

Long-term Health Associations of Childhood Glyphosate Exposure: The CHAMACOS Study

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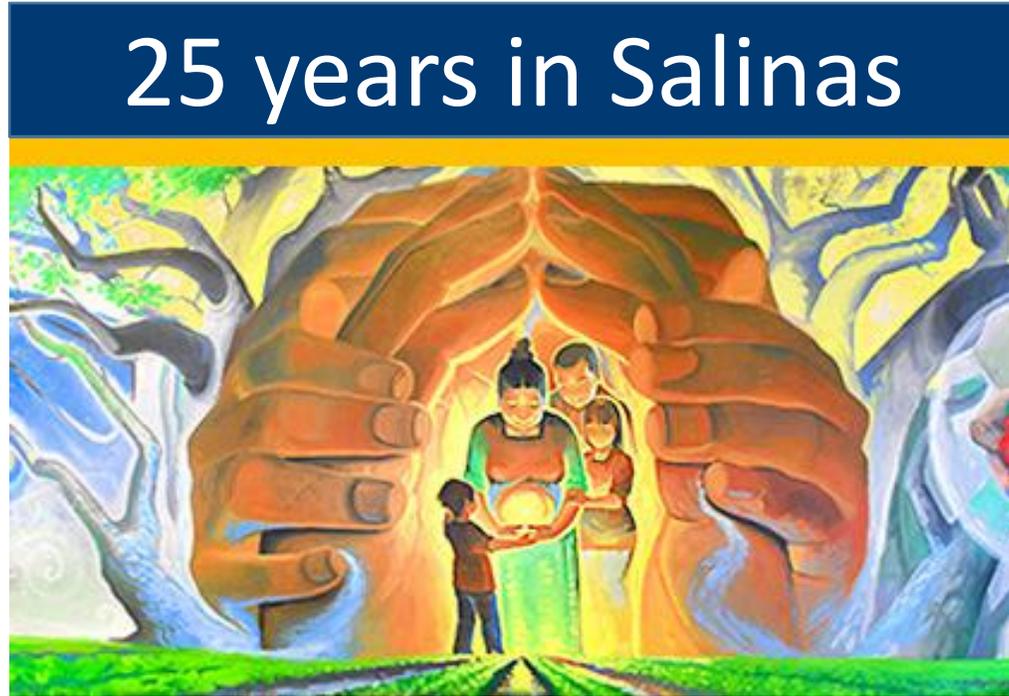
No disclosures

Collaborative for Health and Environment
April 13, 2023

Center for the Health Assessment of Mothers And Children Of Salinas (CHAMACOS)

1998-present

25 years in Salinas



A community-university partnership



Salinas Valley:
The salad bowl of
the Nation.

Shannon1

https://commons.wikimedia.org/wiki/File:Salinas_River_watershed.png

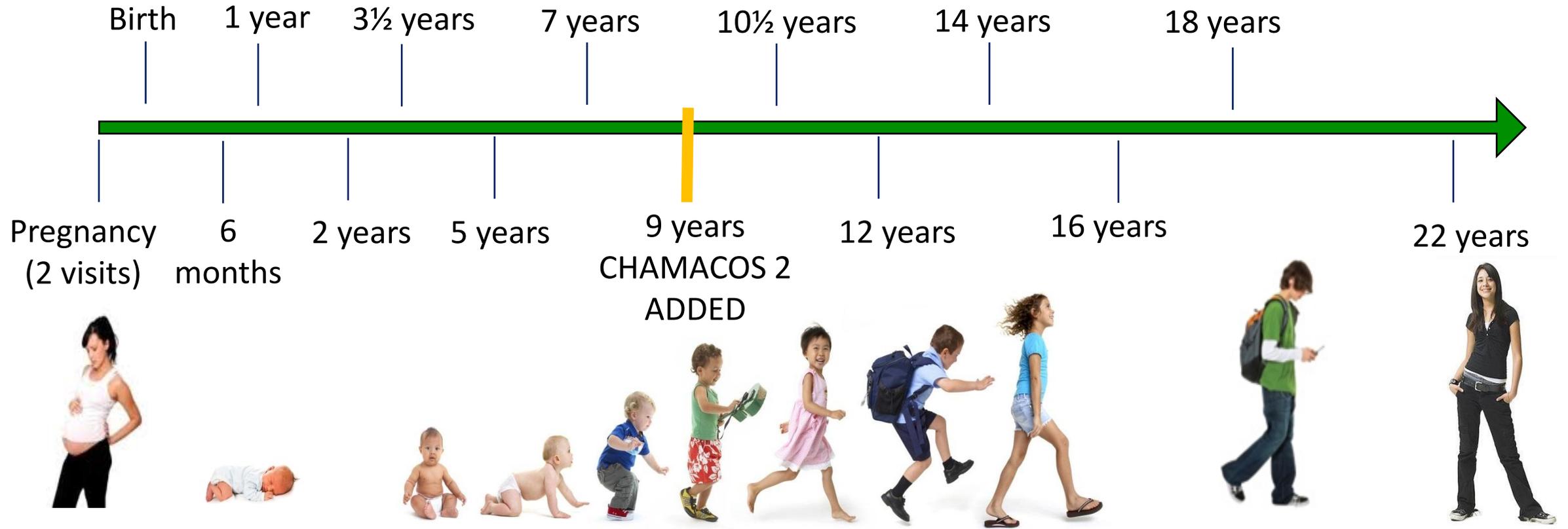


In 1999-2000, we enrolled 601 pregnant women from clinics serving farm workers

- 92% Spanish-speaking
- 85% born in Mexico
- 54% < 5 years in U.S.
- 96% living within 200% of poverty
- 44% 6th grade education or less
- 44% worked in agriculture during pregnancy
- 84% other agricultural workers in home

Since then we have followed the mothers and children and added others at age 9.

They are now 22 years old!



We have evaluated the health and development of the children/youth at each visit

Interviewed mothers and teachers



Tested children



Determined when they entered puberty



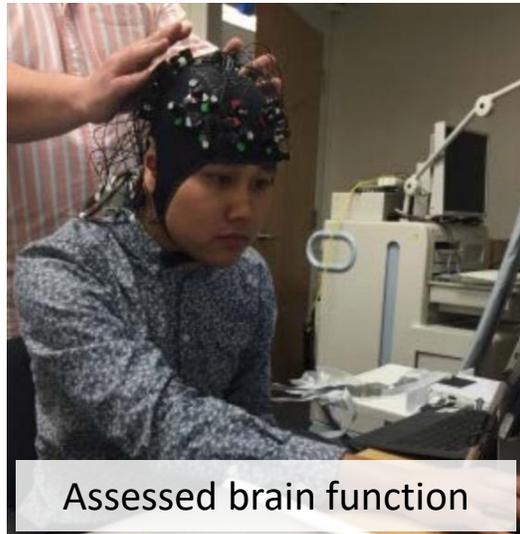
Measured anthropometry, liver and metabolic disorder



Evaluated respiratory function



Assessed brain function



Collected data on risk-taking behaviors



Performed MRIs on mothers



We have also collected samples to measure pesticides and other chemicals

- Mothers
 - ✓ Urine, blood, and breast milk
- Fathers
 - ✓ Urine
- Children
 - ✓ Urine, blood, saliva, hair, teeth
- House dust

