

# Synergistic Effects of Environmental Toxins on Kidney Health Using Ensemble Learning Techniques.

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Malathion diacid and 2,4-D are two common-place pesticides that, combined, decreased kidney function despite neither exhibiting a clear independent effect.

## BACKGROUND

Environmental toxicology is still trying to decipher the **exposome**. While reductionist science has revealed several relationships between exposures and health outcomes, a more holistic approach is expected to reveal other pathological pathways.

**Chronic Kidney Disease of Unknown Aetiology (CKDu)** presents a major health challenge, particularly for agricultural communities.

- Various **risk factors** such as **pesticides**, **heavy metals** and heat stress have been postulated, but with **little firm evidence** to suggest causality.

## METHODS

We applied ensemble learning methods to National Health and Nutrition Examination Survey (NHANES) data to **investigate the independent and combined effect of exposure to various toxins**.

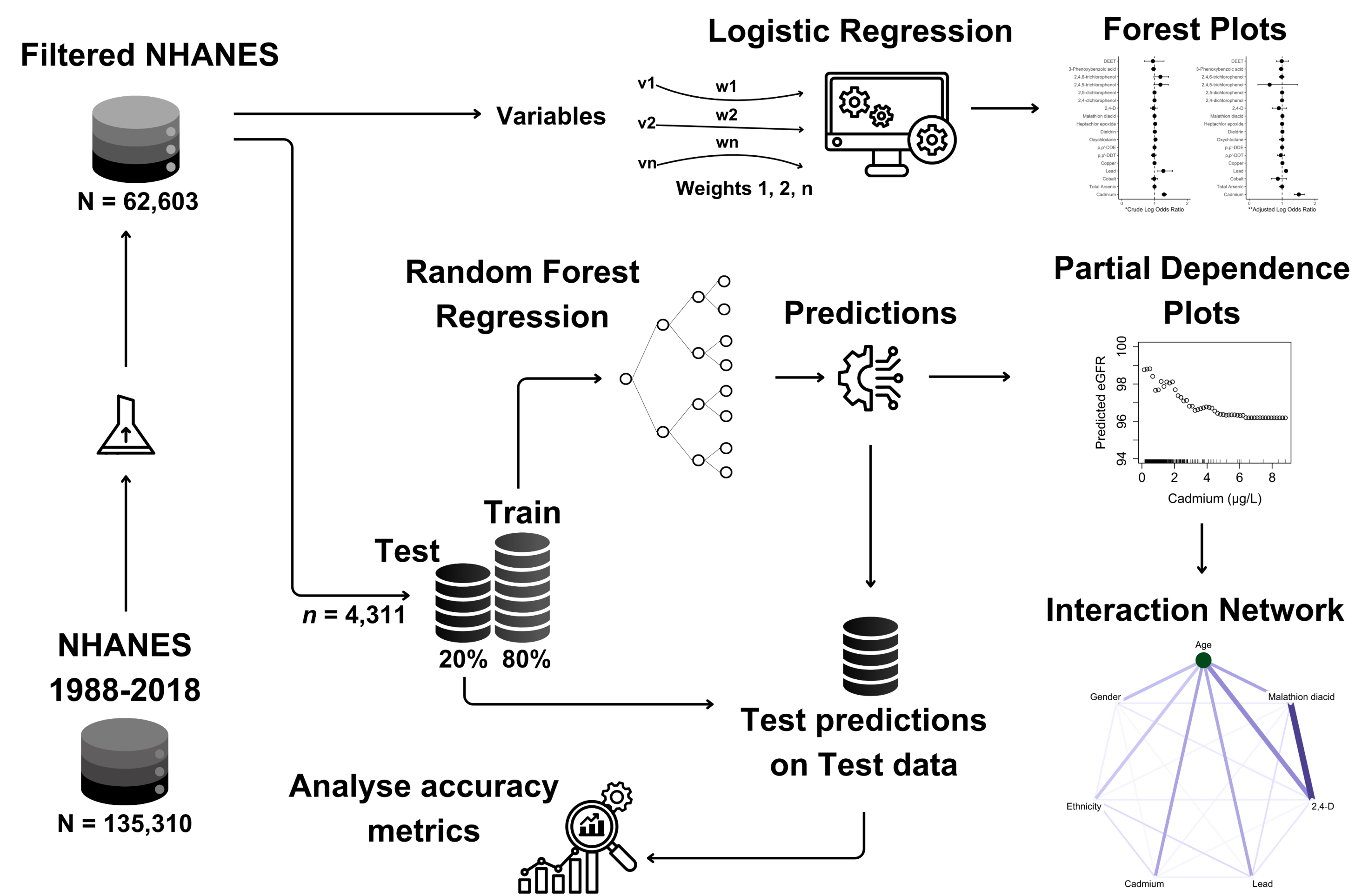


Figure 1. Graphical Methods

## RESULTS

- **Participants with increased cadmium or lead concentrations were at greater risk of decreased renal function.**

Cadmium was calculated to have an adjusted OR of 1.51 (95% CI: 1.37 – 1.68), adjusting for age, ethnicity, PIR and NHANES wave, while lead 1.12 (95% CI: 1.09 – 1.14) adjusting for the same parameters.

