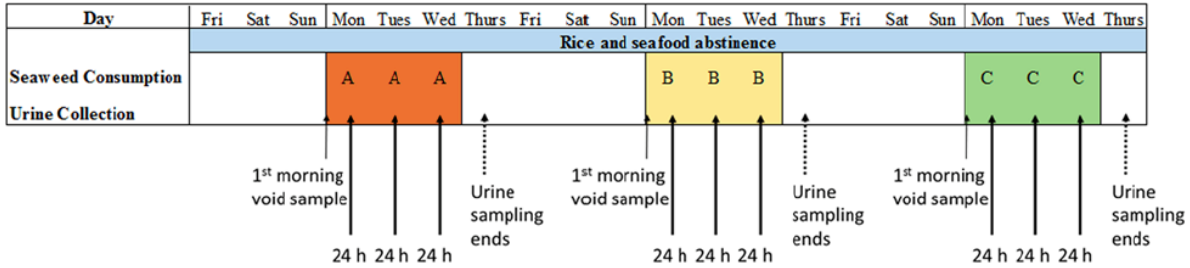
Fig. 2. Linear regression coefficient (beta) between rMED components (g/d, continuous) and urinary and toenail metal exposure among pregnant people from the NHBCS. rMED, relative Mediterranean diet score; NHBCS, New Hampshire Birth Cohort Study. [1]Adjusted by specific gravity, age, pre-pregnancy BMI, pregnant person's education level, smoking status during pregnancy plus metals urine concentrations. [2]Adjusted by toenail sample weight, sample collection season, age, pre-pregnancy BMI, pregnant person's education level, smoking status during pregnancy plus metals toenails concentrations.

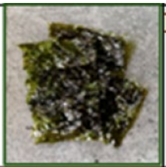
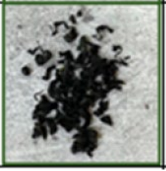
Fish:
AsB, Hg

Do Levels of Toxic Chemicals Relate to Foods People Eat?

Seaweed Feeding Experiment: Multi-Element Analysis

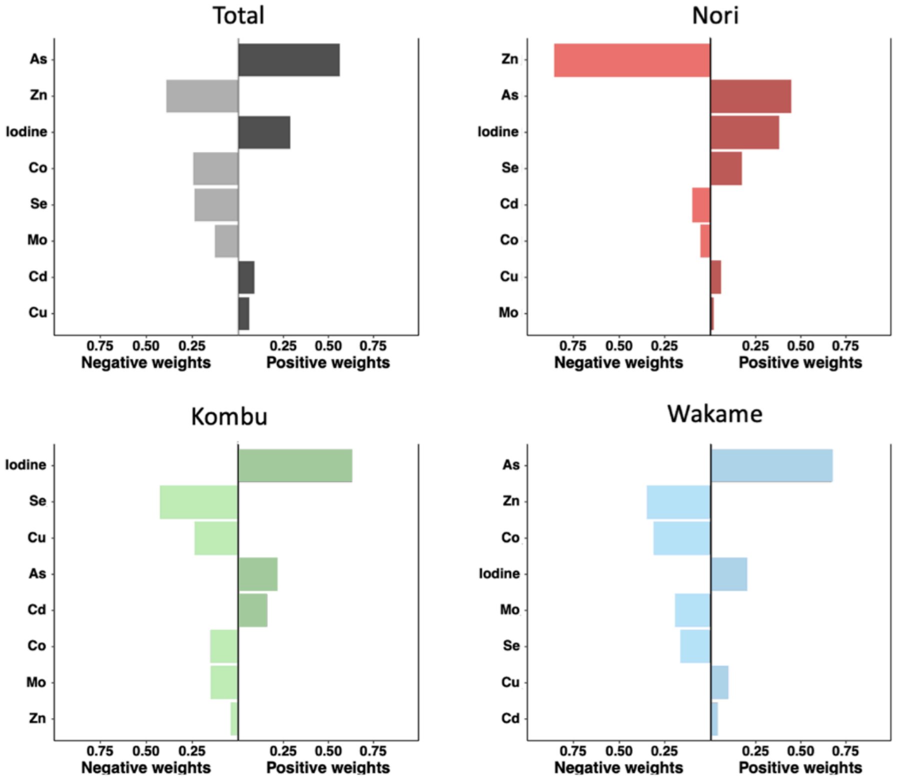
Vivien Taylor, PhD



A) Nori snacks		Dry
B) Kombu		Soaked (1min)
C) Wakame		Soaked (10min)

- 3-week intervention
- 3 common seaweeds
- 3-day, 24 hr urine
- No seafood or rice