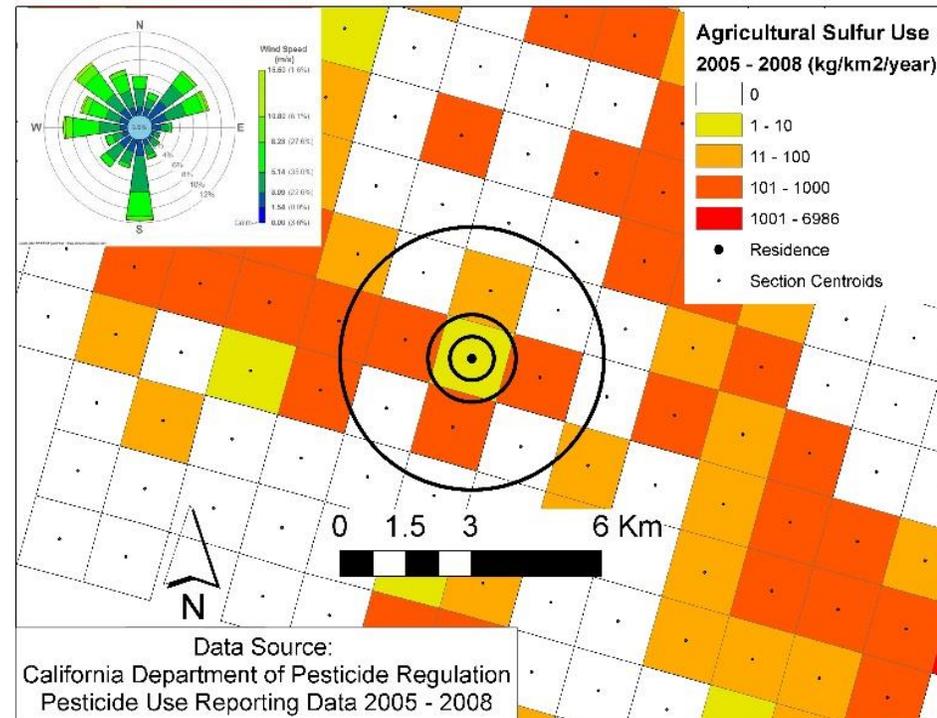
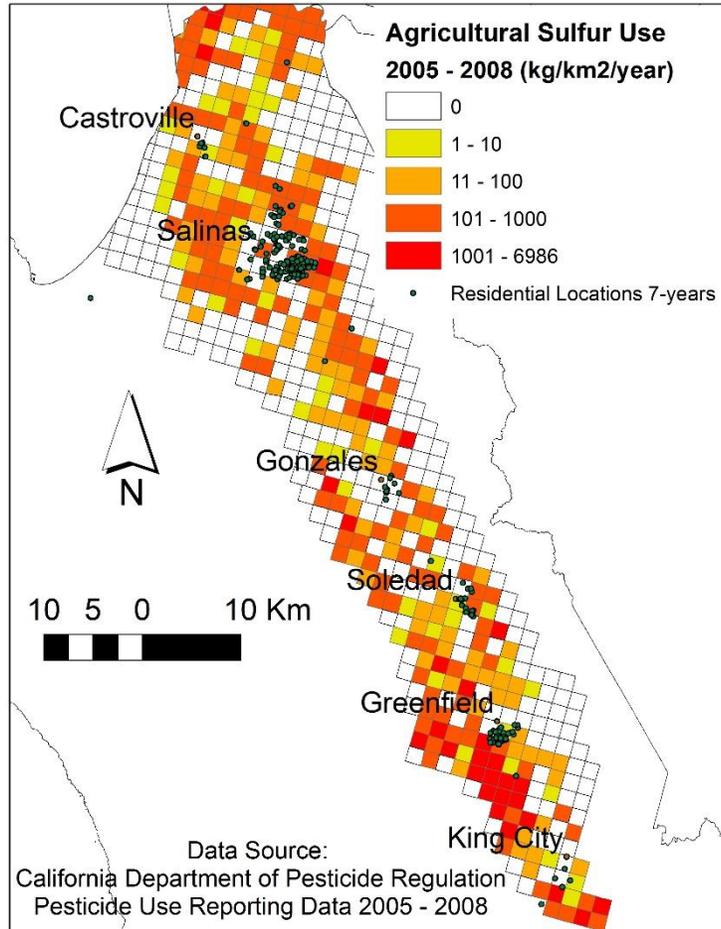


More than 400,000 samples collected and stored!

Geospatial analyses: Pesticide Use Reporting (PUR) data to determine exposure

Maternal and youth exposure levels calculated by:

- Pesticide use per year within 1 km of residence
- Duration of exposure based on housing location changes throughout study



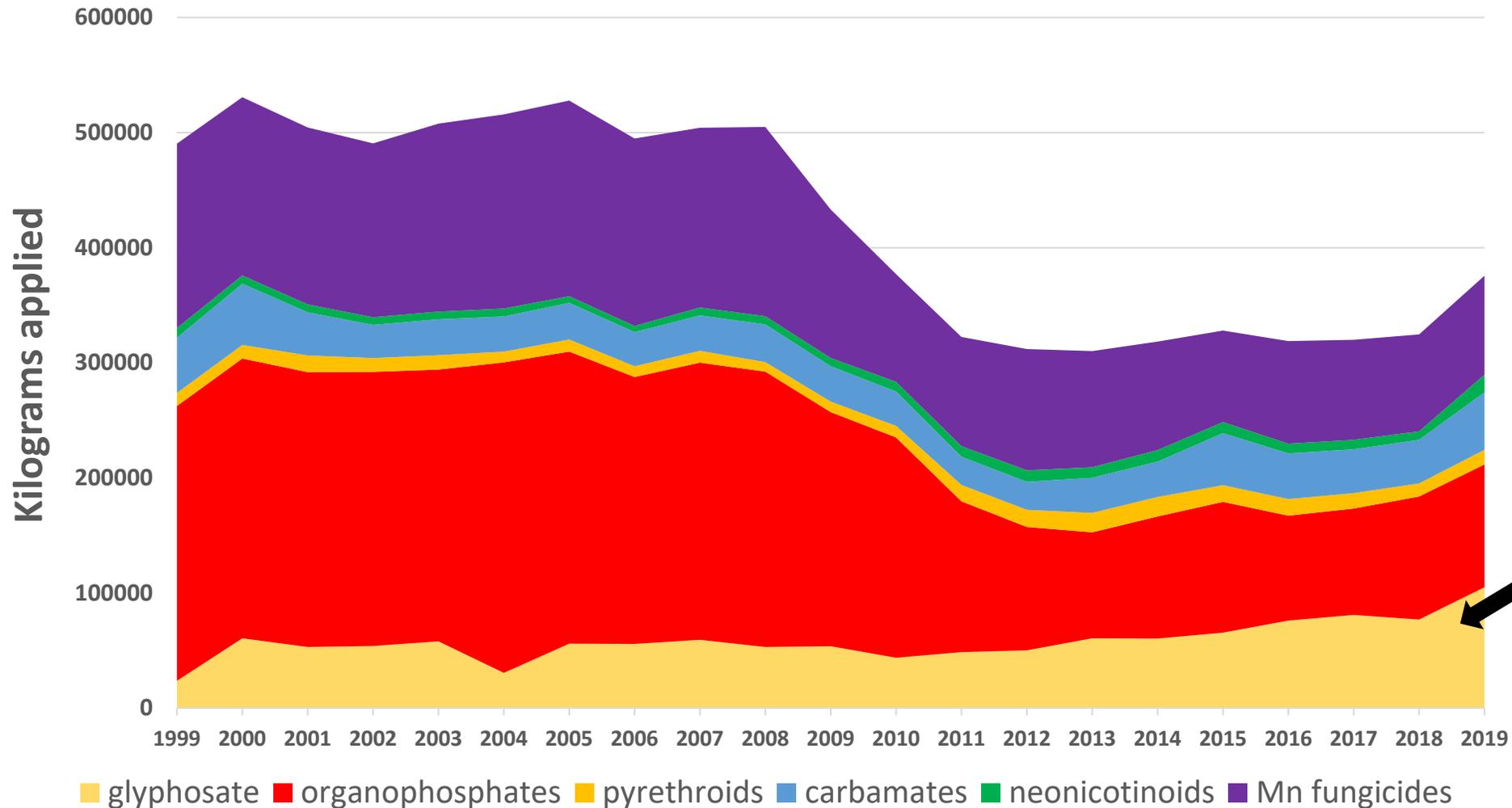
We have studied many pesticides as well as other environmental exposures.

