Pesticide Exposure and Child Health: New Evidence and Putting it into Practice

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Disclosures

- Dr. Karr and Dr. Curl have no disclosures to report

Outline

An introduction to a complex topic

How are children exposed?

Health Impacts

- Acute and chronic toxicity
- Emerging issues
  - Neonics - newer class of insecticides
  - Glyphosate – research in progress
  - COVID killers

Advising your patients

Resources

Complexity….
> 1.2 billion pounds of active ingredient
> 20,700 products
~ 1000 active ingredients
~ 4000 “inerts”

INSECTICIDES

Pyrethroids
Organophosphosphates
Carbamates
Organochlorine
Manganese compounds

Neonicatinoids

HERBICIDES

Bipyridyls
Chlorophenoxy
Glyphosate
Acetanilides
Triazines

FUNGICIDES

Thiocarbamates
Dithiocarbamates
Cupric salts
Tiabendazoles
Triazoles
Dicarboximides
Dinitrophenoles
Organotin compounds
Miscellaneous

RODENTICIDES

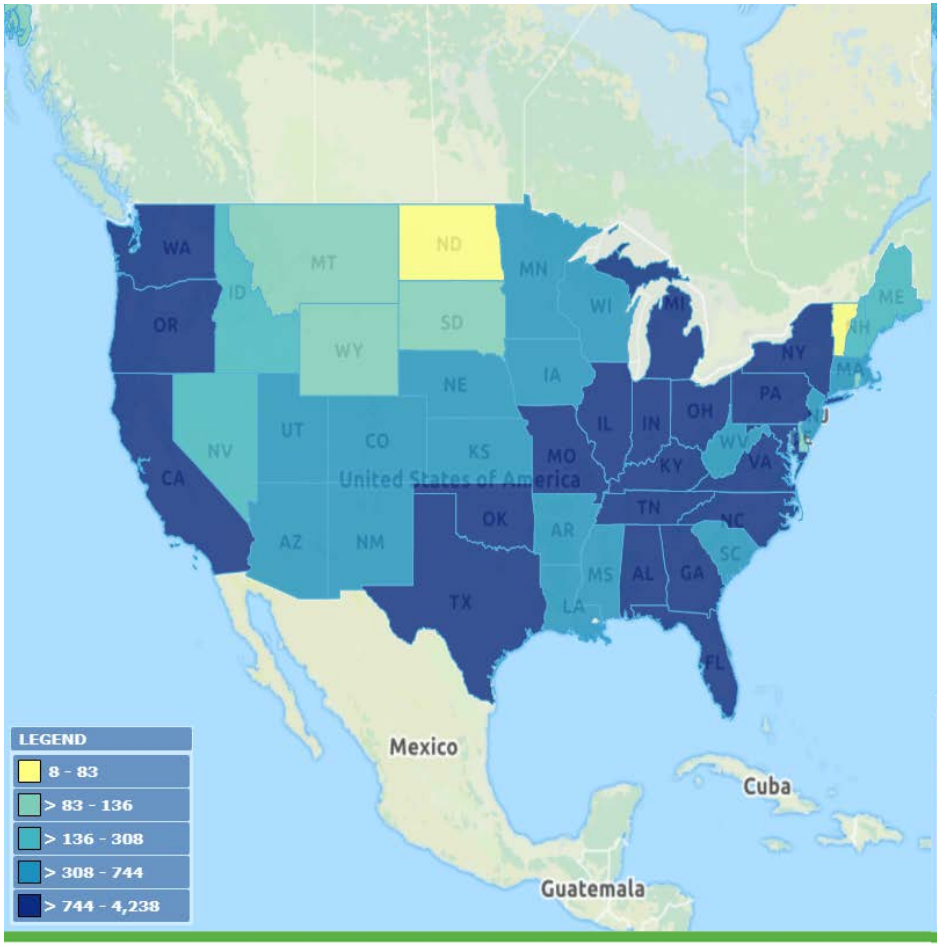
Warfarines
Indanodiones

FUMIGANTS

Aluminium and zinc phosphide
Methyl bromide
Ethylene dibromide

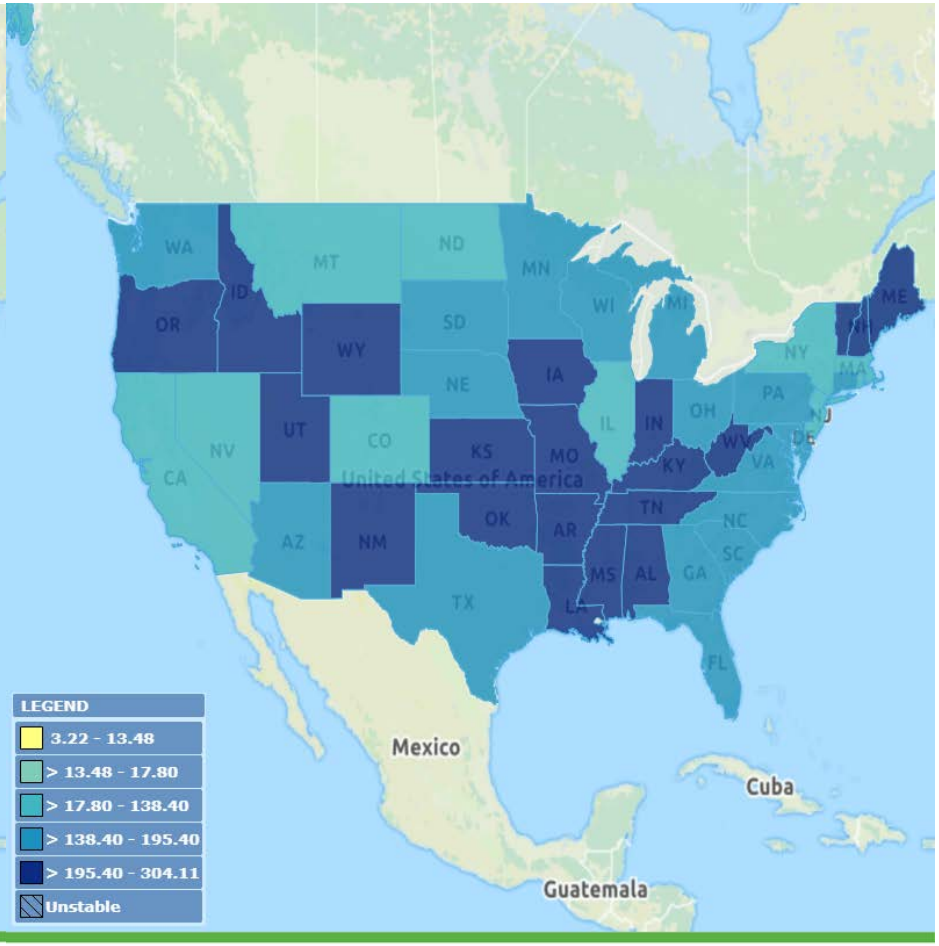
Disinfectants

Reported Child (0-5 year) Pesticide Exposures



PESTICIDE EXPOSURES | REPORTED PESTICIDE EXPOSURES | NUMBER OF REPORTED EXPOSURES TO ALL PESTICIDES | ALL STATES | Child(0-5) | **2017**

Explore more data at ephtracking.cdc.gov/DataExplorer



PESTICIDE EXPOSURES | REPORTED PESTICIDE EXPOSURES | RATE OF REPORTED EXPOSURES TO ALL PESTICIDES PER 100,000 PEOPLE | ALL STATES | Child(0-5) | **2017**

Explore more data at ephtracking.cdc.gov/DataExplorer

The pediatric care provider role

Secondary prevention – timely recognition of acute toxicity concerns

Primary prevention – informed and targeted anticipatory guidance

Chronic pesticide exposure – the importance of diet

"You may not feel any healthier right away, but you'll definitely feel more smug."

Try Organic Food

...or as your grandparents called it, "Food"