Urinary As & Iodine concentrations increased

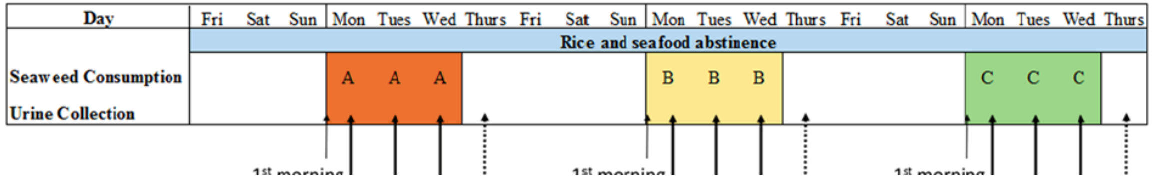


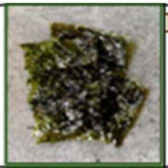
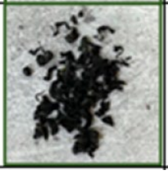
Taylor et al., 2017; Notario-Barandiaran et al., 2024

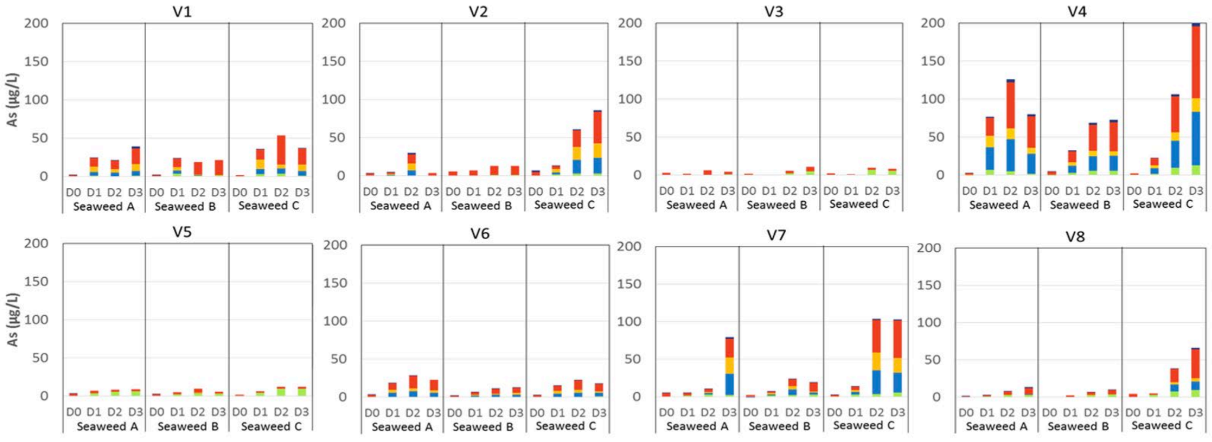
Do Levels of Toxic Chemicals Relate to Foods People Eat?

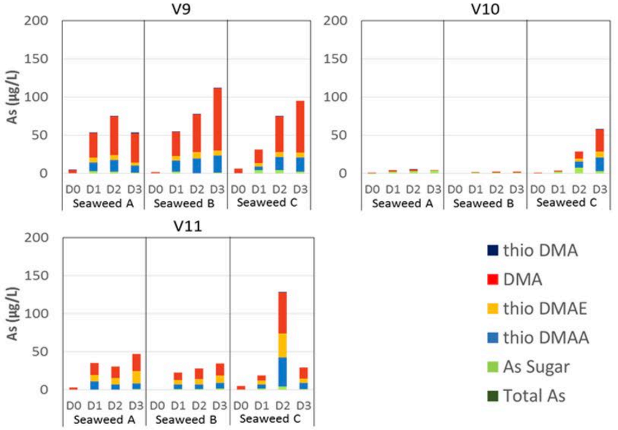
Seaweed Feeding Experiment: Individual As Results

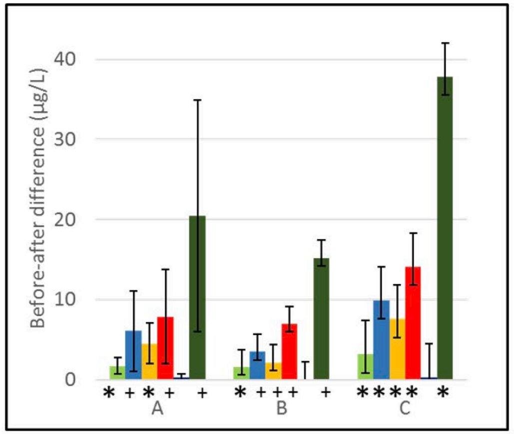
Vivien Taylor, PhD



A) Nori snacks		Dry
B) Kombu		Soaked (1min)
C) Wakame		Soaked (10min)







*Seaweed contains arsenosugars
*Metabolized into multiple forms of As i.e., thiolated compounds
*Large inter-person variability
*Potentially involving the gut microbes