- Pesticides
 - ✓ Organophosphates
 - ✓ Pyrethroids
 - ✓ Fungicides that contain Manganese
 - ✓ Organochlorines (e.g., DDT)
 - ✓ Fumigants such as Methyl Bromide
 - ✓ Glyphosate
 - ✓ Sulfur
- Fire retardants (e.g., PBDEs)
- Bisphenol A (BPA) and other phenols
- Phthalates
- Other chemicals in personal care products
- PM 2.5

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Agricultural pesticide use in Monterey County



Our recent focus has been on glyphosate



- Most commonly-used broad-spectrum herbicide worldwide
- Dramatic increase in U.S. in last two decades
- Controls grass and weeds; used in agriculture, forestry, right of way, parks, golf courses, and yards
- Found primarily in grains and legumes
- Eliminated in urine as glyphosate and as aminomethylphosphonic acid (AMPA)

Main health outcome of concern has been cancer

- **IARC: Probable Carcinogenic to Humans** (2A) in 2015
- **EPA** “no risks of concern to human health when glyphosate is used according to the label and that **it is not a carcinogen**” in 2020
- **European Commission extends use of glyphosate** until Dec 2023 while continues to peer review (July 2023)

Controversial glyphosate weedkiller wins new five-year lease in Europe

EU votes to reauthorise the pesticide, ending a bitterly fought battle that saw 1.3 million people sign a petition calling for a ban



In Roundup case, U.S. judge cuts \$2 billion verdict against Bayer to \$86 million

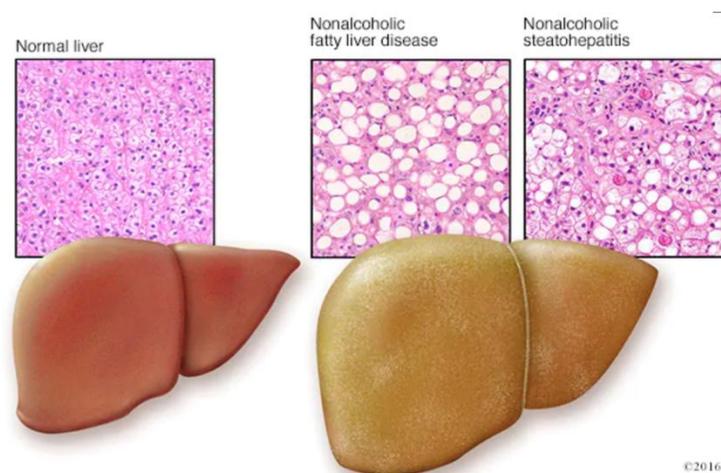
Reuters, July 2019

U.S. government says verdict in Bayer's Roundup case should be reversed

Reuters, December 2019

Glyphosate Excretion is Associated With Steatohepatitis and Advanced Liver Fibrosis in Patients With Fatty Liver Disease

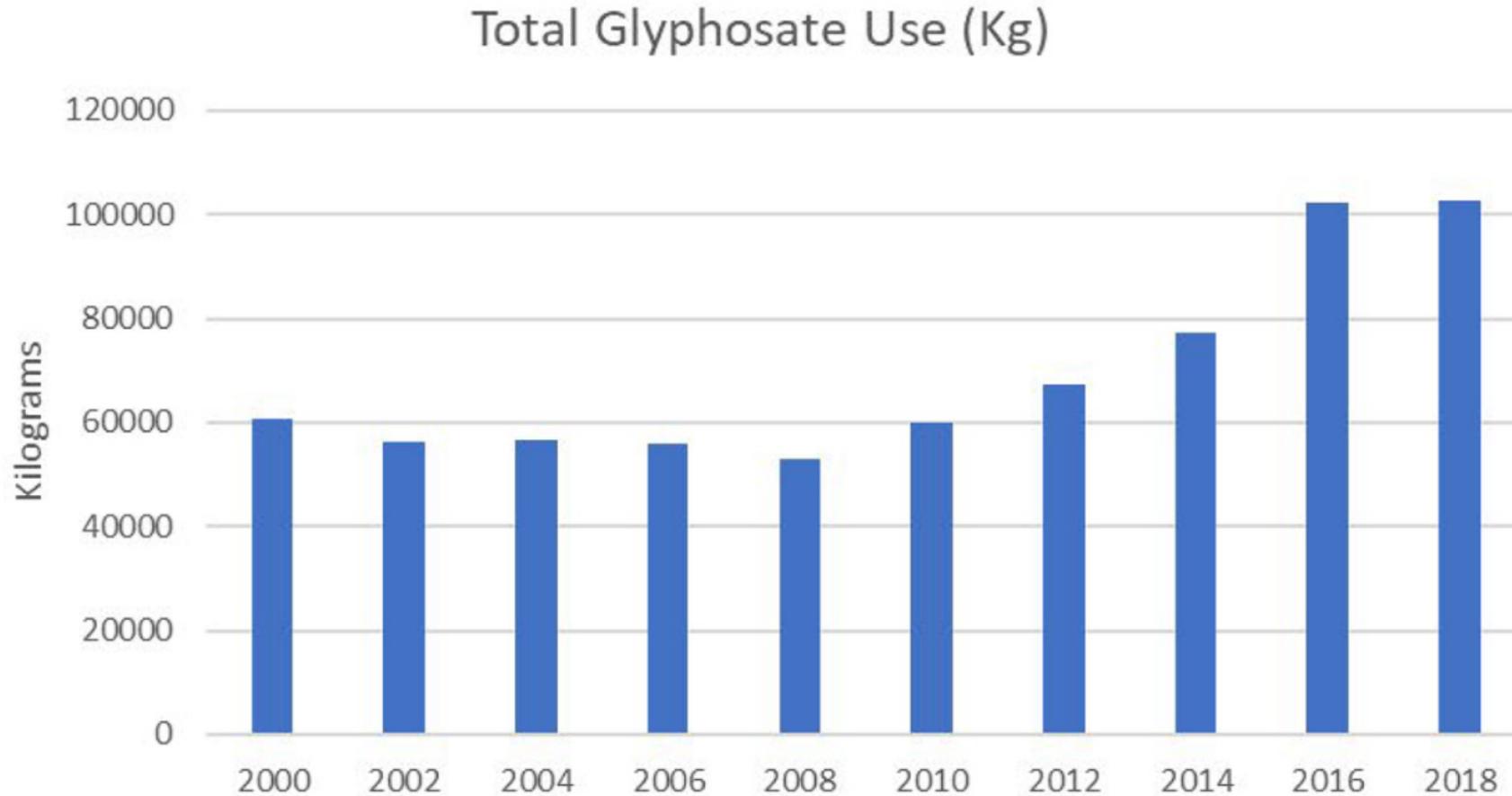
Paul J. Mills,^{*} Cyrielle Caussy,^{‡,§} and Rohit Loomba^{‡,||}



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- 63 cases of Non-alcoholic steatohepatitis – Stage 2, 3, or 4
- 34 controls without advanced fibrosis – Stage 0 or 1
- Fasting urine measured for AMPA and glyphosate; calculated glyphosate residues
- AMPA and glyphosate residue significantly elevated in NASH vs. non-NASH; adjusted for sex, age, and BMI
- Significant increase with severity of NASH

Glyphosate use has increased in recent years: Monterey County



Methods

■ Participants

- 480 mother-child (18 y) dyads from CHAMACOS with residential information and blood measures
- A nested case-control study
 - 60 cases with liver inflammation defined by elevated liver transaminases (AST or ALT)
 - 91 controls with normal liver transaminases, frequency matched on sex

