

Aolin Wang,^{1,2} Jackie M. Schwartz,¹ Roy R. Gerona,³ Thomas Lin,³ Rachel Morello-Frosch,⁴ Marina Sirota,² Tracey J. Woodruff¹

¹Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, California, USA

²Institute for Computational Health Sciences, University of California, San Francisco, California, USA

³Clinical Toxicology and Environmental Biomonitoring Lab, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, California, USA

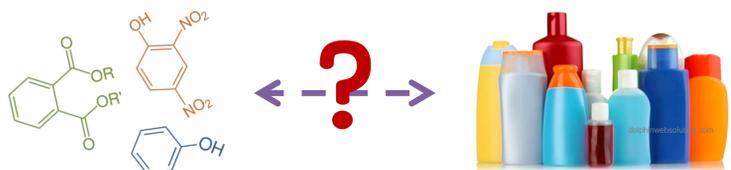
⁴School of Public Health and Department of Environmental Science, Policy and Management, University of California, Berkeley, California, USA

Introduction

- Consumer products are important sources of exposure to endocrine disrupting chemicals (EDCs), such as phthalates and environmental phenols (including parabens, triclosan, and bisphenol-A)
- Due to non-equal health risks, it is important to monitor the various EDCs among pregnant women and identify sources of exposure
- We developed a suspect screening method to screen for environmental phenols and phthalate metabolites using high resolution mass spectrometry.

Aims: 1) profile the pattern of suspect phenols and phthalate metabolites detected in serum samples from a racially and economically diverse cohort of pregnant women, and consumer product use including use of personal care products (PCPs) or household cleaning products (HCPs);

2) assess the relationship between suspect detection and PCPs or HCPs.



Methods

Study sample

Seventy-five serum samples were collected at delivery from pregnant women receiving care at Zuckerberg San Francisco General Hospital or UCSF Medical Center.

Consumer product use information and demographic variables including age, race/ethnicity, educational attainment, annual household income were collected using structured questionnaire during face-to-face interview.

Chemical analysis and data processing (Fig 1)

We used liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) with Agilent QTOF/MS 6550 instrument. We used Agilent MassHunter Qualitative Analysis software Find By Formula algorithm to generate a list of exact mass matches – compounds whose exact masses (acquired in the LC-QTOF/MS analysis) matched the exact masses of chemicals in the suspect database. Additional data processing steps for all accurate mass matches included visual inspections/reviews of the total ion chromatogram peaks and differentiation of isomers based on LC-QTOF/MS retention time. When a mass spectral feature matches to a chemical in our suspect database, we call this feature a “suspect phenol” or a “suspect phthalate metabolite” as they are not confirmed compounds.

Statistical analysis

We used pairwise t-tests to assess the demographic differences in the number of PCPs, HCPs, suspect phenols, or suspect phthalate metabolites. Due to the high dimensionality of the data with relatively small sample size, we used a two-stage approach to assess the relationship between suspect detection and daily use of PCP or HCP: 1) used linear regression with adjustment for race to assess the relationship between number of suspects detected and specific category of daily use of PCP or HCP (Y/N), 2) used Chi-squared tests or linear regression to identify the specific suspect phenols or phthalate metabolites whose detection (Y/N) or relative concentration (measured by the chromatogram peak area) are associated with significant product use predictors identified from stage 1) analysis. All tests were corrected for multiple comparison using the false discovery rate (FDR) method.

Fig 1. Flow chart for data generation, processing, and analysis

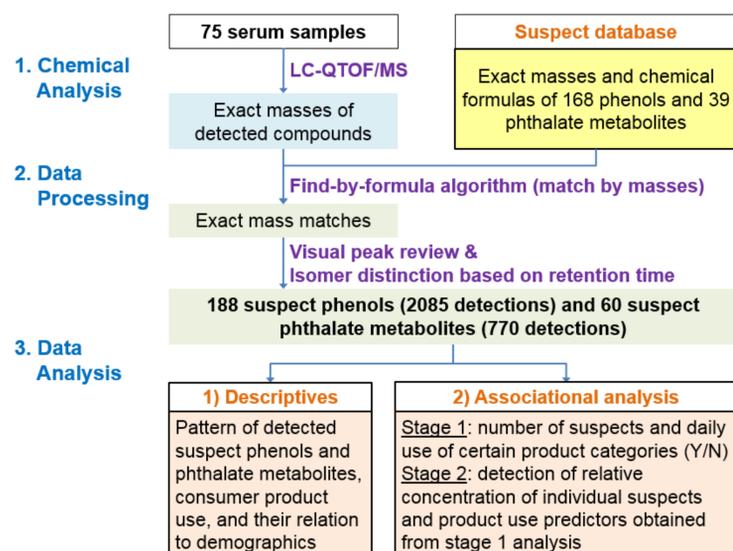
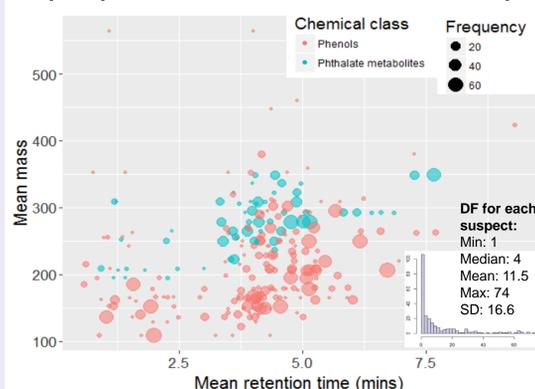
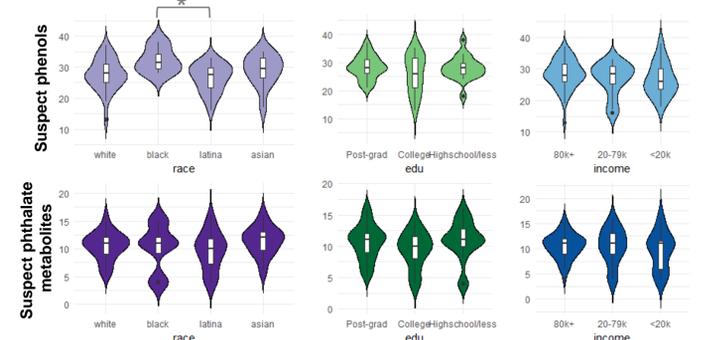