Trials – costly, large samples & long follow-up to capture clinical outcomes

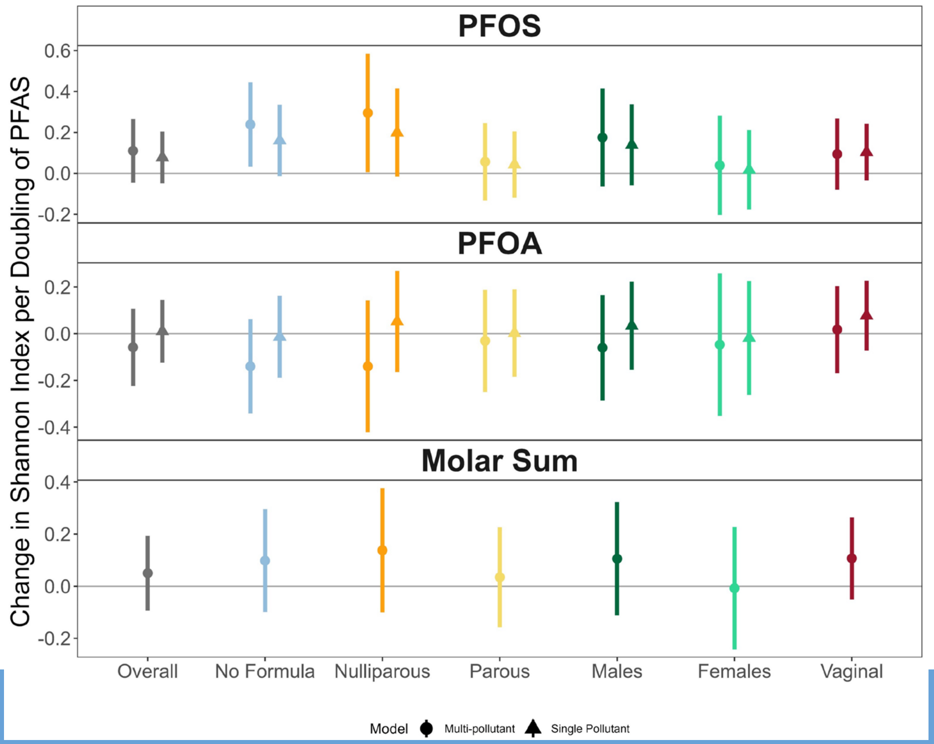
Taylor et al., 2017; Notario-Barandiaran et al., 2024

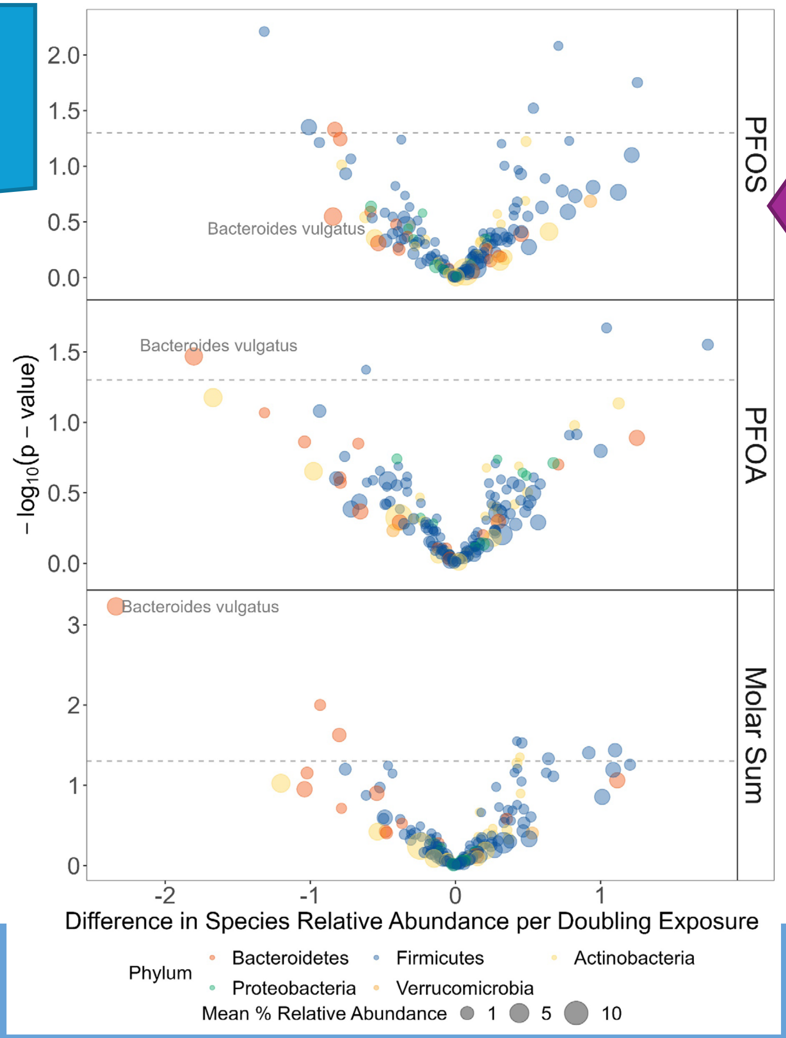
How do these exposures impact our health?