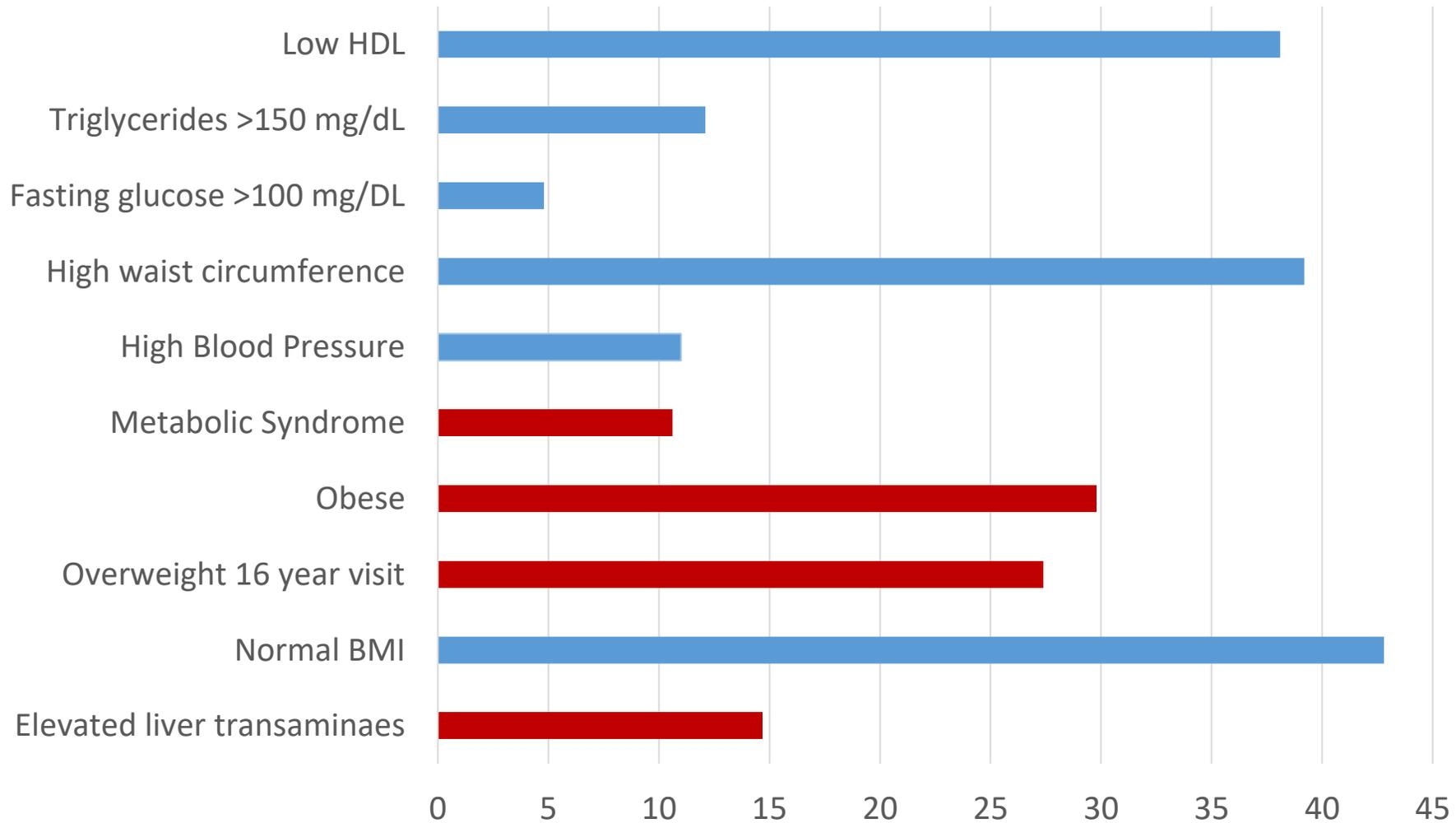
■ Exposure measures

- PUR data on Ag use of glyphosate near residences: Pregnancy to age 5 years
- Urine measurement of glyphosate and AMPA; calculation of glyphosate residue (Quebec)
 - Mother during pregnancy — 26 weeks gestation
 - Child at 5, 14, 18 years of age

Methods

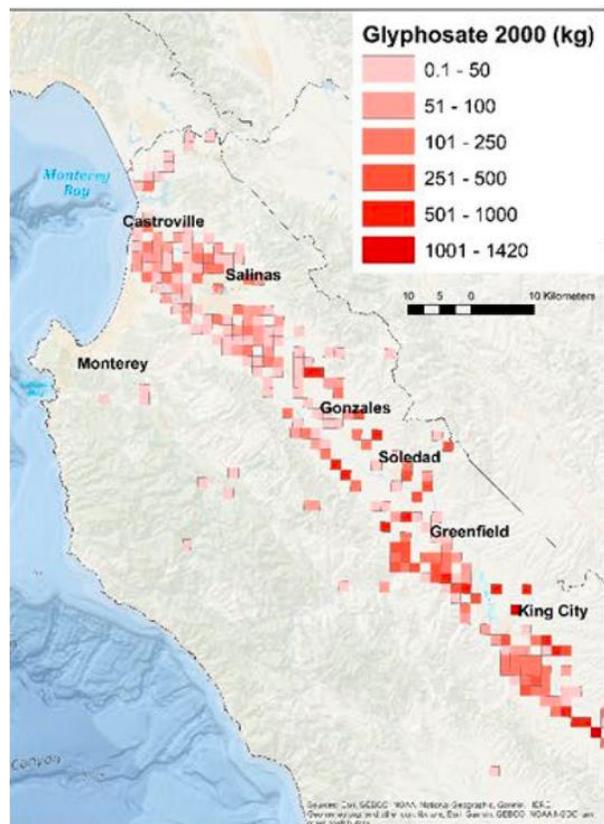
- Outcome measures at 18 years of age
 - Liver transaminases in blood — ALT and AST
 - Metabolic syndrome — any 3:
 - high systolic blood pressure or diastolic blood pressure
 - large waist circumference
 - elevated fasting serum glucose
 - elevated serum triglycerides
 - low HDL cholesterol

Cardiometabolic outcomes in CHAMACOS at 18-year visit

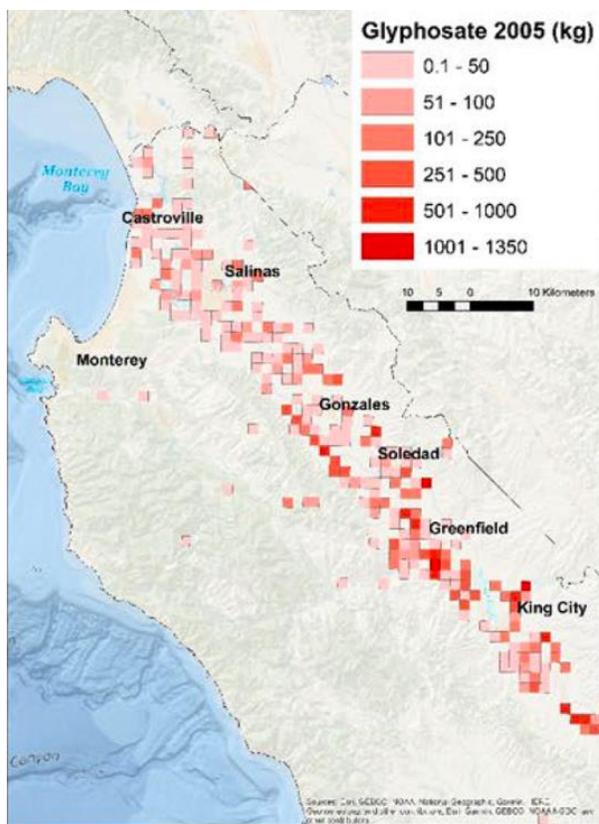


Agricultural use of glyphosate in the Salinas Valley: In utero and age 5, 14, and 18 years