Fox News

GREEN YOUR WORLD

New study finds organic foods are healthier than conventionally grown foods

WebMD

Organic Foods Not Necessarily Better

Study Questions Health Benefits of Eating Organic

The New York Times

ENVIRONMENT

Study of Organic Crops Finds Fewer Pesticides and More Antioxidants

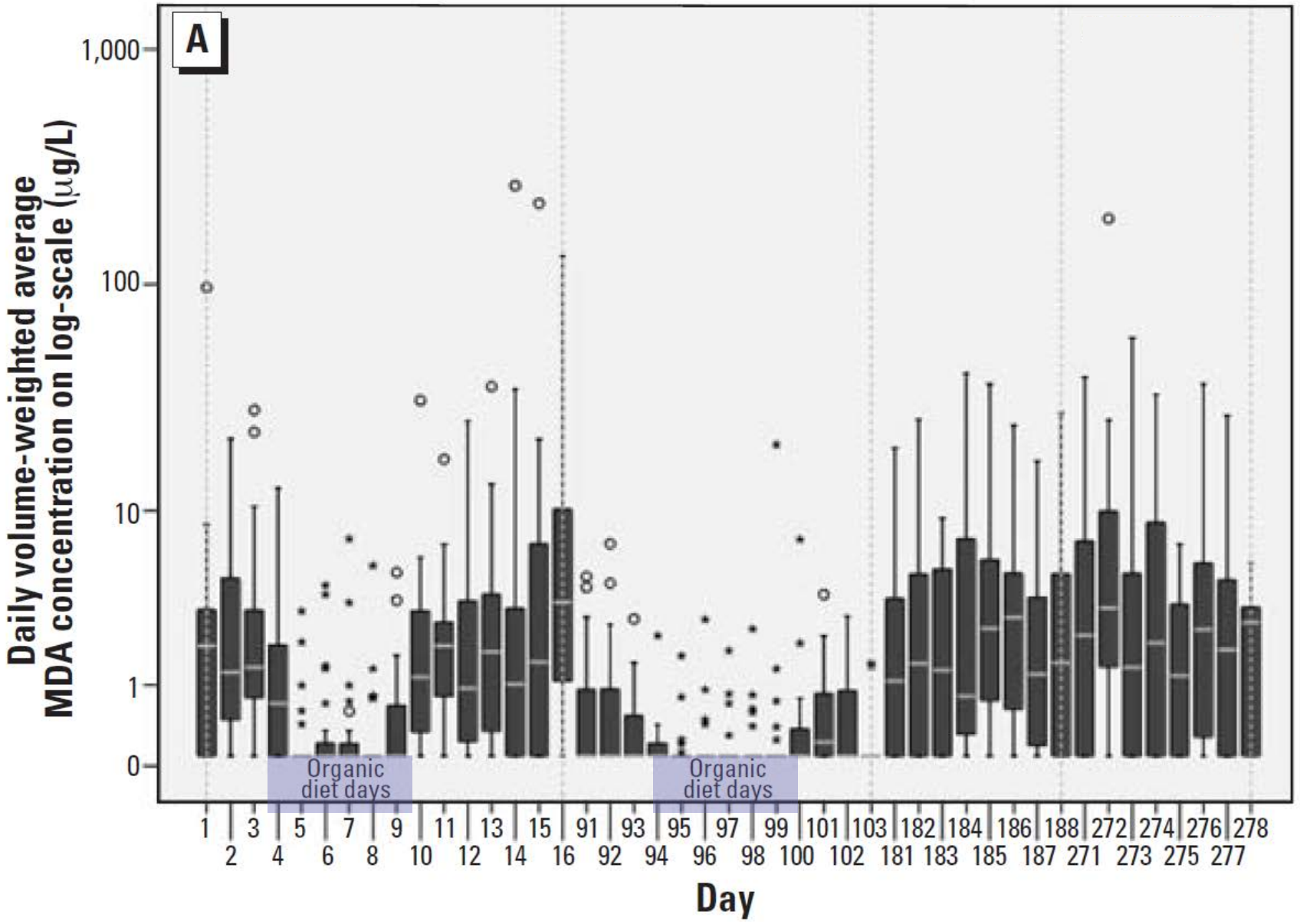
Time Magazine

NUTRITION

Is It Worth Buying Organic? Maybe Not

New research questions whether organic produce and meats are really more nutritious or healthier than conventional varieties

(**MORE:** Does Organic Food Turn You into a Jerk?)


A
Daily volume-weighted average
MDA concentration on log-scale (μg/L)
1,000
100
10
1
0
Organic
diet days
Organic
diet days
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 91 92 93 94 95 96 97 98 99 100 101 102 103 181 182 183 184 185 186 187 188 271 272 273 274 275 276 277 278
Day

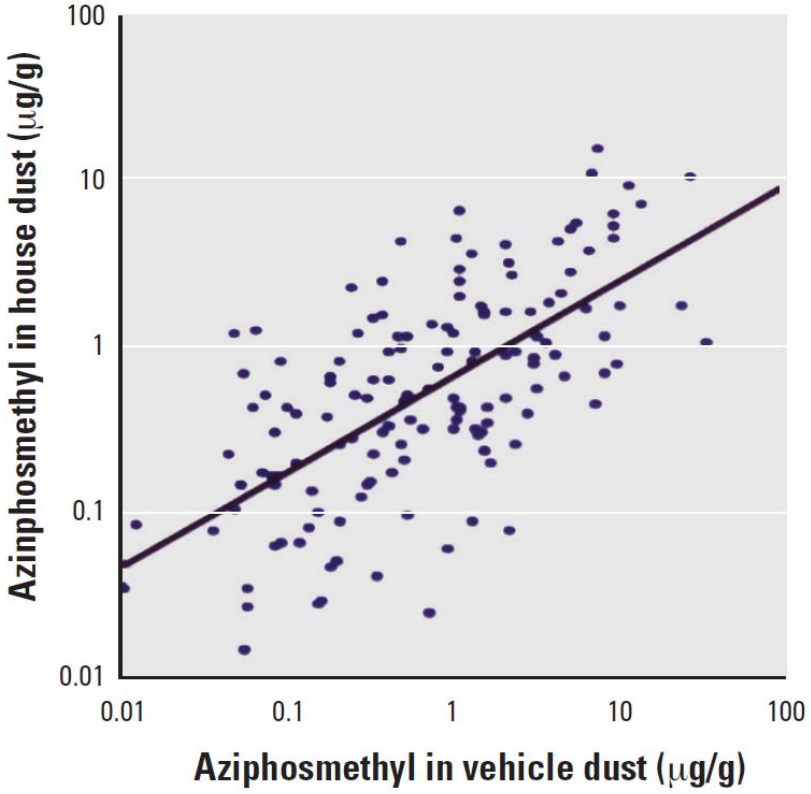
Pesticide “spray drift” can be a problem for workers, neighboring crops and agricultural communities.

Parental Take-Home

Evaluation of Take-Home Organophosphorus Pesticide Exposure among Agricultural Workers and Their Children

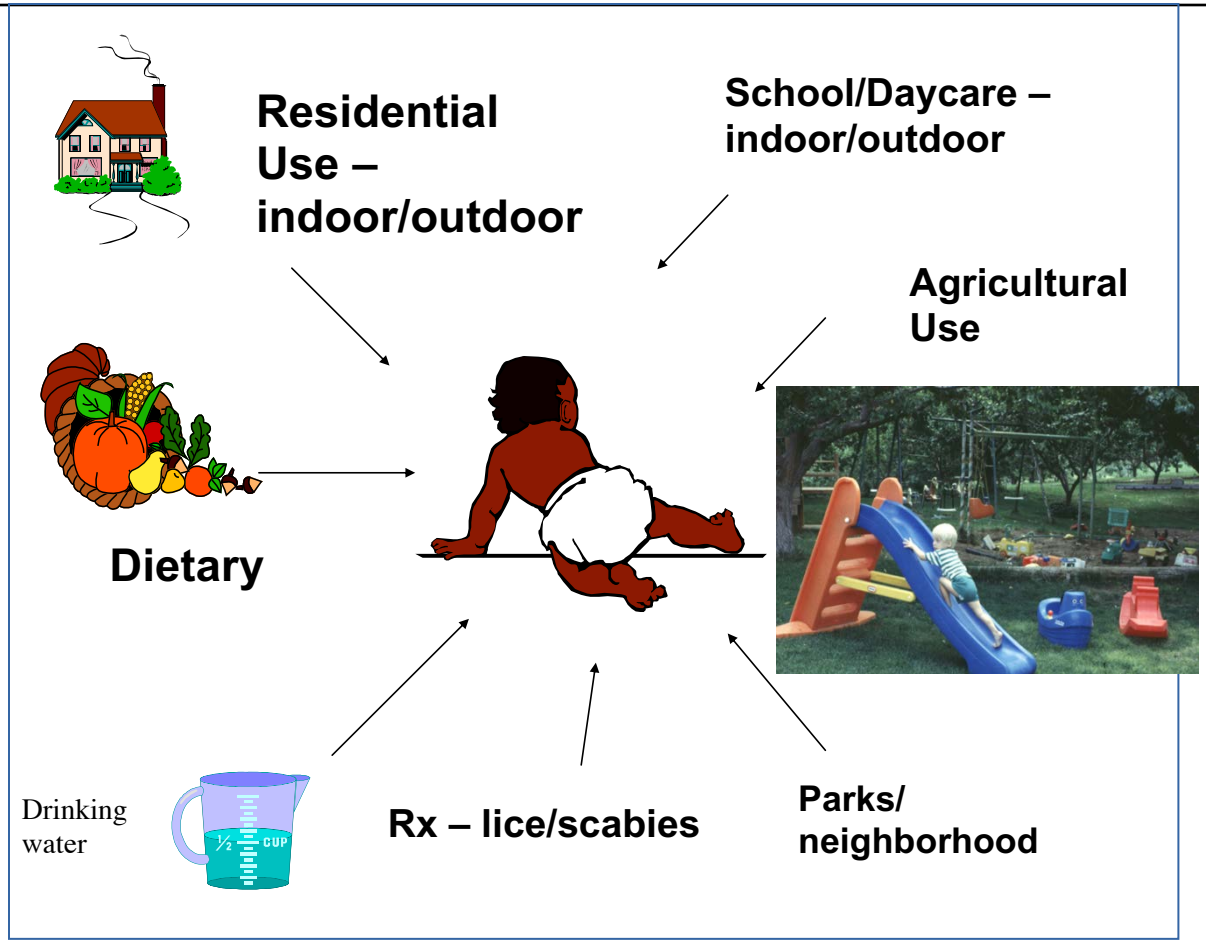
Cynthia L. Curl,[1] Richard A. Fenske,[1] John C. Kissel,[1] Jeffry H. Shirai,[1] Thomas F. Moate,[2] William Griffith,[1] Gloria Coronado,[3] and Beti Thompson[3,4]

[1]Department of Environmental Health, School of Public Health and Community Medicine, University of Washington, Seattle, Washington, USA; [2]SNBL USA Ltd., Everett, Washington, USA; [3]Cancer Prevention Research Program, The Fred Hutchinson Cancer Research Center, Seattle, Washington, USA; [4]Department of Health Services, School of Public Health and Community Medicine, University of Washington, Seattle, Washington, USA



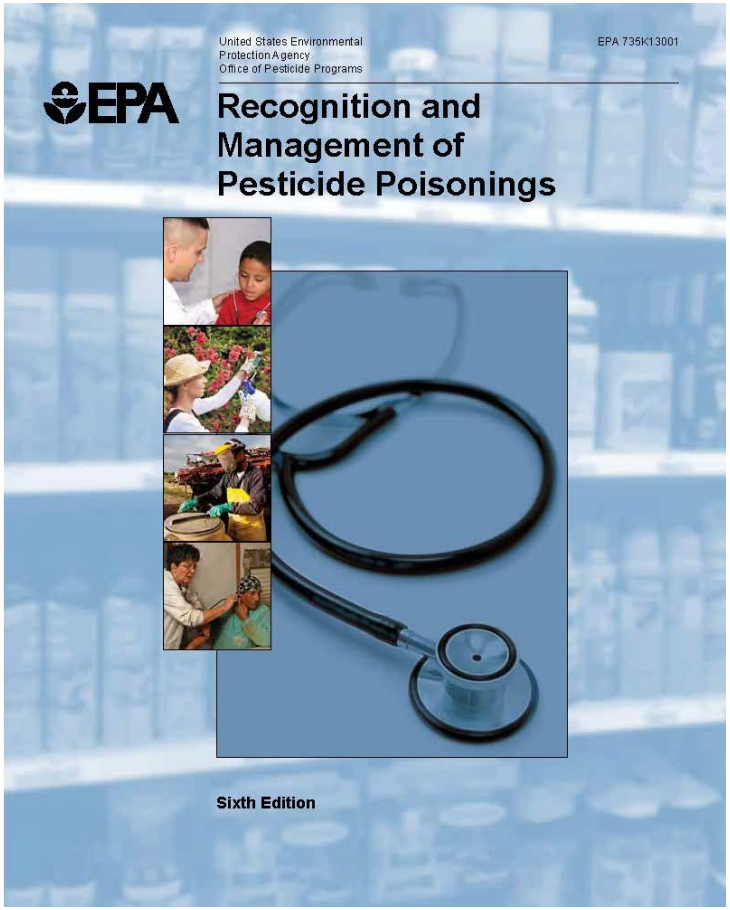
This is why we should protect our kids. We need to get rid of any pesticides that we could bring home from the fields. Here are some tips.