Human Milk PFAS and the Infant Gut Microbiome

Hannah Laue, ScD

Increased PFOS associated with **increased bacterial diversity** at six weeks, which has been associated with increased odds of early-life infection.





Increased PFOA associated with decreased *Bacteroides vulgatus* at one year, which has been implicated in type I diabetes.

nh birth cohort study

Laue et al. Environ Epidemiol. 2023;(1):p e238.

How do these exposures impact our health?

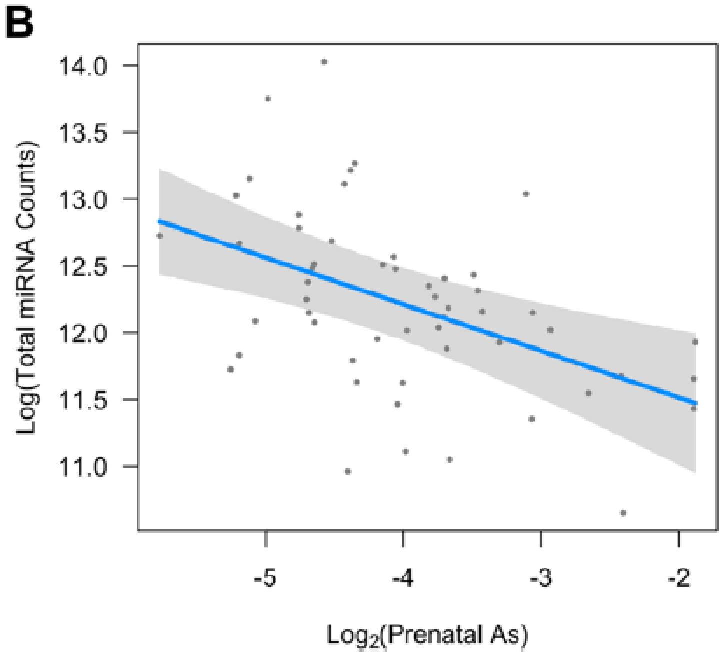
Human Milk Extracellular Vesicle (EV) miRNA:
a transgenerational epigenetic mechanism that may be impacted by chemical hazards in our food

Exposure and Health (2023) 15:731–743
https://doi.org/10.1007/s12403-022-00520-1

ORIGINAL PAPER

Periconceptional and Prenatal Exposure to Metals and Extracellular Vesicle and Particle miRNAs in Human Milk: A Pilot Study

Caitlin G. Howe[1] · David A. Armstrong[2,3] · Meghan E. Muse[1] · Diane Gilbert-Diamond[1] · Jiang Gui[4] · Anne G. Hoen[1] · Thomas J. Palys[1] · Roxanna L. Barnaby[5] · Bruce A. Stanton[5] · Brian P. Jackson[6] · Brock C. Christensen[1] · Margaret R. Karagas[1]



EV/P miRNA carried to an infant during lactation

Within the suite of elements, arsenic associated with a reduced number of miRNA in human milk EVs