- **Participants with increased malathion diacid or 2,4-D concentrations had non-significant effect on renal function**
- **Despite malathion diacid and 2,4-D exhibiting no effect upon kidney function independently of covariates, participants with combined exposures exhibited a multiplicative effect indicative of synergy, decreasing renal function.**

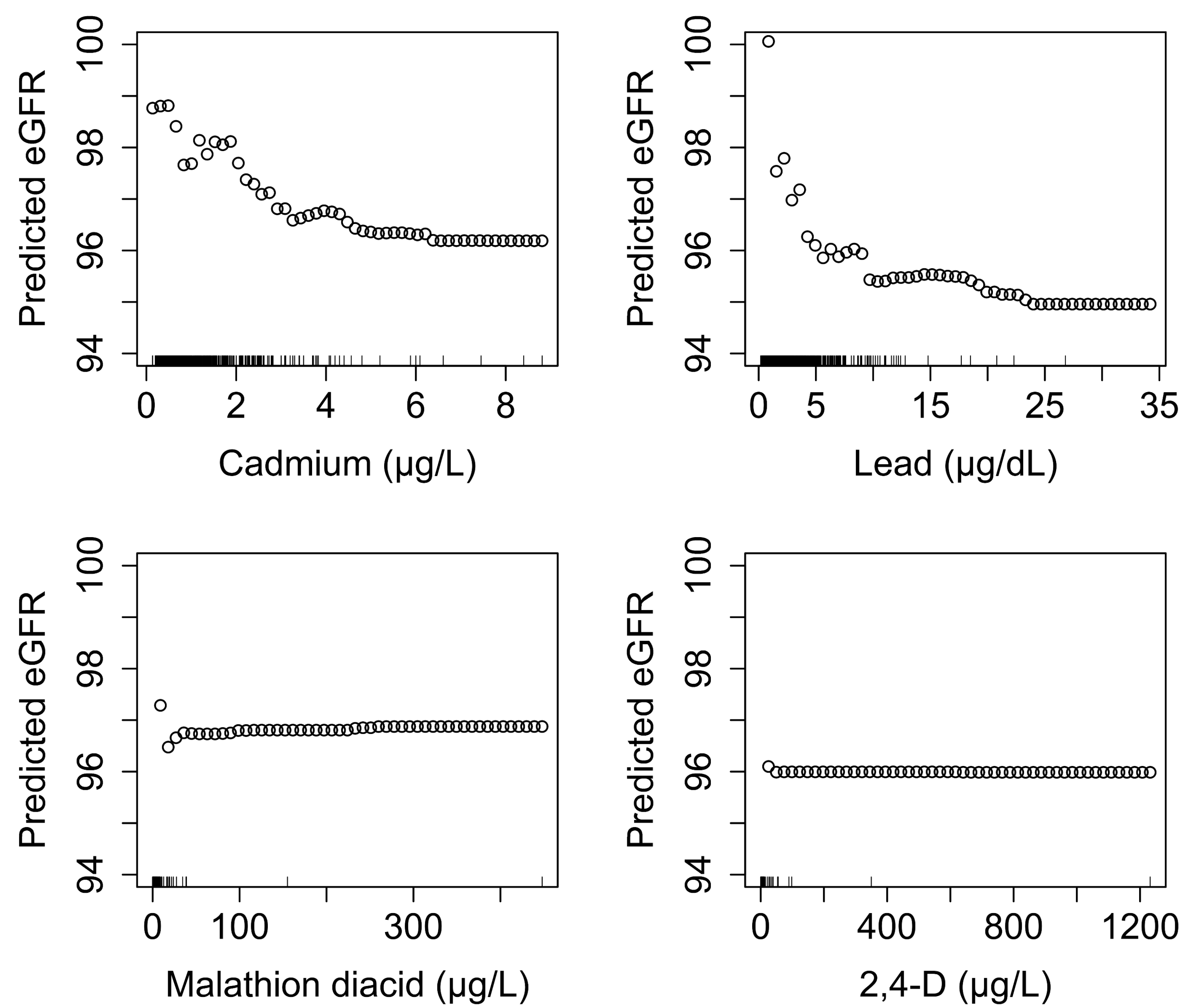


Figure 2. Independent predictions of eGFR for each toxin. Cadmium and Lead both decreased eGFR as their concentration increased. In comparison, malathion diacid and 2,4-D did not exhibit an effect at any concentration