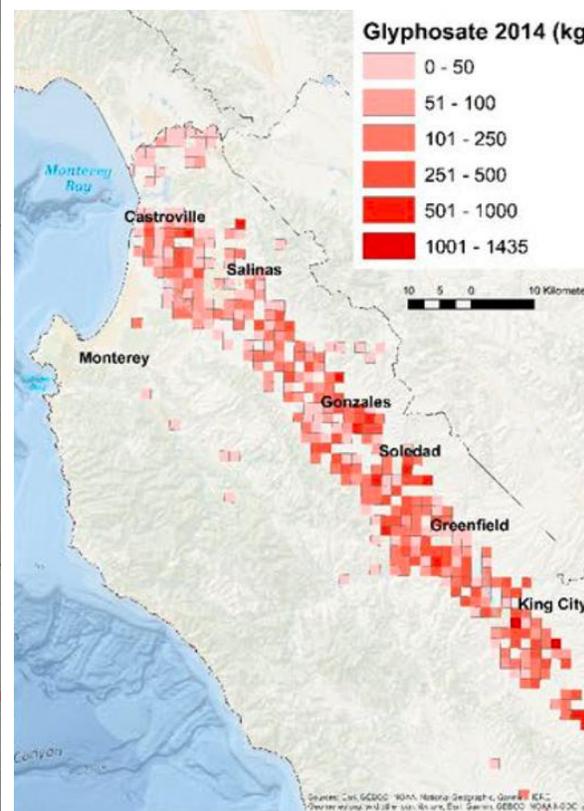
In Utero: 2000



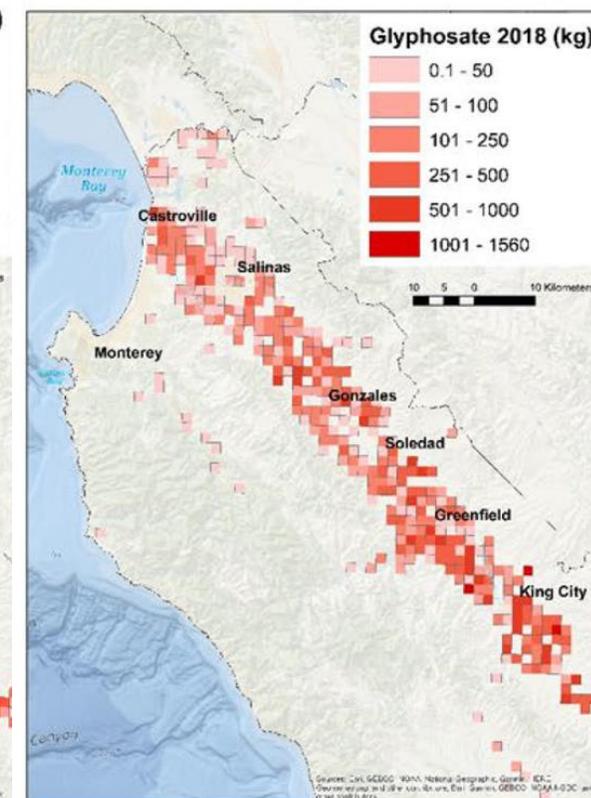
5 years: 2005



14 years: 2014



18 years: 2018

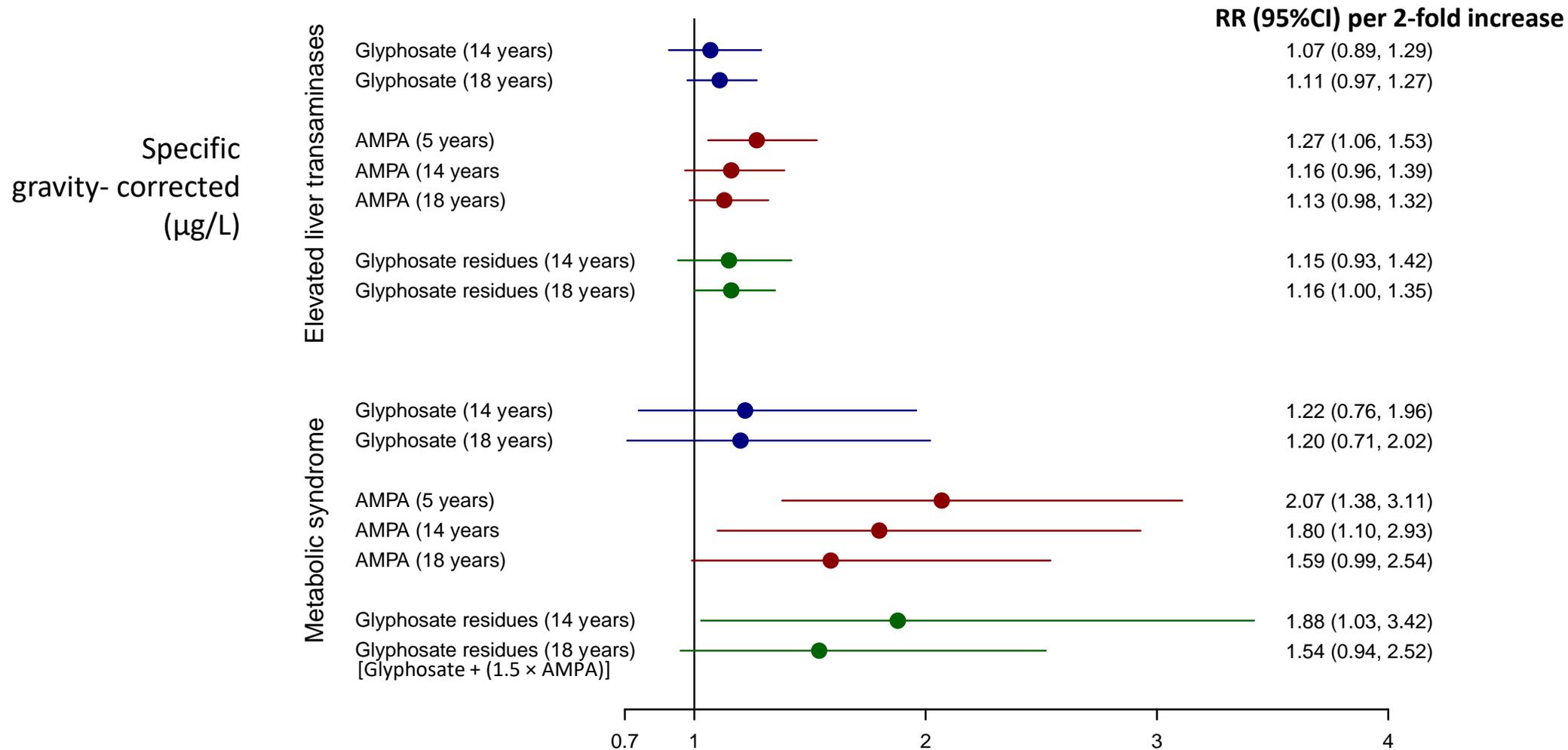


Looked at the relationship in 3 main ways:

- Pregnancy, 5, 14, 18-year urinary glyphosate, AMPA and glyphosate Residues* (only include if > 50% detection)
 - Each exposure time point separately
 - Using multiple informant models to consider all exposures in the same model
- PUR: Pregnancy and childhood averaged 0-5 years