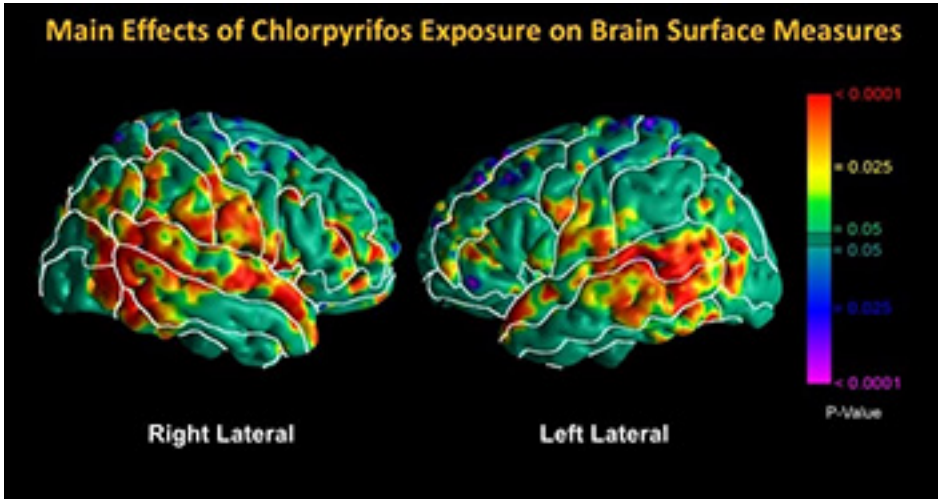
Multiple sources of exposure



Wu X et al. Env Health 2013

Pediatric Health Implications





www.niehs.nih.gov/research/supported/success/2016/rauh/index.cfm

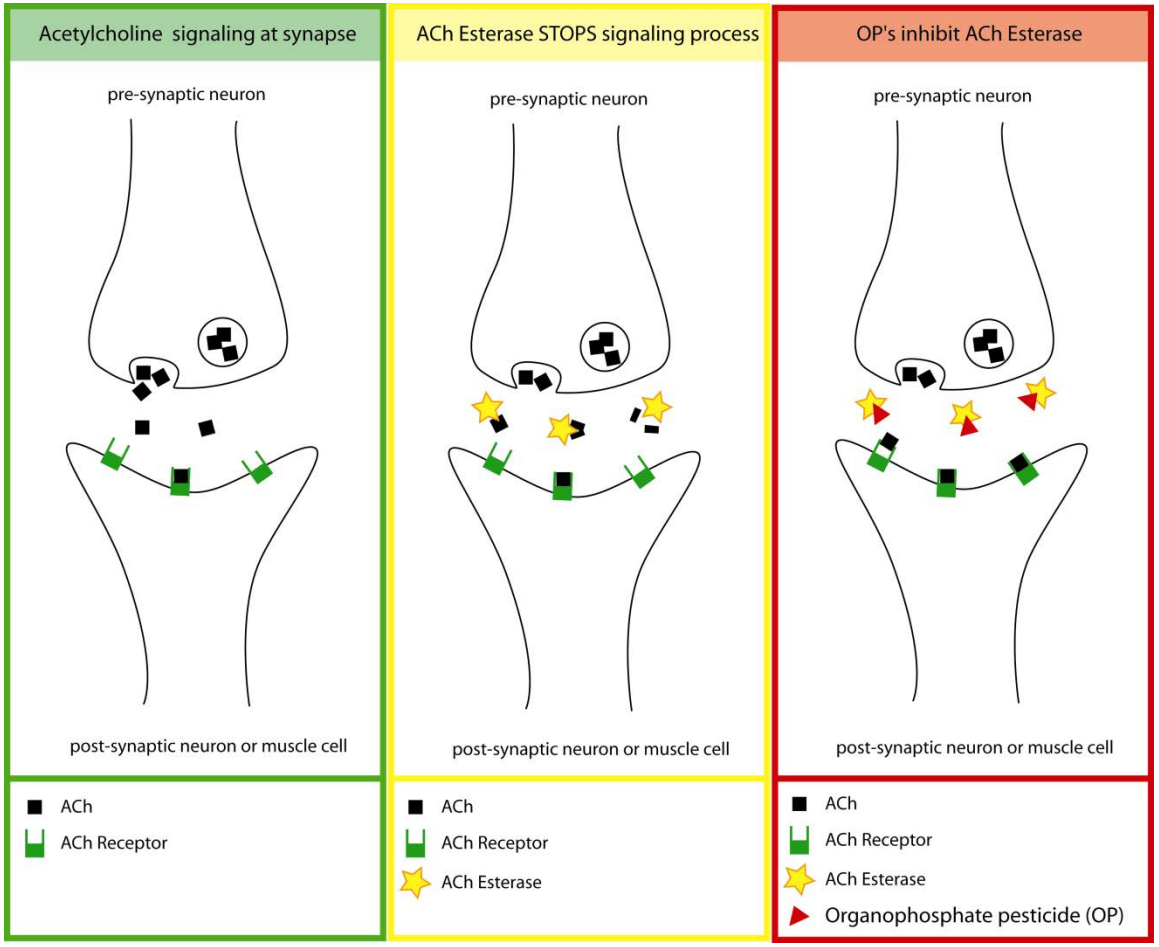
www.epa.gov/pesticide-worker-safety/recognition-and-management-pesticide-poisonings

Organophosphate/N Methyl Carbamate Insecticides

- **Important in acute poisoning reports**
- Widely used in agriculture, some home garden products
- Variable acute toxicity but many = high (class I and II)
- Well absorbed via inhalation, dermal, ingestion

- Malathion, Chlorpyrifos (Dursban), Phosmet, Carbaryl (Sevin), Methyl parathion (Pesticide label lists active ingredient)

OP/Carbamates Acute Neurotoxicity : Cholinesterase Inhibition



Nausea, vomiting, diarrhea
Weakness, twitching, paralysis
Visual blurriness (meiosis), Confusion, lightheadedness, coma

Hypersecretion:
Tearing
Bronchial secretions, wheezing, edema
Sweating, salivation, urination

Signs and Symptoms in a CHILD

More likely to have hypotonia & mental status changes such as lethargy and coma, seizures

eg. seizure occurrence based on case series:

- adults 2-3%
- children 22-25%

Classic cholinergic excess signs of hypersecretion are less likely to occur, particularly at initial presentation

Often mistaken for viral illness (respiratory infection, gastroenteritis, meningitis)

Case series found 80% of children with organophosphate poisoning were transferred with the wrong diagnosis

Zweiner RJ, et al. Organophosphate and carbamate poisoning in infants and children. *Pediatrics* 1988;81:121-6. Sofer S. Carbamate and organophosphate poisoning in early childhood. *Ped Emer Care* 1989;5:222-5.

Pyrethroid Insecticides

Also neurotoxic but…. *Generally* less acutely toxic compared to OPs/ carbamates

Sites of action = Na & Cl channels; GABA, nicotinic acetylcholine, & peripheral benzodiazepine receptors = varied acute neurotoxicity

Generally low skin absorption (exposure via ingestion, inhalation)

- Type I – (permethrin)
- Type II (contain a cyano group) – cypermethrin, fenvalerate

TYPE II are more commonly associated with poisonings

Pyrethroid signs/symptoms

- Nonspecific symptoms - headache, fatigue, vomiting, diarrhea, and irritability
- Reflex hyperexcitability, tremor, choreoathetosis
- Similarities to OPS-hypersecretion, muscle fasciculation, pulmonary symptoms and seizures

And for lower dose exposures, (without symptoms above)

- Paresthesias - Skin irritation and paresthesias (burn/tingle/numb), often face (most commonly reported for Type II group)

International Journal of
Environmental Research and Public Health

Case Report

Home Use of a Pyrethroid-Containing Pesticide and Facial Paresthesia in a Toddler: A Case Report

Alexandra Perkins [1,2], Frederick Walters [3], Jennifer Sievert [4], Blaine Rhodes [4], Barbara Morrissey [4] and Catherine J. Karr [2,5,*]

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2 Northwest Pediatric Environmental Health Specialty Unit, Seattle, WA 98105, USA
3 Bainbridge Pediatrics, Bainbridge Island, WA 98110, USA; fwalters@bainbridgepediatrics.com
4 Washington State Department of Health, P.O. Box 47825, Olympia, WA 98504, USA; Jennifer.Sievert@doh.wa.gov (J.S.); Blaine.Rhodes@doh.wa.gov (B.R.); Barbara.Morrissey@doh.wa.gov (B.M.)
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Int J Env Res Public Health 2016