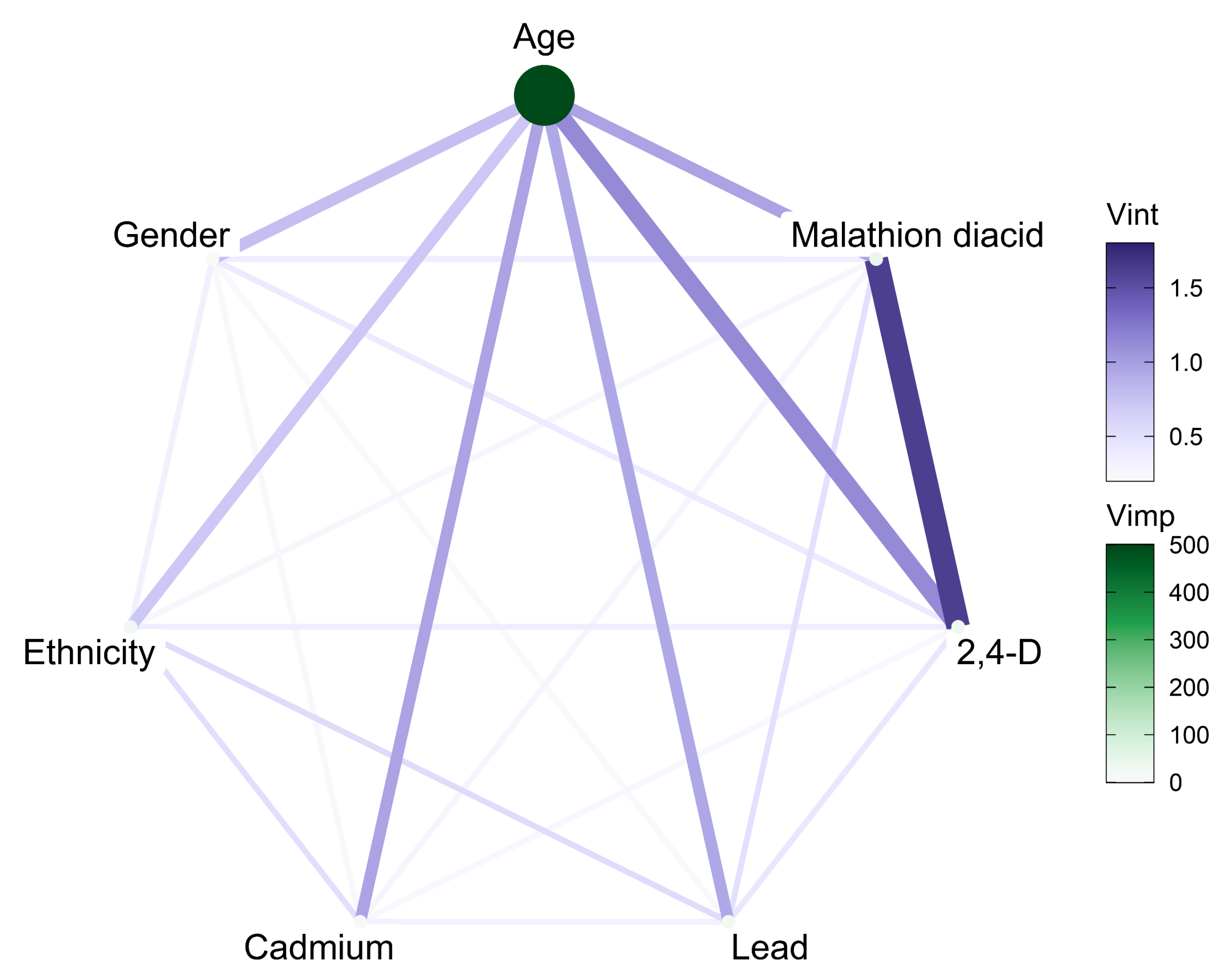


Figure 3. Interaction network. Malathion diacid and 2,4-D exhibit a strong, multiplicative interaction, H-statistic = 1.91. Age had the greatest %incMSE, thus most influential predictor of eGFR

## CONCLUSIONS

There is a complex relationship between environmental exposures and human health and research is needed to decipher the exposome