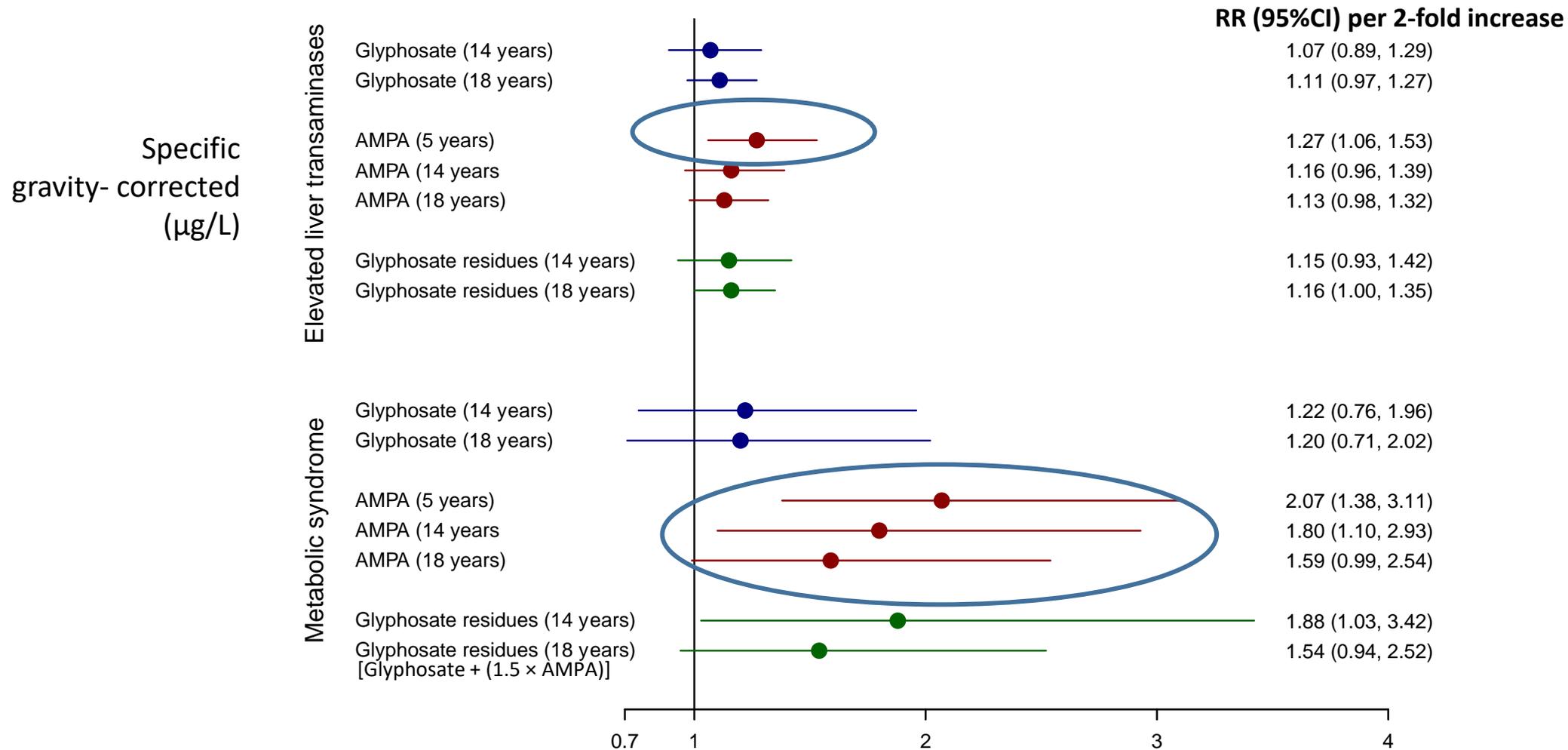
* Glyphosate + (1.5 × AMPA)

Urinary glyphosate, AMPA and glyphosate residues and elevated liver inflammation and metabolic syndrome



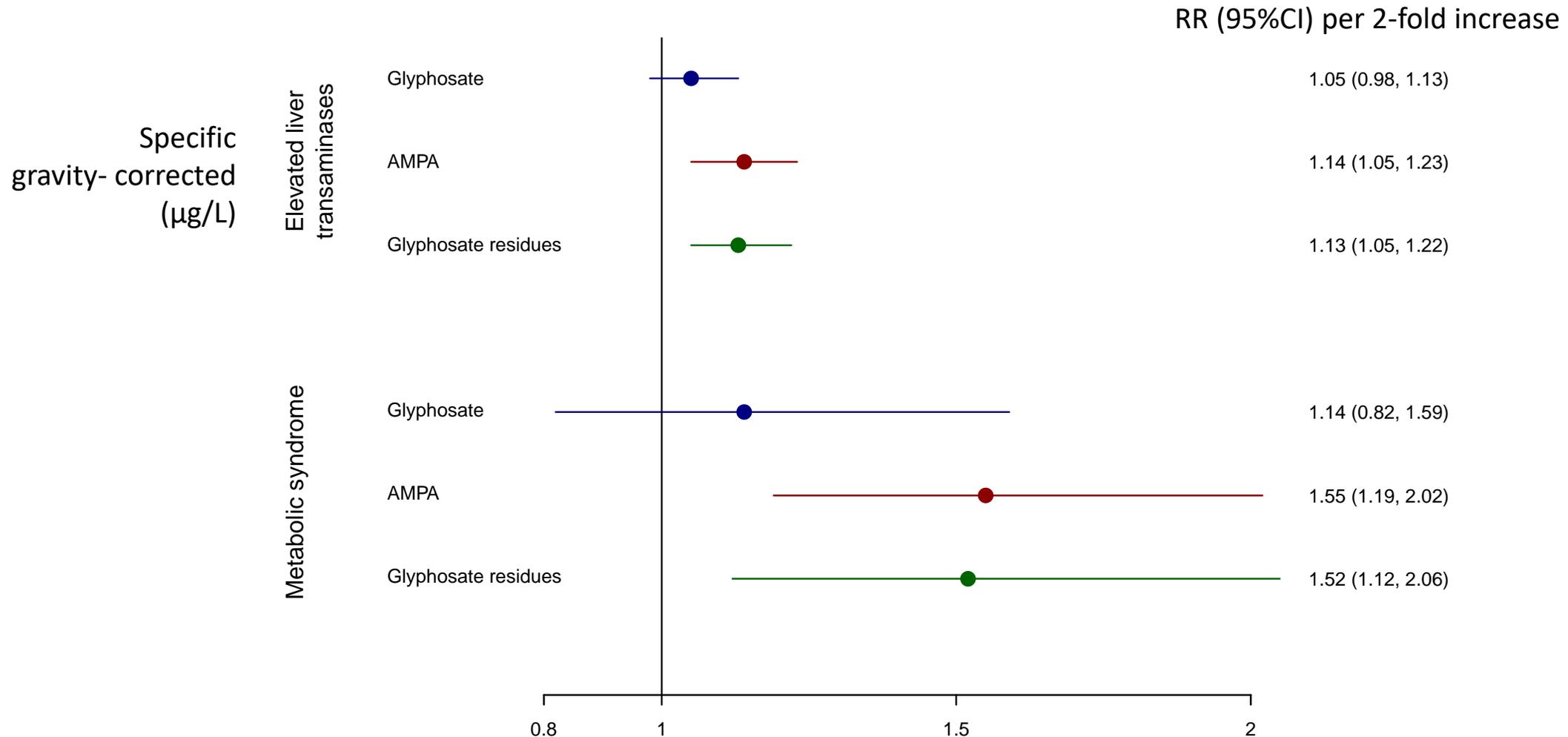
Models adjusted for sex, alcohol use at 18 y (never/ever), maternal prepregnancy BMI, parental work in agriculture during pregnancy (yes/no), household poverty status at 18 y (above vs. below the poverty threshold), and food security at 18 y (high/marginal security vs. low and very low security).