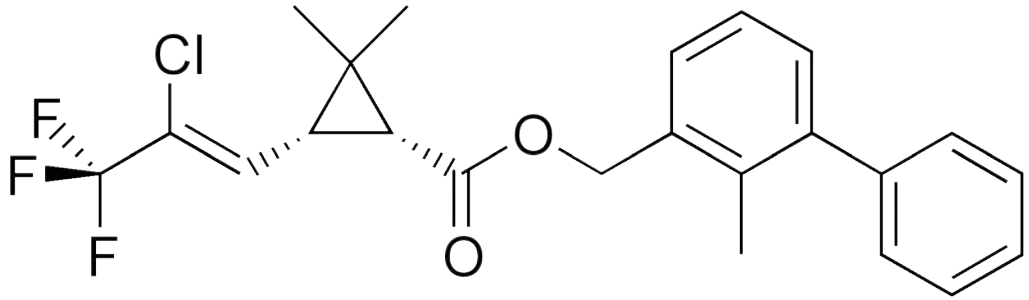
Case – call to NW PEHSU

13 month old, previously healthy male

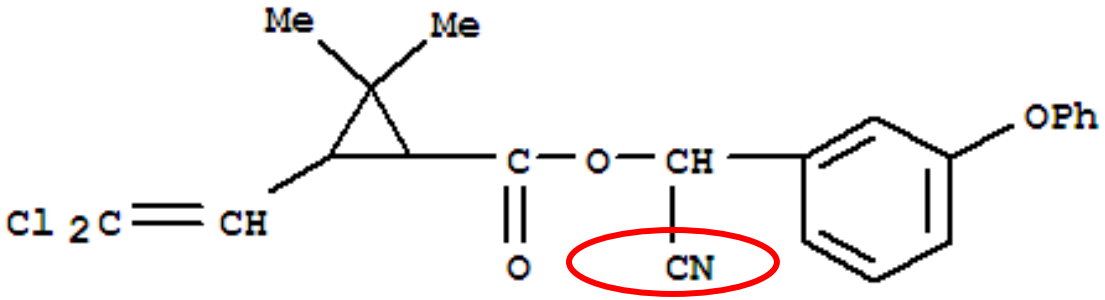
Acute onset of facial movements that seem like “twitching”

“…may be coincidental, but I think the timing is somewhat concerning that the family recently has been spraying for ants the last 2 weeks”

Combination Spray: Synthetic Pyrethroids



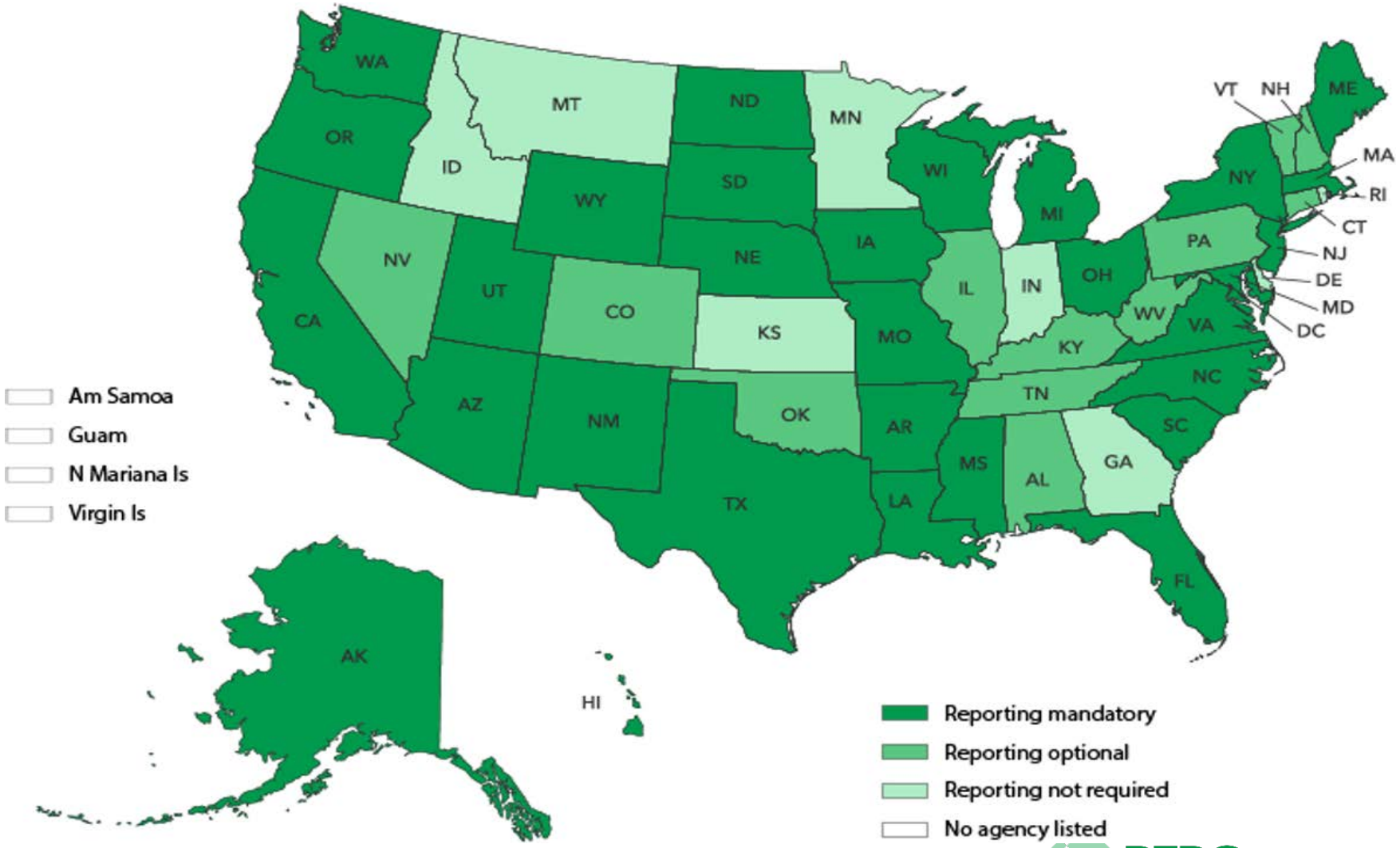
Bifenthrin (Type I)



Most commonly associated with human poisoning

Zeta-Cypermethrin
(Type II – cyano group)

Pesticide Reporting Requirements



http://pesticideresources.org/med/

PERC-med
Pesticide Educational Resources Collaborative - Medical

PEHSU, WA DOH Response

2 metabolites of cypermethrin could be tested in WA DOH State Lab

3 Phenoxybenzoic Acid (PBA) and Trans-DCCA

	Sx start & continue		**Sx resolve, no notable sequelae**			
	10/24/13-10/31/13 Pesticide applied	11/01/13 DOH education Use stopped, clean up, safe pest control	11/15/13	12/20/14	WA kids 6-11 years 50th % (95% CI)	WA kids 6-11 years 95th % (95% CI)
3-PBA mcg/g Cr		**2.22**		**0.329**	0.53 (0.41-0.69)	7.47 (2.86-15.4)
trans-DCCA Mcg/g Cr		**3.82**		**0.453**	< LOD < LOD-0.421)	2.61 (1.4-15.8)

DOH Pesticide Incident Summary Report – Confirmed pesticide related illness

Chronic low dose effects

Mechanisms ≠ acute toxicity mechanisms

Concern for developmental toxicity

Epidemiological associations with major chronic morbidities of childhood:

Neurodevelopment/Neurobehavior (ADHD, Autism, Learning disability)

Pediatric cancer (Leukemia, brain)

Birth outcomes (premature birth, fetal growth, birth defects)

Other emerging data – asthma, diabetes

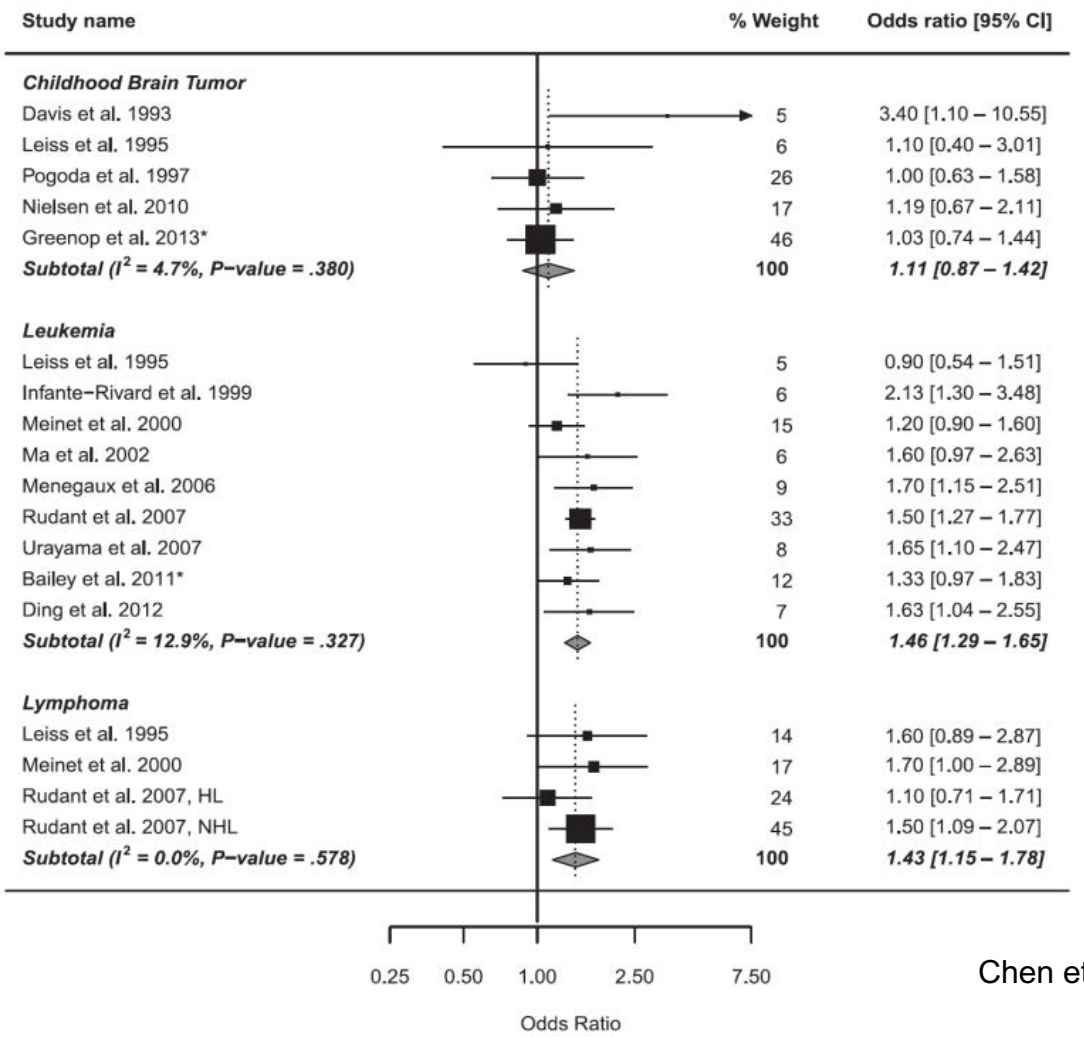
Roberts JR, Karr CJ; Council on Environmental Health. American Academy of Pediatrics. Pesticide exposure in children. Technical Report. Pediatrics. 2012;130(6): *e1765 -e1788*