Specific miRNA may be important for reducing inflammation

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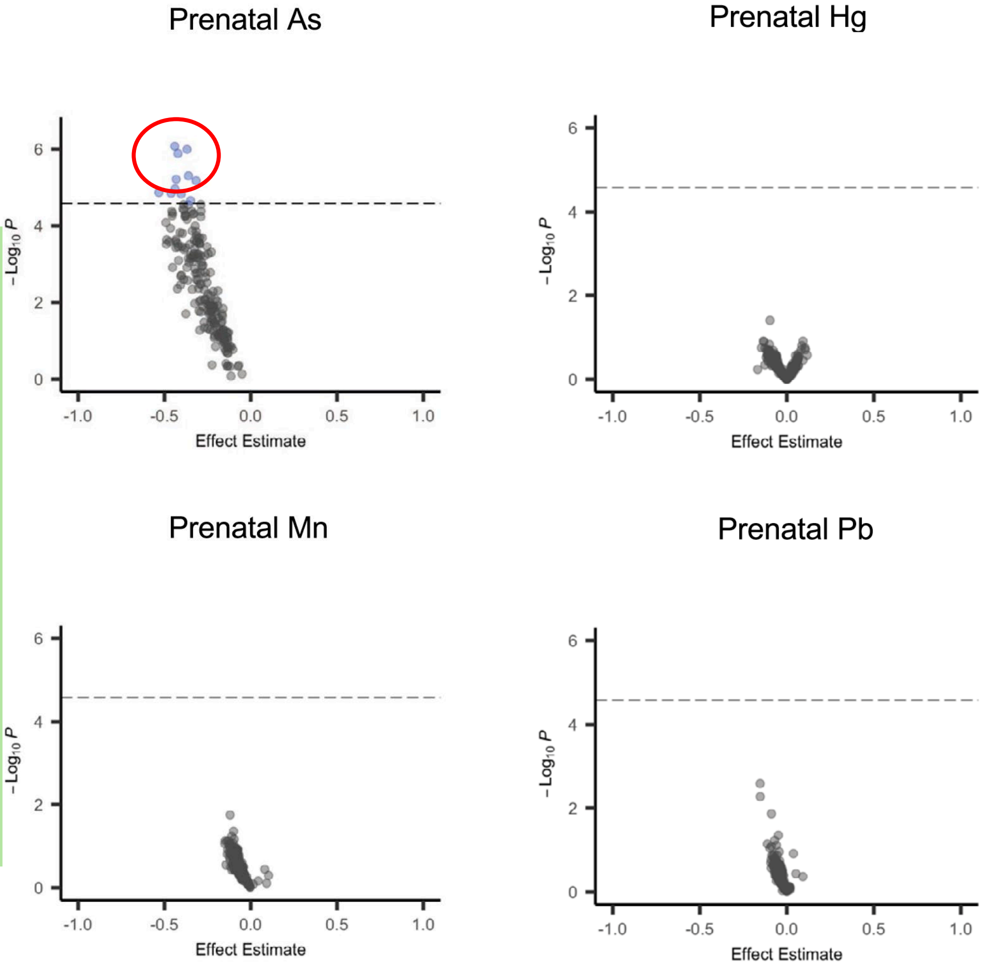
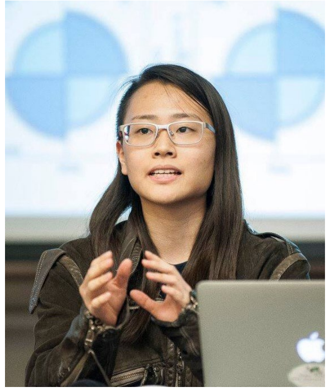
Caitlin Howe, PhD



How do these exposures impact our health?