Urinary glyphosate, AMPA and glyphosate residues and elevated liver inflammation and metabolic syndrome



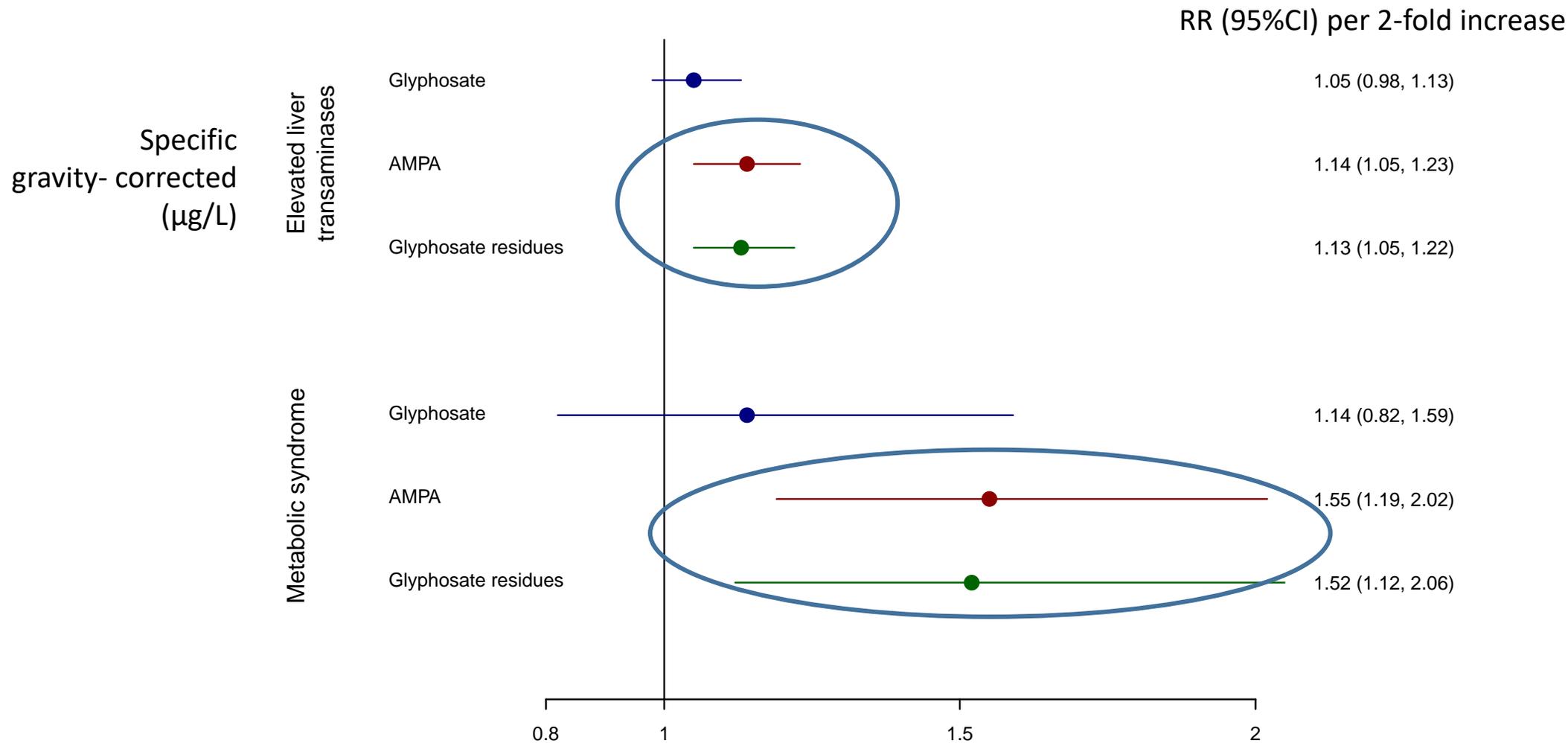
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Consideration of multiple exposure periods (multiple informant models)



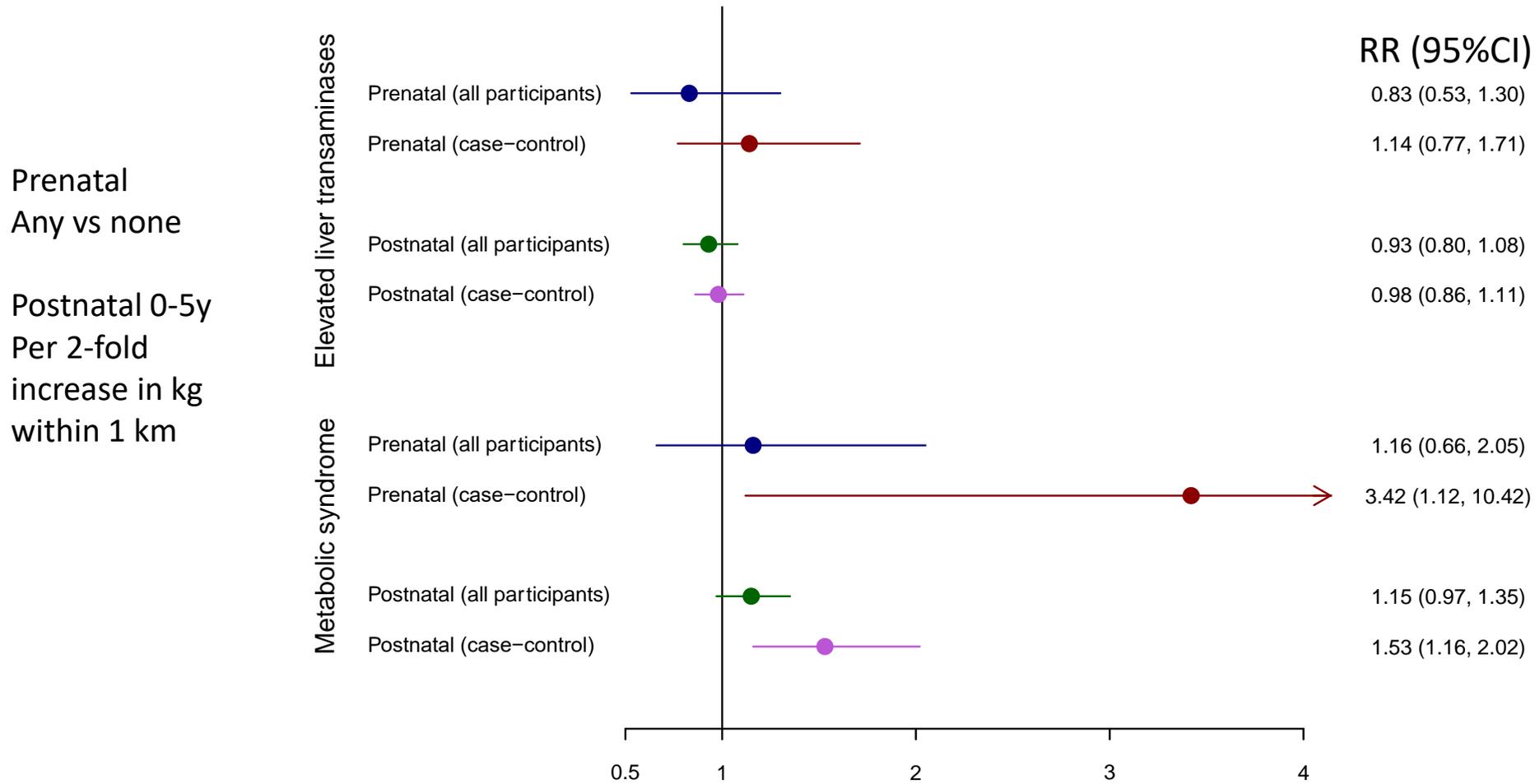
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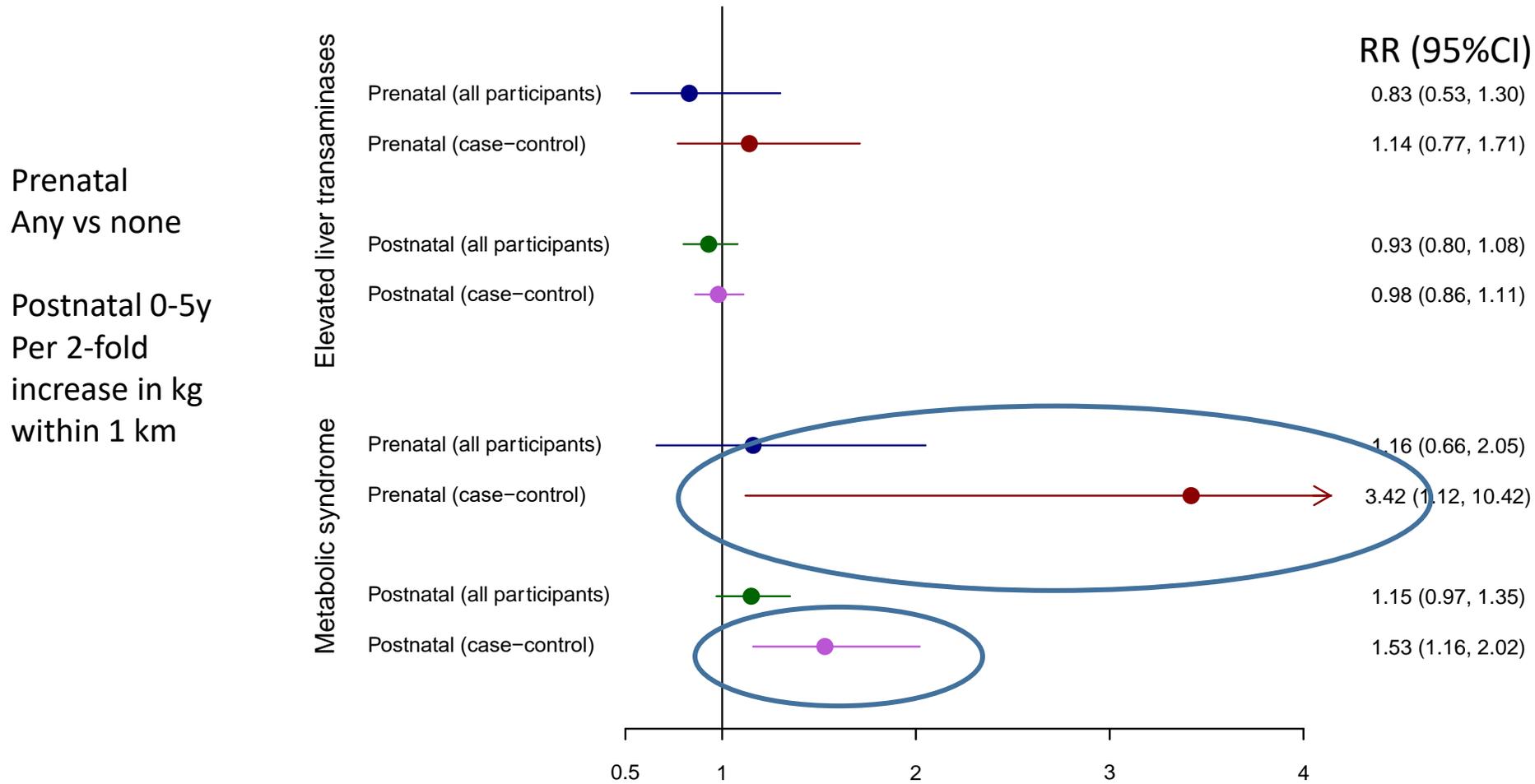
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Glyphosate use in agriculture near residence during mother's pregnancy or during 0-5 years in relation to liver inflammation and metabolic syndrome