Significant Evidence Base: Early Life Chronic OP/PYR Pesticide Exposure & Adverse neurodevelopmental outcomes

	Organophosphates	**Pyrethroids**
Biological Plausibility/Toxicological Mechanisms	Many Studies	Several studies
Epi (X-Sectional)	↑ ADHD	↑ Special Ed, LD/ADHD
Epi (Prospective Cohort)	Many studies: Neonatal reflexes Toddler MDI/PDI Behavior (CBCL/BSID) Cognition (IQ) Symptoms ASD/ADHD	Several studies: Toddler MDI Cognition Behav probs/EF (BASC/BRIEF)

Eskenazi Env Health Perpect 2007, Bouchard Pediatrics 2010, Horton Pediatrics 2011, L Quirós-Alcalá Env Health 2017, Oulhote 2013, Viel Env Int 2015, Schuman Env Health 2015; Watkins 2016, Furlong Neurotox 2017, Liu Env Health Perspect 2016, Jusko Env Health Perspect 2019

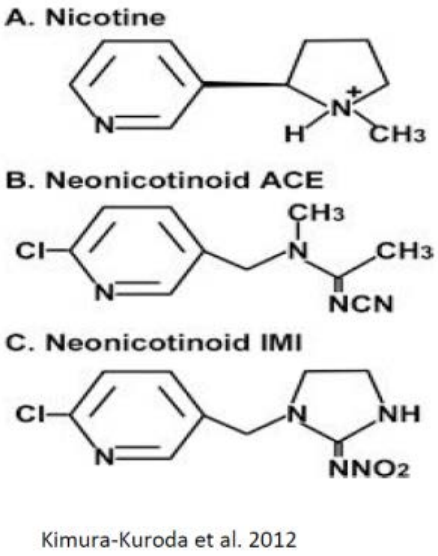
Meta analysis childhood cancers and exposure to home pesticides in childhood



Chen et al. Pediatrics. 2015

Neonicatinoids

- Newer class – developed to replace organophosphates/carbamates
- Exponential growth- in use in agriculture,
  also pet products
- Chemically similar to nicotine -nicotinic acetylcholine receptor (nAChR)
- Highly persistent in soil, crops
- Acetimiprid (ACE), Imidacloprid (IMI), thiamethoxam (THO), clothianidin (CLO)



Kimura-Kuroda et al. 2012

Neonics – child health concern???

- Animal models – endocrine disruption, reproductive toxicity
- Cross placenta and blood brain barrier
- New biomonitoring data – CDC/NHANES (Espina et al. Env Res 2019)
  - ~50% US population = at least one urinary metabolite detected
  - Children 3–5 years of age had higher concentrations of N-desmethyl acetamiprid than any other age groups
- Systematic review 2017, n = 4 population based epi studies (Cimino et al. Env Health Persp 2017)

  Tetralogy of Fallot (AOR 2.4, 95% CI: 1.1, 5.4)

  Anencephaly (AOR 2.9, 95% CI: 1.0, 8.2)

  ASD (AOR 1.3, 95% (CrI): 0.78, 2.2)

GLYPHOSATE “Round Up”

My students’ textbook, page 343: “[Glyphosate] has no teratogenic, developmental or reproductive effects. Genotoxicity and carcinogenicity studies in animals were negative.”

The New York Times

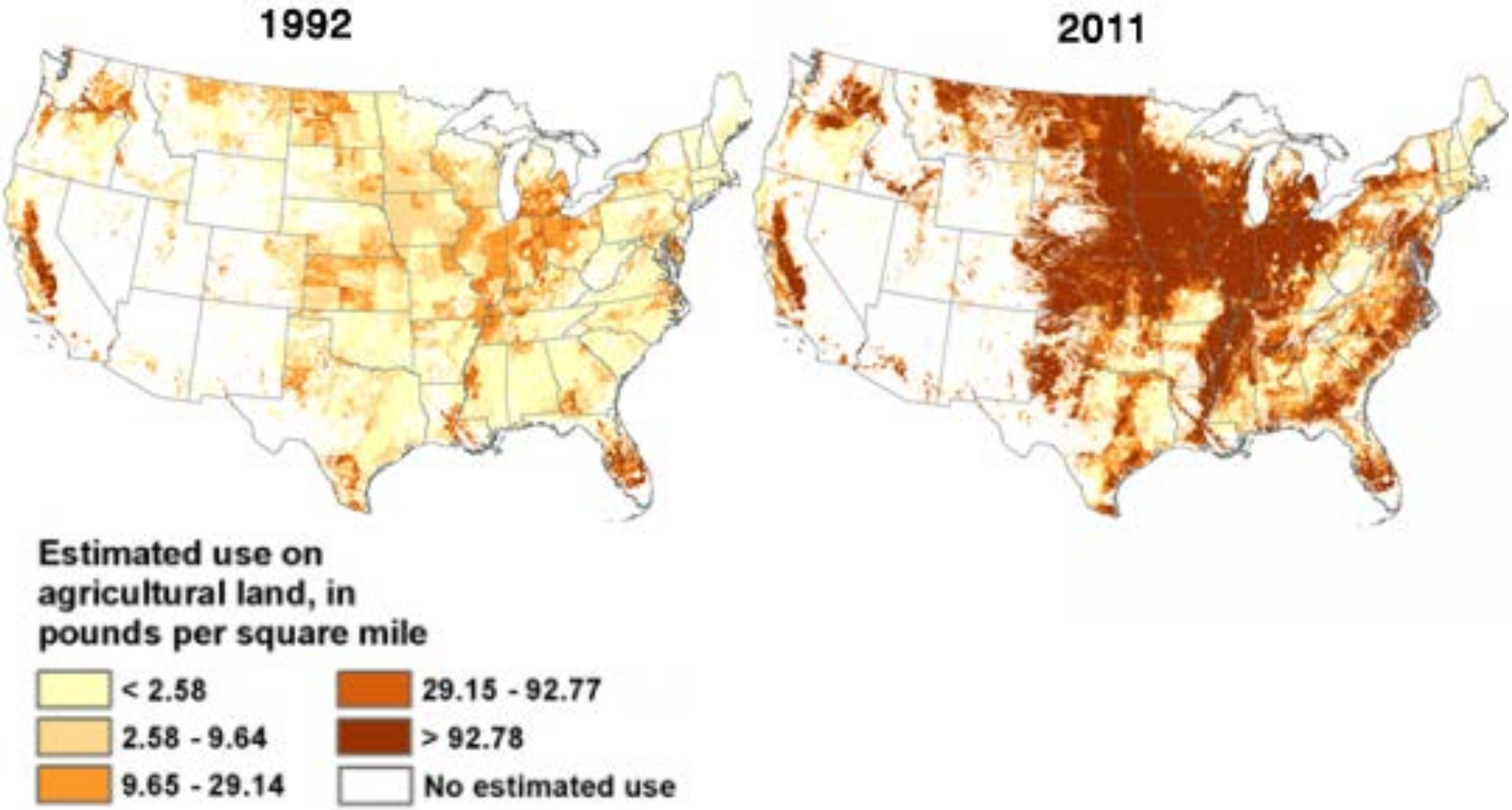
$2 Billion Verdict Against Monsanto Is Third to Find Roundup Caused Cancer

Alva Pilliod, left, and Alberta Pilliod, third from left, with their lawyers after a jury ordered Monsanto to pay the Pilliods $2 billion in damages. Paul Elias/Associated Press