Risks and benefits of foods on clinical outcomes



Yuka Moroishi, PhD

Rice cereal contains As, and As is associated with immune-related outcomes

scientific reports

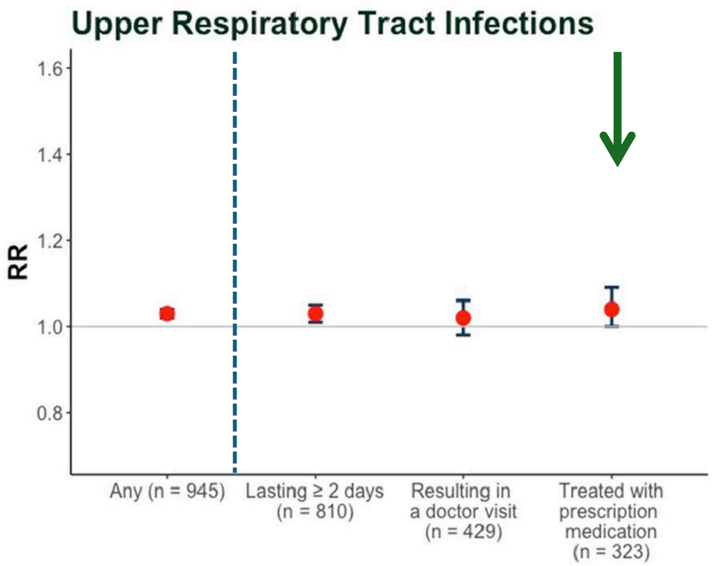
OPEN

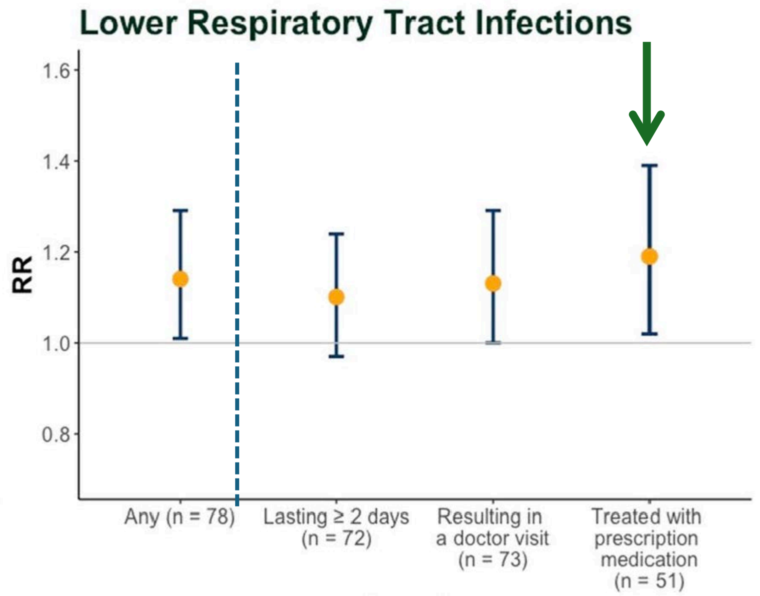
Check for updates

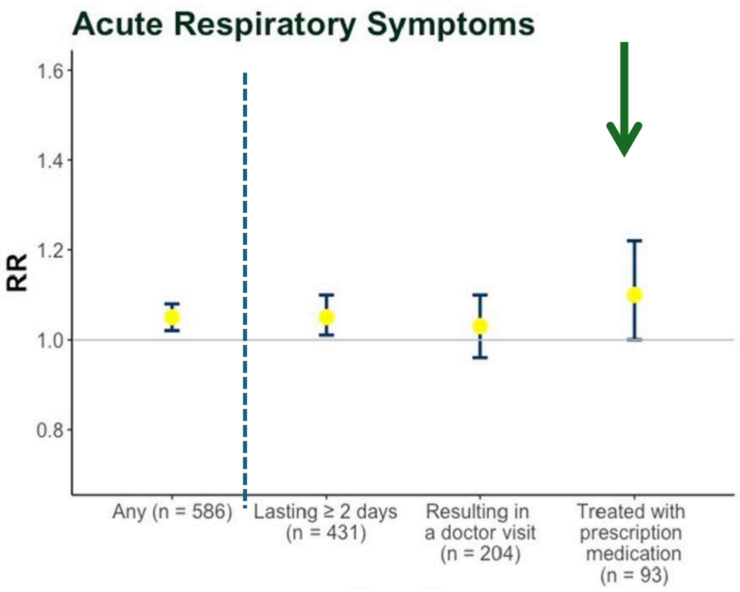
Infant infections, respiratory symptoms, and allergy in relation to timing of rice cereal introduction in a United States cohort

Yuka Moroishi[1,2], Antonio J. Signes-Pastor[1], Zhigang Li[3], Kathryn L. Cottingham[4,5], Brian P. Jackson[6], Tracy Punshon[4,5], Juliette Madan[1,5,7], Kari Nadeau[8], Jiang Gui[2] & Margaret R. Karagas[1,5]✉

Earlier introduction of rice cereal associated with higher risks of URI, LRI & respiratory symptoms







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How do these exposures impact our health?

American Society for Nutrition
Excellence in Nutrition Research and Practice

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

Original Research Article

Association of maternal fish consumption and ω-3 supplement use during pregnancy with child autism-related outcomes: results from a cohort consortium analysis

Kristen Lyall[1,*], Matt Westlake[2], Rashelle J Musci[3], Kennedy Gachigi[4], Emily S Barrett[5], Theresa M Bastain[6], Nicole R Bush[7], Claudia Buss[8], Carlos A Camargo Jr.[9], Lisa A Croen[10], Dana Dabelea[11], Anne L Dunlop[12], Amy J Elliott[13,14], Assiamira Ferrara[10], Akhgar Ghassabian[15], James E Gern[16], Marion E Hare[17], Irva Hertz-Picciotto[18], Alison E Hipwell[19], Christine W Hockett[13,14], Margaret R Karagas[20], Claudia Lugo-Candelas[21], Thomas G O'Connor[22], Rebecca J Schmidt[18], Joseph B Stanford[23], Jennifer K Straughen[24], Coral L Shuster[25], Robert O Wright[26], Rosalind J Wright[26], Qi Zhao[17], Emily Oken[27], on behalf of program collaborators for Environmental influences on Child Health Outcomes, ECHO Components, Coordinating Center, Data Analysis Center, Person-Reported Outcomes Core, ECHO Awardees and Cohorts

Large, geographically, racially/ethnically diverse prospective national cohort

Ideas are welcomed!

Association of maternal fish intake and (i)-3 supplement use during pregnancy with child autism diagnosis.

	n	Adjusted OR (95% CI)
Fish intake		
No	664	1.0 (referent)
Yes	3275	0.84 (0.77, 0.92)
Fish intake categories		
Never	664	1.0 (referent)
<1x/wk	1373	0.81 (0.71, 0.92)
1-2x/wk	1167	0.89, (0.75, 1.06)
>2x/wk	735	0.84 (0.73, 0.97)

Reduced risk, no dose-response relationship

How do these exposures impact our health?