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Glyphosate use in agriculture near residence during mother's pregnancy or during 0-5 years in relation to liver inflammation and metabolic syndrome



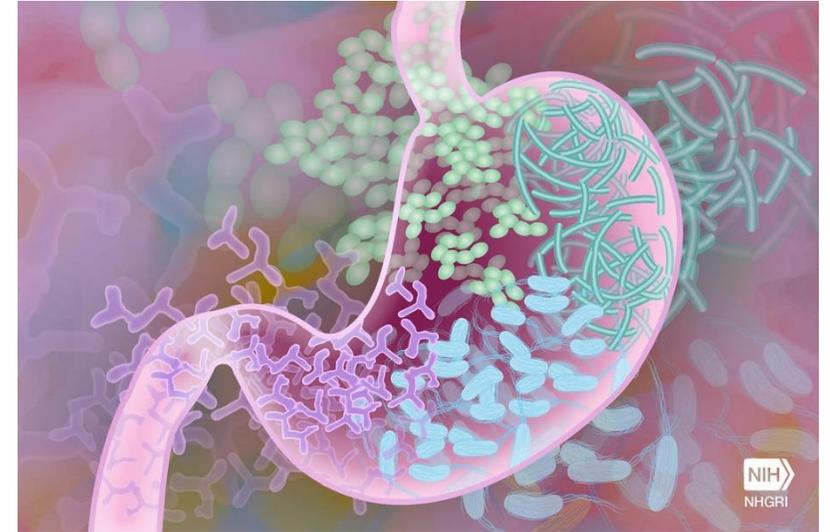
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Other results...

- Results are not mediated by the BMI alone
- Higher detection for AMPA than for glyphosate — but correlated
- Highest detection at age 14 years — even higher than at 18 years
- 18-years olds who fasted had lower levels
- Diet correlated
 - 5y: Cold cereal associated with higher AMPA and glyphosate residue concentrations
 - 14y: Calories, carbohydrate intake and hot cereal, bread, and fruits and vegetables and glyphosate
- PUR not correlated with glyphosate, weakly with AMPA

Potential mechanisms

- Via oxidative stress?
- Via alteration of gut microbiota?
- Via endocrine disruption?



De long and Hollaway, 2017; Prasad et al., 2022; Roberts and Sindhu, 2009; Martini et al., 2012, 2016; Mesnage et al., 2021; Romano et al., 2012; Martinez and Al-Ahmad, 2019; Myers et al., 2016; Guerro et al., 2022.

Limitations

- Short half-life chemical
- Single spot urine sample albeit multiple times (pregnancy and childhood)
- PUR do not reflect all nearby exposures (schools, workplaces, non-ag, differences by formulation)
- Inaccurate dietary recall
- Exposure was low during the prenatal period, although during childhood within the range of other studies for glyphosate
- Pathways of AMPA unknown although likely from food and water



Strengths

- California's unique PUR data
- Two measures of exposure and include AMPA
- Longitudinal study of a farmworker population
- Exposures are not higher than the US population



A photograph of a sandy beach with footprints leading towards the ocean. The text "[next steps]" is written in a handwritten style on the sand. The scene includes a small stream of water on the left, green seaweed, and a smooth rock on the right. The lighting is bright, suggesting a sunny day.

[next steps]

Future studies

- Longer follow-up in longitudinal studies.
- Larger sample sizes to look at sex differences.
- Other health outcomes not just cancer and include reproductive and endocrine function.
- Glyphosate and AMPA within pesticide mixtures.
- Studies with frequent measures of exposure and include pregnancy
- Studies to understand pathways of AMPA exposure.

In last 5 years, emerging human health data...

- Lower birthweight (Birth cohort)
- Shortened gestation (Gly and AMPA) (Birth cohort)
- Preterm delivery (Gly and AMPA)(Birth cohort nested case-control)
- Higher NICU admission (Birth cohort)
- Developmental delay (Case-control)
- Wilms Tumor (Meta-analysis)
- Oxidative stress (AMPA) (Children cross-sectional)
- Decrease in estradiol and testosterone (NHANES, cross-sectional)

Conclusions

- Exposure to glyphosate, the most commonly used herbicide worldwide, and AMPA, a degradation product of glyphosate and amino-phosphonates, in early childhood was **linked to liver inflammation and/or cardiometabolic disease** in young adulthood.
- Although previous research on glyphosate in humans has largely focused on its potential carcinogenicity, this study indicates the **need for further investigation** of its association with metabolic and liver outcomes.

Eskenazi et al., published March 1, 2023, Environmental Health Perspectives Vol 131 (3)



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ECHO: 1UG3OD023356

*And a very special
thanks to the families
who have
participated!*



Thank YOU!!!



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