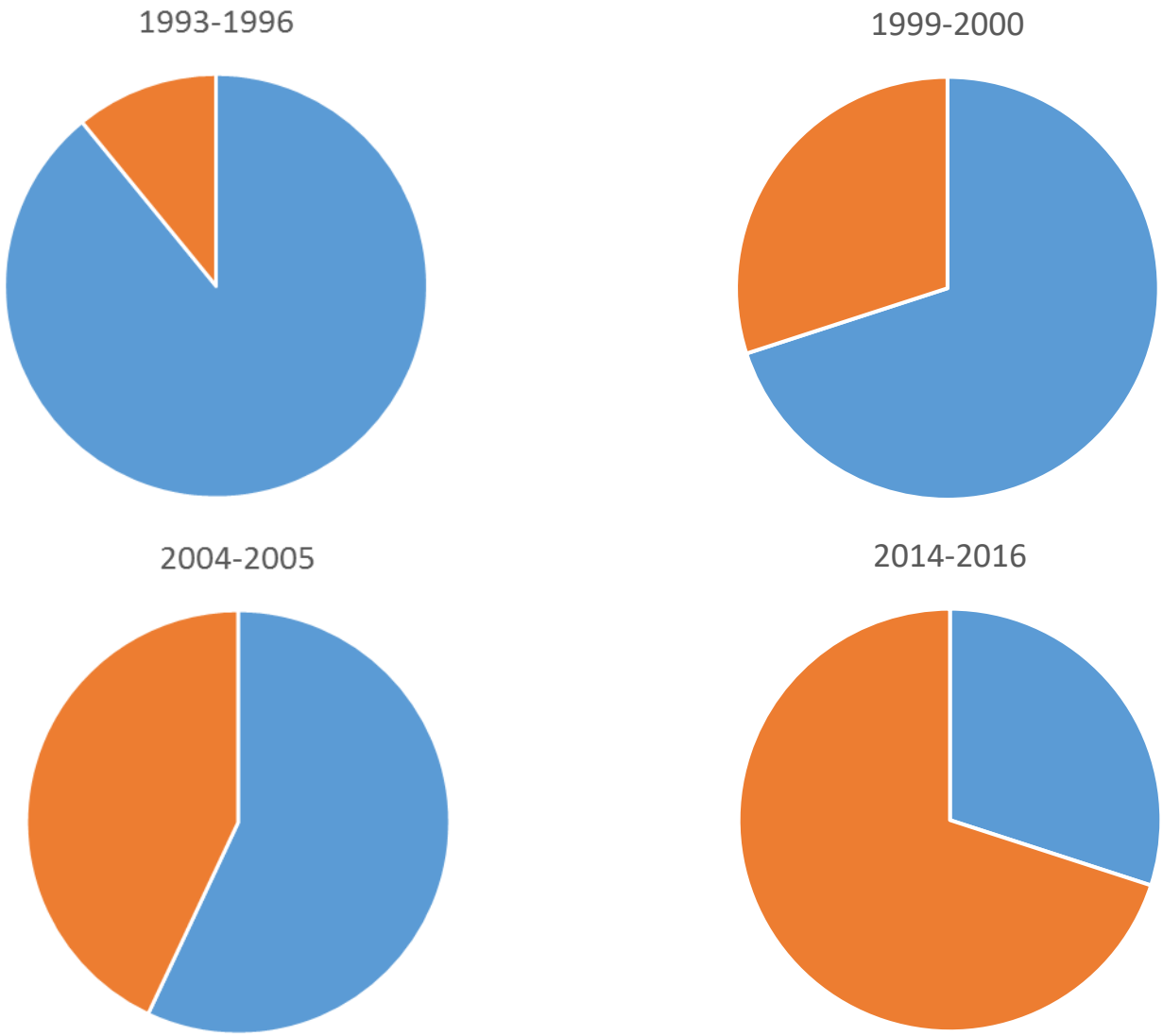
By Patricia Cohen

May 13, 2019

Estimated Agricultural Use for Glyphosate



Percent of San Bernardino study participants with measurable exposure to glyphosate



Source: Journal of the American Medical Association (JAMA), Oct 2017

NEWS

POLITICS U.S. NEWS BUSINESS WORLD TECH & MEDIA THINK SPORTS

Popular weed killer's alleged link to cancer stirs widespread concern

Two juries have implicated Roundup as the cause of cancer in frequent users, but major public health agencies disagree over whether it is a carcinogen.

Roundup products for sale at a store in San Rafael, California on July 9, 2018. Josh Edelson / AFP - Getty Images file

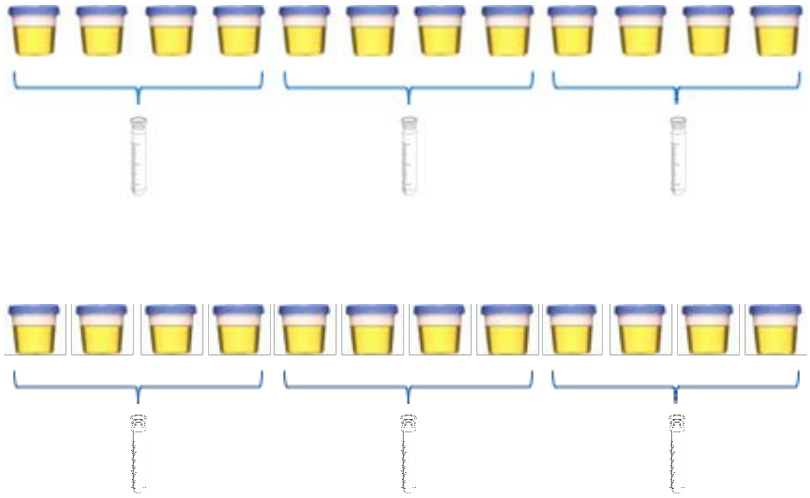
April 1, 2019

Cynthia Curl, an environmental health scientist at Boise State University in Idaho who studies the chemical, said, "many assumptions have been made about the safety of glyphosate that are now being actively questioned. We will see an explosion of information about glyphosate, and it's about time. We're really playing catch-up on this one."

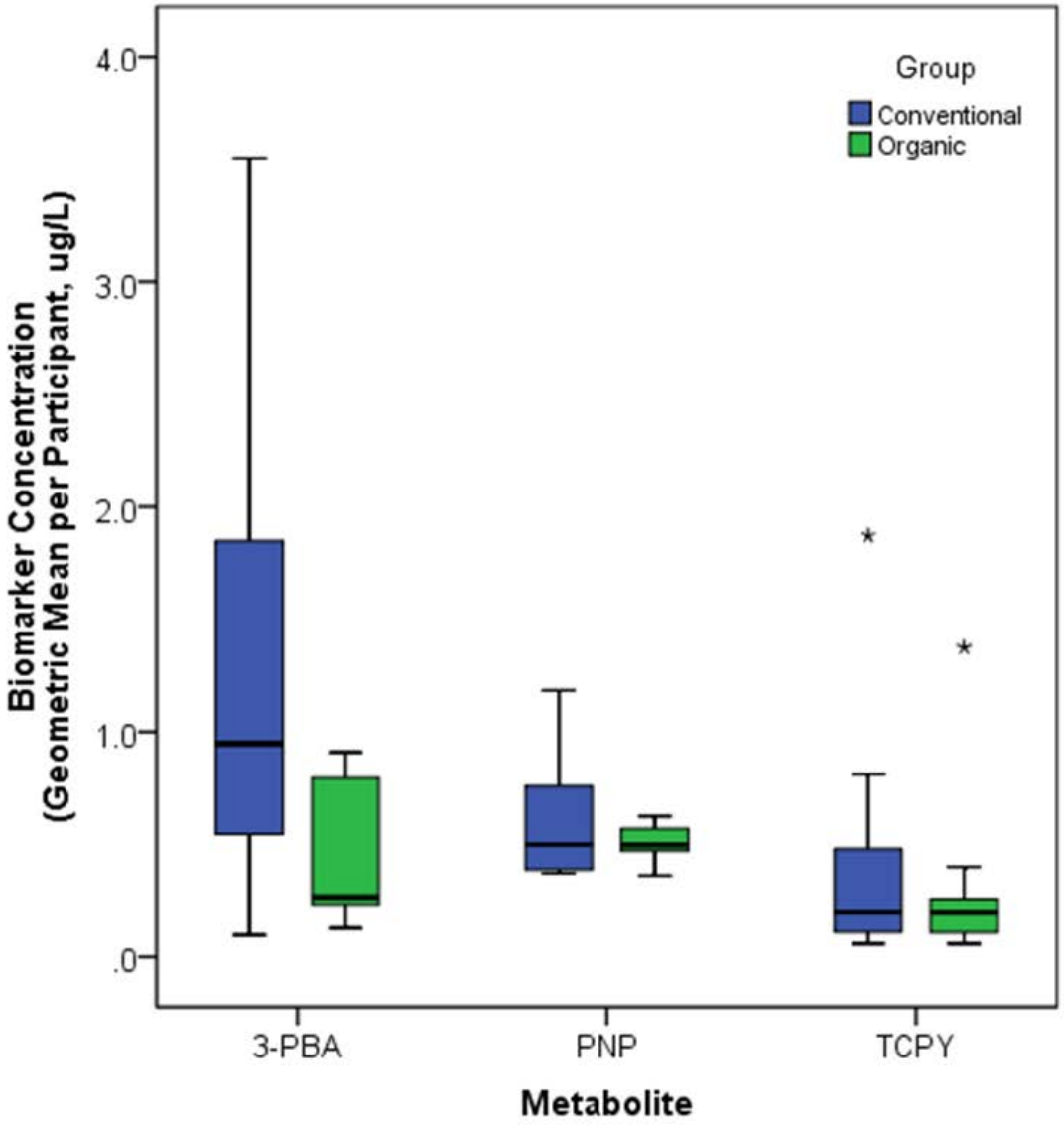
Conventional Group

Organic Group

1 baseline sample



24 weekly samples composited in 1 mL aliquots to create six “monthly” aggregate samples representing the **second and third** trimesters