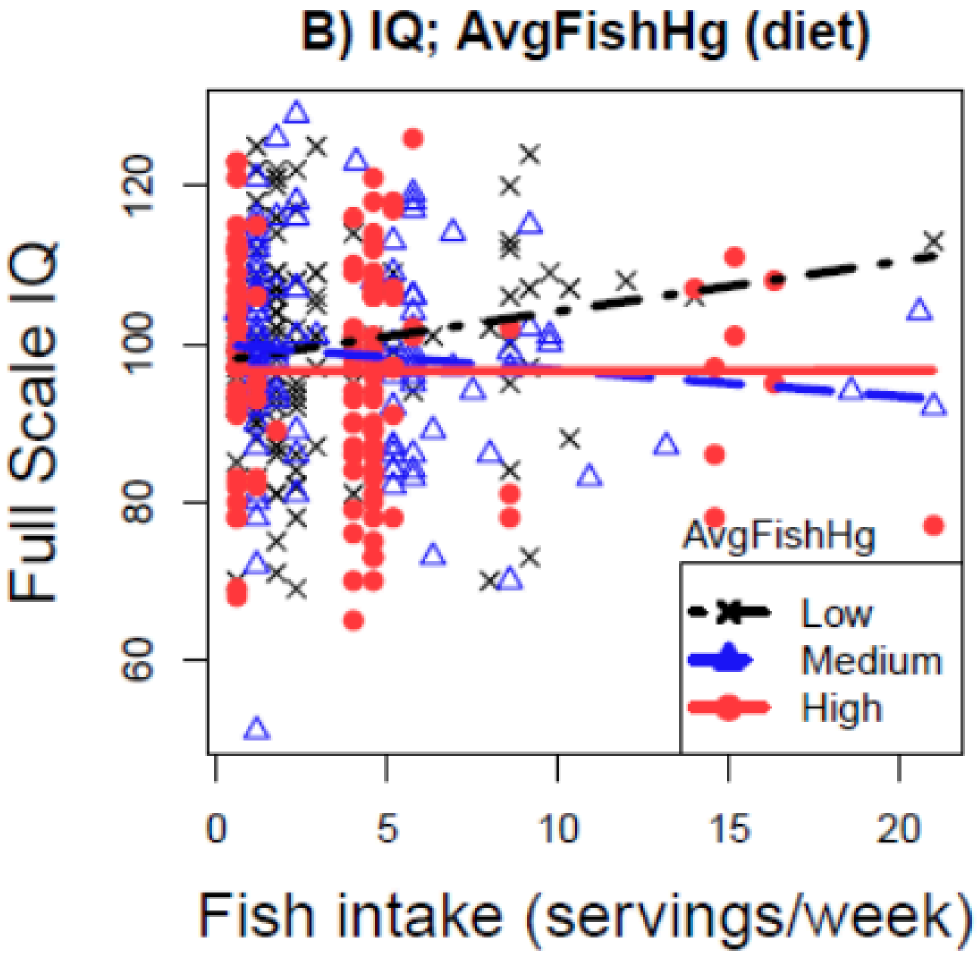
Weighing the risks vs benefits of foods

> Am J Epidemiol. 2024 Jun 28:kwae149. doi: 10.1093/aje/kwae149. Online ahead of print.

A Novel Approach to Assessing the Joint Effects of Mercury and Fish Consumption on Neurodevelopment in the New Bedford Cohort

Sally W Thurston [1,2], David Ruppert [3,4], Susan A Korrick [5,6]

N=361



Association with fish consumption varied by Hg concentrations of fish

https://pubmed.ncbi.nlm.nih.gov/38940366/

How does this inform decision making?

ADVICE ABOUT EATING FISH

For Those Who Might Become or Are Pregnant or Breastfeeding and Children Ages 1 – 11 Years

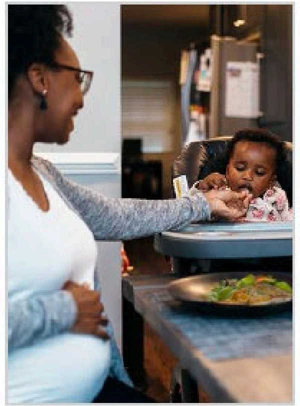
U.S. FOOD & DRUG ADMINISTRATION

Fish‡ provide key nutrients that support a child's brain development.

Fish are part of a healthy eating pattern and provide key nutrients during pregnancy, breastfeeding, and/or early childhood to support a **child's brain development**:

- Omega-3 (called DHA and EPA) and omega-6 fats
- Iron
- Iodine (during pregnancy)
- Choline

Choline also supports development of the **baby's spinal cord**. Fish provide iron and zinc to support **children's immune systems**. Fish are a source of other nutrients like protein, vitamin B12, vitamin D, and selenium too.



Choose a variety of fish that are lower in mercury.

Best Choices
Good Choices
Choices to Avoid

While it is important to limit mercury in the diets of those who are pregnant or breastfeeding and children, many types of fish are both nutritious and lower in mercury.

This chart can help you choose which fish to eat, and how often to eat them, based on their mercury levels.

What is a serving? As a guide, use the palm of your hand.

Pregnancy and breastfeeding:
1 serving is 4 ounces

Eat 2 to 3 servings a week from the "Best Choices" list
(OR 1 serving from the "Good Choices" list).

Childhood:
On average, a serving is about:

1 ounce at age 1 to 3
2 ounces at age 4 to 7
3 ounces at age 8 to 10
4 ounces at age 11

Eat 2 servings a week from the "Best Choices" list.

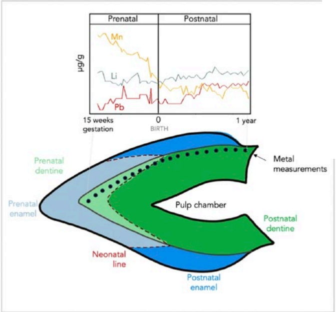
https://www.fda.gov/food/consumers/advice-about-eating-fish

Summary of Study Designs

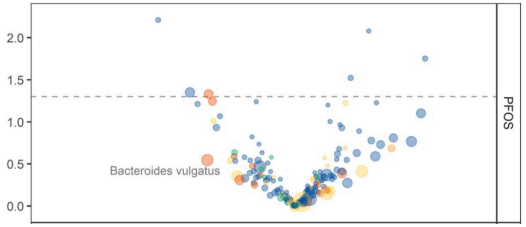
National, Cross-Sectional Data

nhanes
The Nation's Mobile Health Survey

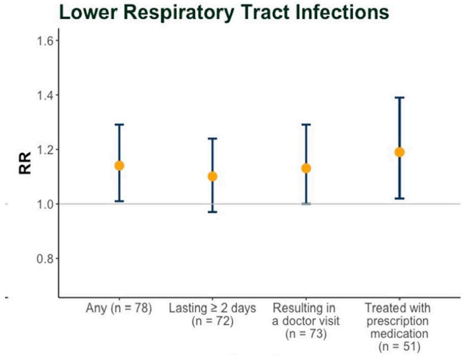
Biomarkers of Exposure Trajectories



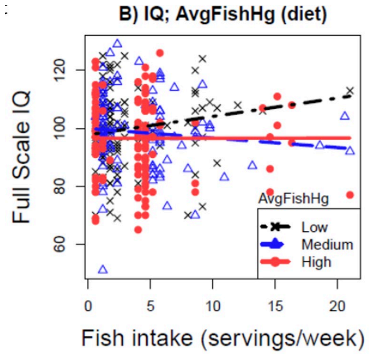
Intermediary/Mediating Outcomes



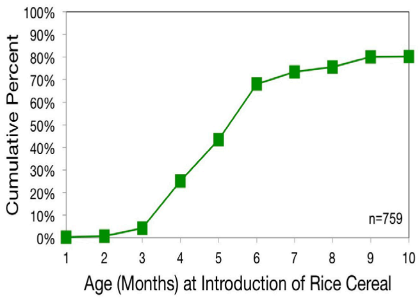
Relevant Clinical Outcomes



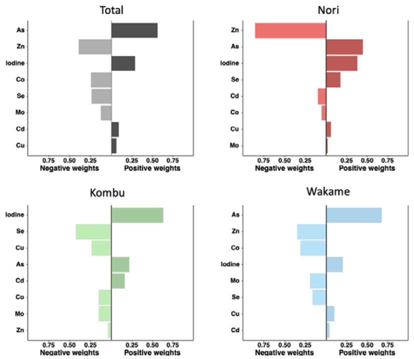
Teasing Apart Effects of Nutrients-Toxicants



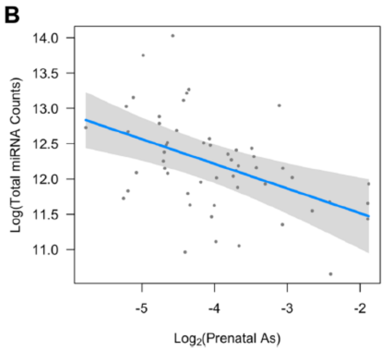
Prospective Studies



Experimental Designs to Identify Novel Exposures



Transgenerational Effects/Novel Mechanisms



Consortium Efforts

ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

Informing Guidelines

FDA U.S. FOOD & DRUG ADMINISTRATION

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