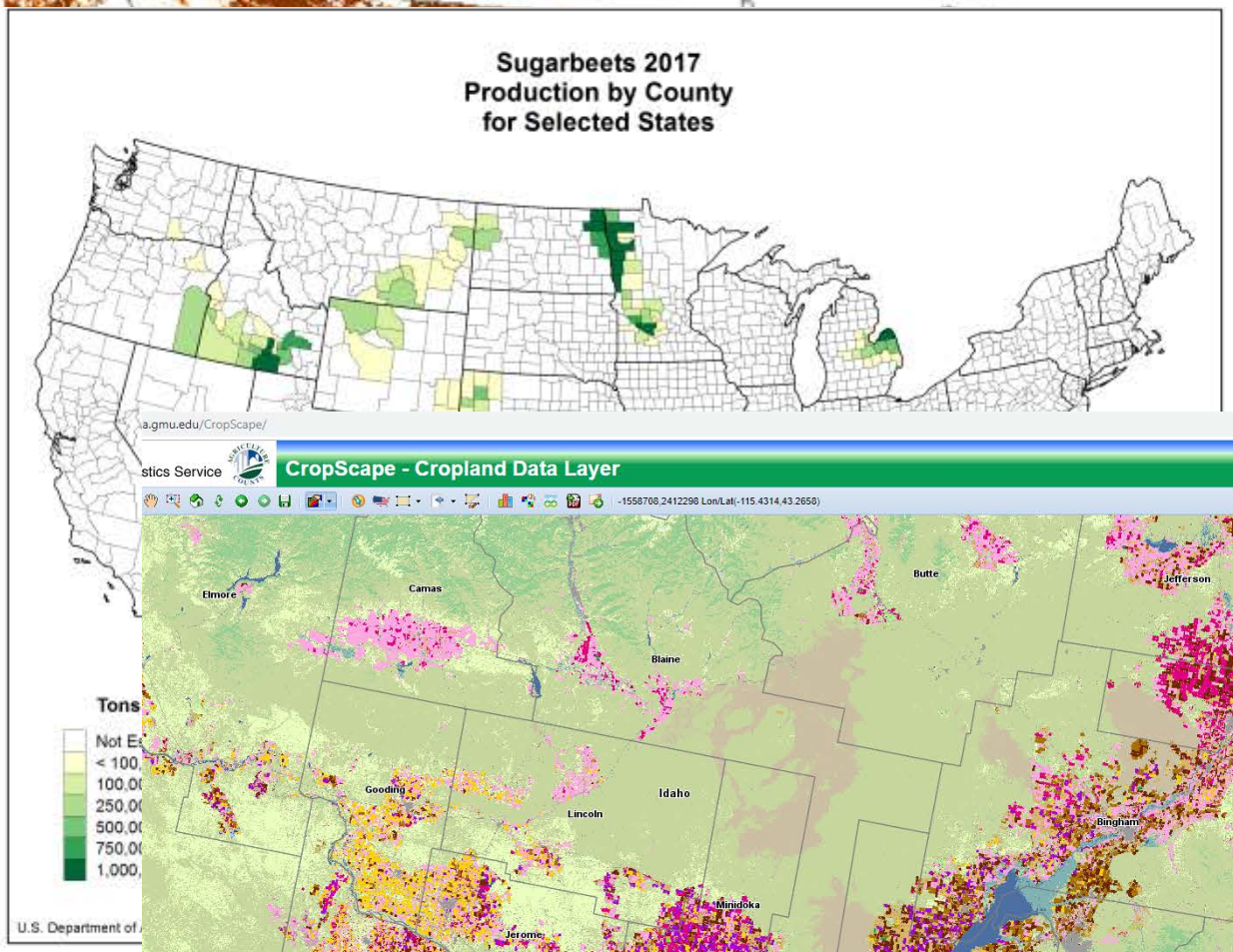
Curl et al. 2019 Environment International

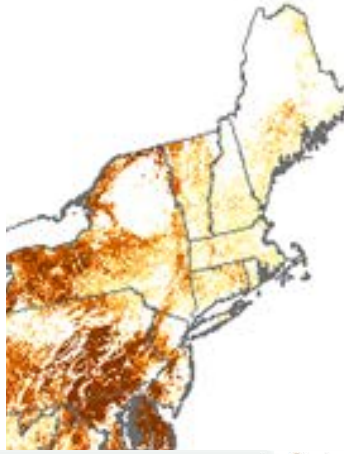
Measurement of Agricultural and Dietary Glyphosate Exposure among Pregnant Women

- To gain a better understanding of pregnant women's exposure to glyphosate
- (If exposed) to understand how much of that exposure is coming from where they live and how much is coming from what they eat

Estimated Agricultural Use for Glyphosate , 2014 (Preliminary)

EPest-Low



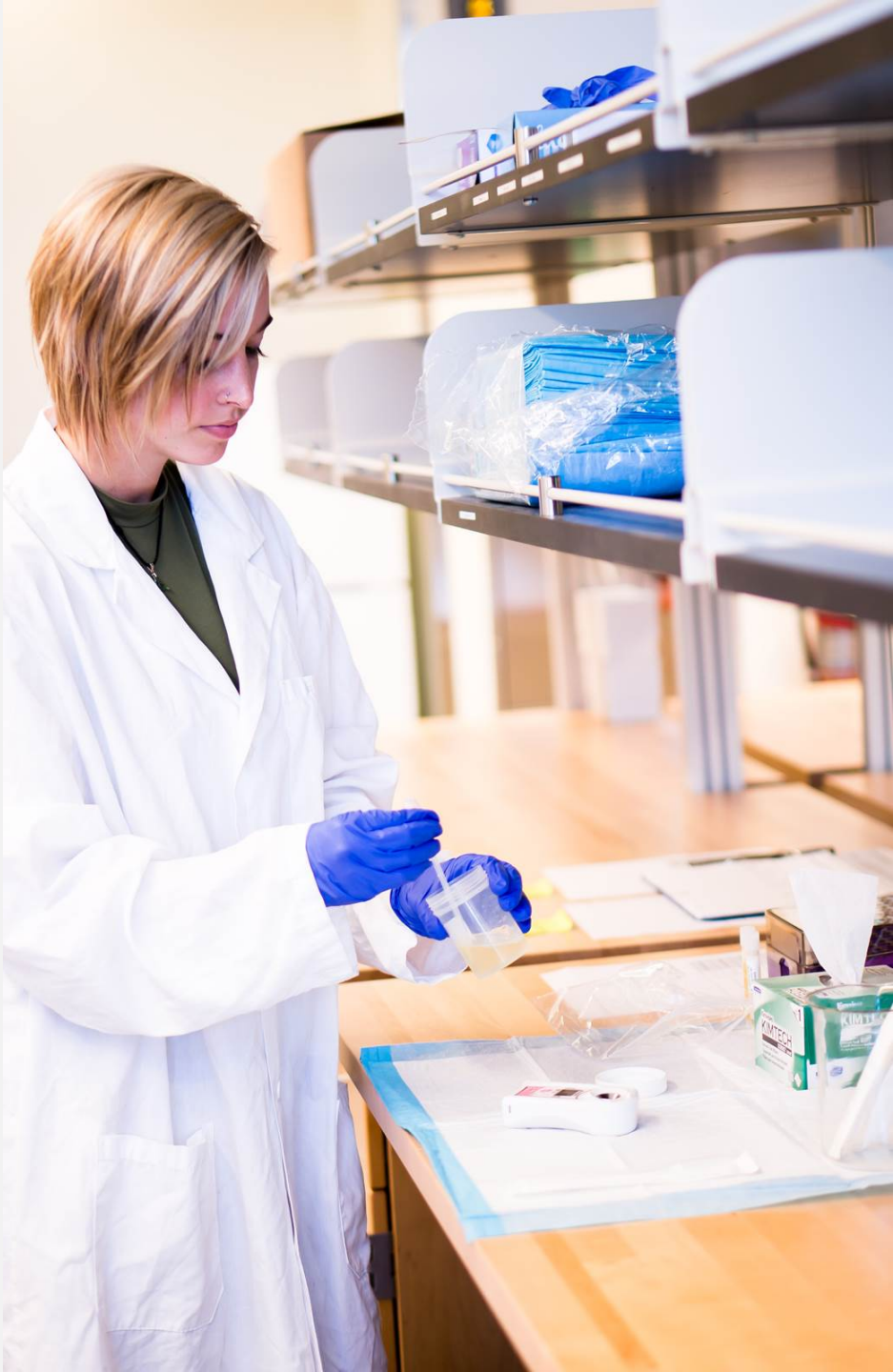


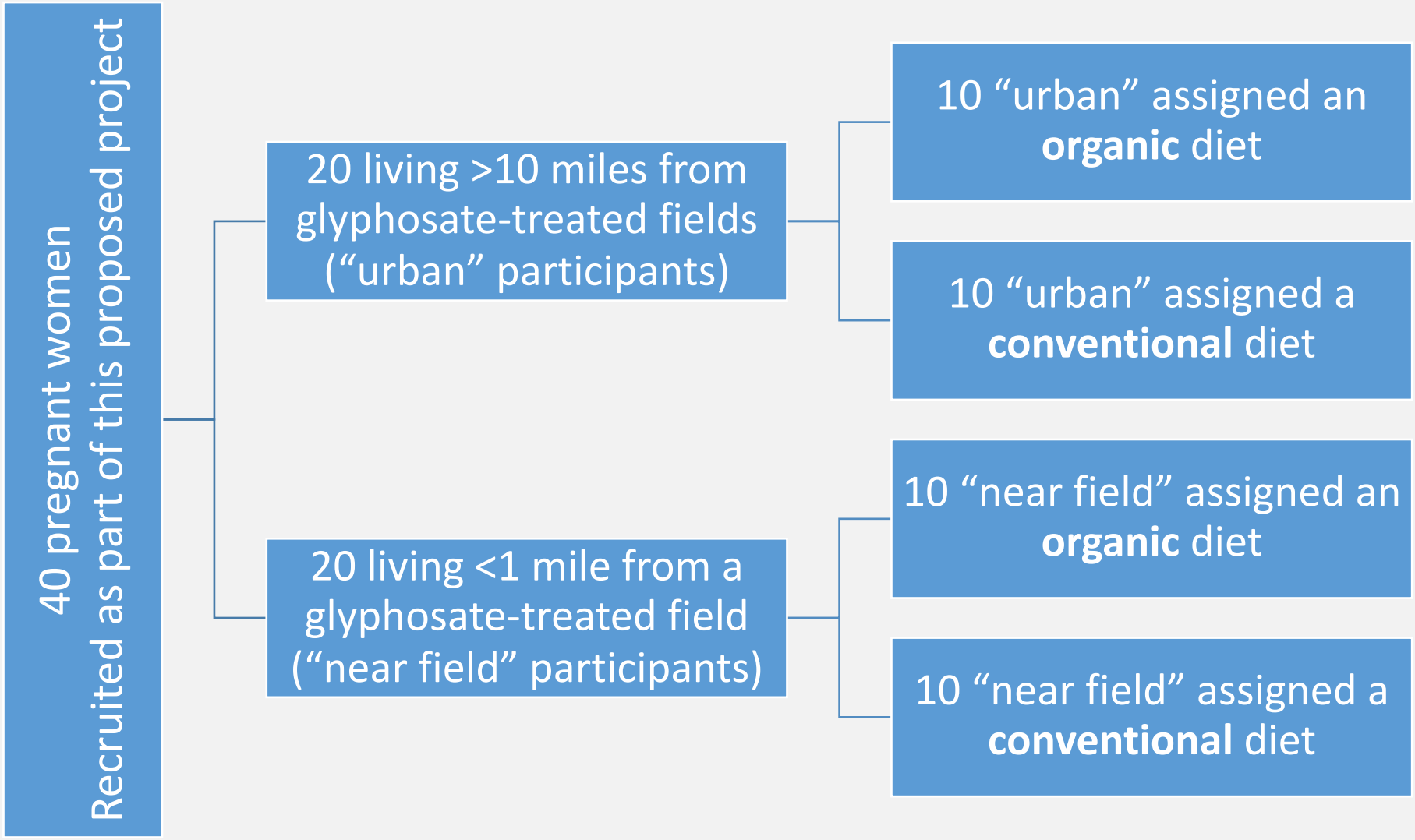
Estimate
agricultu
pounds

< 4.
4.52
21.13 - 88.06
> 88.06
No estimated

Participants will take part in a two-week organic and conventional dietary intervention study, in a cross-over design.

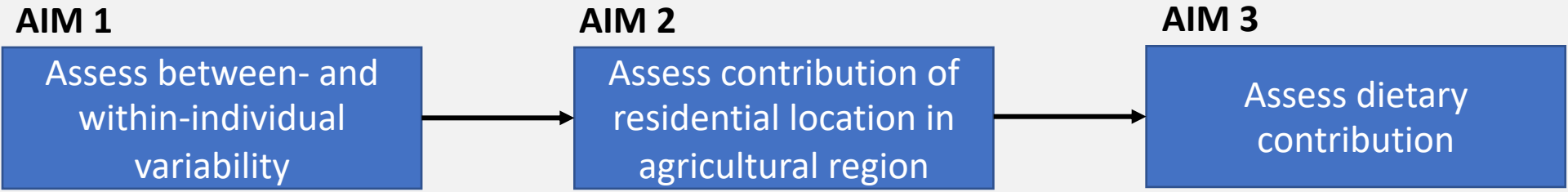
We will collect weekly urine samples throughout pregnancy, and daily urine samples during the dietary intervention, for a total of 36 samples per participant, and 1,440 samples in total.




40 pregnant women
Recruited as part of this proposed project
20 living >10 miles from glyphosate-treated fields ("urban" participants)
20 living <1 mile from a glyphosate-treated field ("near field" participants)
10 "urban" assigned an **organic** diet
10 "urban" assigned a **conventional** diet
10 "near field" assigned an **organic** diet
10 "near field" assigned a **conventional** diet

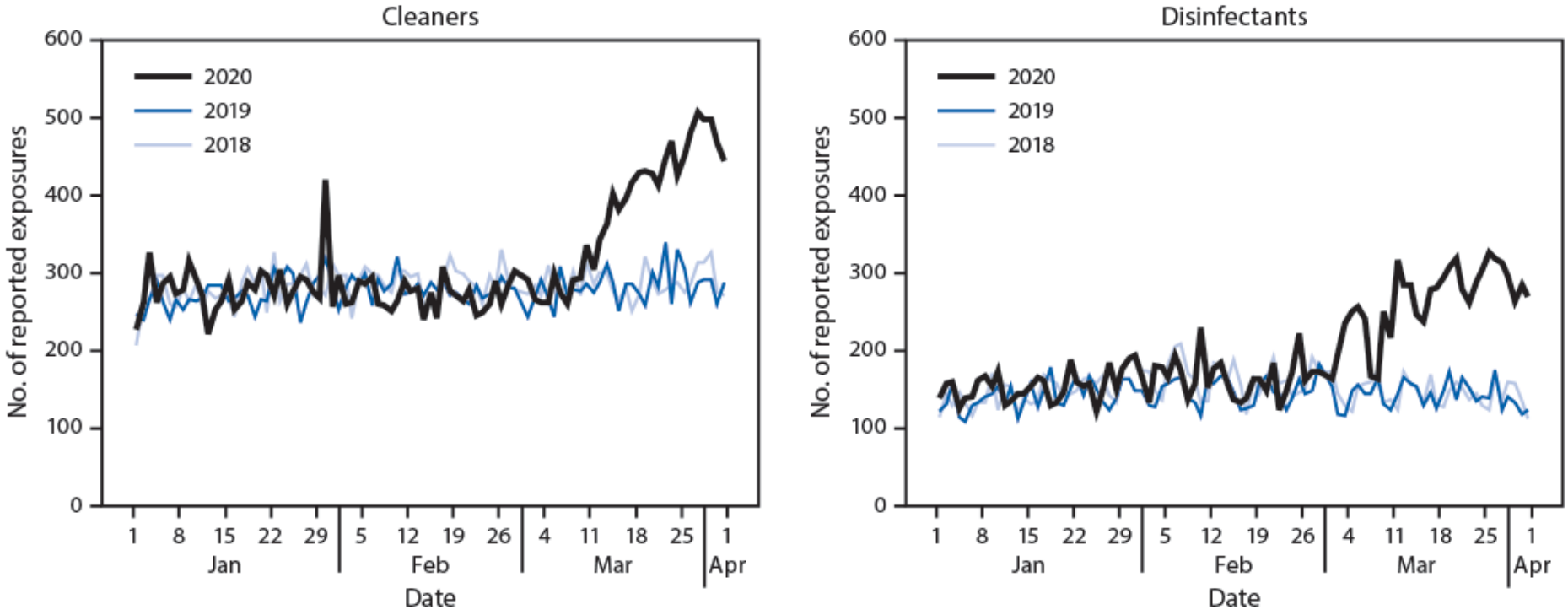
Despite its extensive use, frequent environmental presence and potential toxicity, very little biomonitoring data exists to characterize human exposure to glyphosate.

This project aims to assess glyphosate exposure among a cohort of pregnant women and to quantify the relative contribution of agricultural and dietary sources to this exposure.



Antimicrobial Pesticides: COVID-19 Killers

Daily Exposures to Cleaners and Disinfectants
Reported to US Poison Control Centers
January-March 2018, 2019, 2020



MMWR April 24, 2020 / 69(16);496–498

Educate Families on Appropriate Use

- Know when & which surfaces should be cleaned and/or disinfected
- Cleaning with soap & water is sufficient (in most cases) for households where no one is sick
- Sanitize or wash hands when returning home before touching anything
- Choose safer sanitizers/disinfectants – look for the seal – and know what to avoid

  Bleach, Quaternary Ammonium Compounds = asthmagens
- Follow label directions – allow for proper dry time, never mix products/chemicals
- Store cleaners, sanitizers, disinfectants, & cleaning tools out of reach from kids
- Keep areas well-ventilated during use

Safer options are available

Look for Safer Choice, Green Seal®, Ecologo® and Design for the Environment (DfE) labels on products.

Key Terms

Cleaner

Removes germs, dirt, and impurities from surfaces or objects. Works by using soap/detergent, water and friction to physically remove dirt and germs from surfaces. Cleaning before disinfecting reduces spreading infection more than disinfecting alone.

Sanitizer

Reduces germs on surfaces to levels considered safe for public health (usually 99.99%). Products must be EPA registered.

Disinfectant

Destroys almost all infectious germs, when used as the label directs on a surface. No effect on dirt, soil, or dust. Should be used where required by law, in high-risk and high-touch areas, or in case of infectious disease. Products must be EPA registered.

www.deohs.washington.edu/pehsu/

Non acute exposure “cases”

I’m worried about the pesticides in my garden/home/job – how can I protect my child?

Is organic food worth it?

What do low everyday low doses mean for health?

Encourage organic?

Why?

- **Organic produce reduces pesticide exposure in children** and there is evidence of potential adverse health impacts in children with low dose exposure
- **Organic farming brings other environmental and occupational health benefits**

Why not?

- Don't want to discourage IMPORTANCE of fruit/vegetable in diet
- Expense

See Healthychildren.org "Is organic worth the price"? and "AAP weighs in for first time on organic foods for children"

Advising patients

- Wash and scrub produce with water (cleansers not necessary), throw away the outer leaves of leafy vegetables, and trim the skin and fat from poultry, fish and meats.
- Purchase organic when possible, but not at the expense of a diet rich in a variety of fresh fruits and vegetables.

Key Anticipatory Guidance

- Informed by Env Hx – occupational exposures in the household, young workers? Pesticide use/storage at home?
- Recommend wash hands and face and change out of contaminated clothes and shoes before returning home, entering car, and wash contaminated clothes separately from the rest of the laundry.
- Discuss safe storage
- Encourage use of low toxicity or non toxic pest control approaches for home/garden pest problems.

Resources

1. **EPA Recognition and Management of Pesticide Poisoning. 6th Edition**. Free online or request free copy. *https://www.epa.gov/pesticide-worker-safety/recognition-and-management-pesticide-poisonings*

2. **NW Pediatric Environmental Health Specialty Unit (NW PEHSU**). 1-877-KID CHEM (Monday-Friday during office hours) or kidchem@uw.edu. *(for acute management – Poison Center) https://deohs.washington.edu/pehsu/*

Factsheets available – pesticides, covid cleaning/disinfecting

3. **PERC- MED**. Pesticide Education Resource Collaborative – Medical *http://pesticideresources.org/med/*

4. Roberts JR, Karr CJ; Council on Environmental Health. American Academy of Pediatrics. **Pesticide exposure in children. Technical Report. Pediatrics. 2012;130(6): *e1765 -e1788***. *https://pediatrics.aappublications.org/content/130/6/e1765.short*

6. US **EPA Citizens Guide to Pest Control and Pesticides**: how to use, choose, store, and dispose of pest control products safely. *https://www.epa.gov/sites/production/files/2017-08/documents/citizens_guide_to_pest_control_and_pesticide_safety.pdf*

7. **Project LEAF (Limiting Exposures Around Families)**

Printable brochures (Eng/Spn) for ag workers on reducing pesticide exposure in children, including take-home exposures from occupational sources. *https://afop.org/health-safety/pesticide-safety/take-home-exposures/*

Northwest PEHSU
Pediatric Environmental Health Specialty Units

Disclaimer and acknowledgements

This material was supported by the American Academy of Pediatrics (AAP) and funded (in part) by the cooperative agreement award number 5 NU61TS000296-02-00 from the Agency for Toxic Substances and Disease Registry (ATSDR).

Acknowledgement: The U.S. Environmental Protection Agency (EPA) supports the PEHSU by providing partial funding to ATSDR under Inter-Agency Agreement number DW-75-95877701. Neither EPA nor ATSDR endorse the purchase of any commercial products or services mentioned in PEHSU publications.

Thank - you

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