Fig 2. Overview of 188 suspect phenols and 60 suspect phthalate metabolites in 75 serum samples



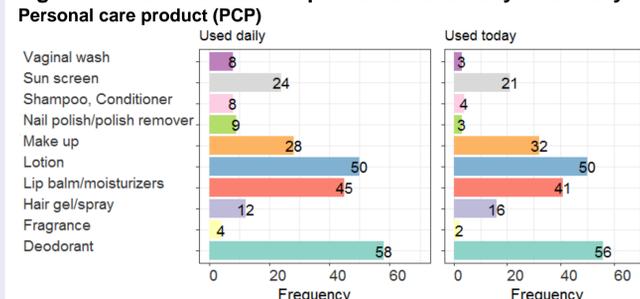
Only 10 suspects were detected over 80% among 75 women. A large number of suspects were detected in only one sample.

Fig 3. Number of suspects by race/ethnicity, education, and income

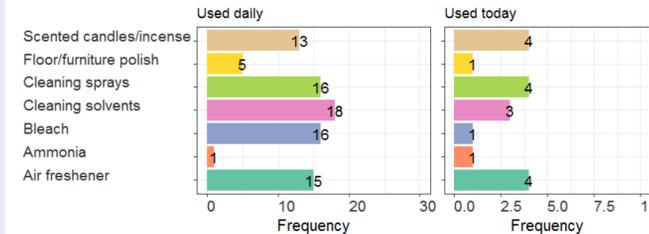


We detected an average of **28 (SD: 5)** suspect phenols and **10 (SD: 3)** suspect phthalate metabolites. Compared to African American women, Latinas or whites had 6 and 4 fewer suspect phenols respectively, although *p*-values from pair-wise t-test were no longer significant after multiple comparison adjustment.

Fig 4. Number of consumer products used daily and today



Household cleaning product (HCP)



Daily use of PCPs were highly correlated with its use today ($\text{corr} = 0.79, p < 0.001$) whereas daily use of HCPs were only moderately correlated its use today ($\text{corr} = 0.35, p = 0.002$). Number of PCPs used daily did not differ by demographics. Asians and Whites (compared to Latinas) and women with at least some college education (compared to high school or less education) or household income $\geq \$80,000$ (compared to $< \$20,000$) used two fewer HCP daily on average.

Fig 5. Number of products used daily by demographics

* Indicates significant pair-wise comparisons after FDR adjustment.

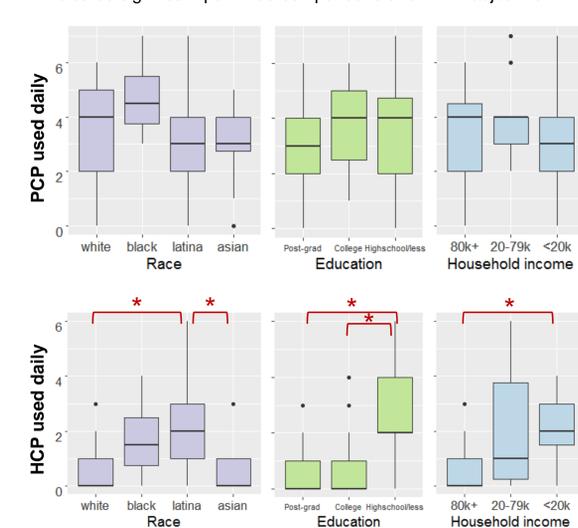
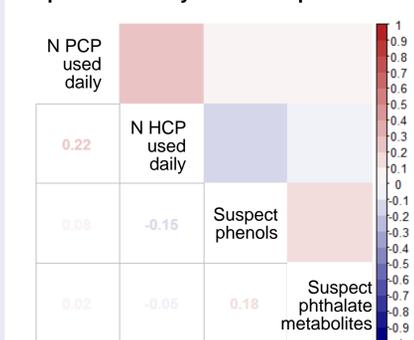


Fig 6. Correlation between number of suspects and daily consumer product use



The number of PCP or HCP used daily was **not correlated** with the overall number of suspect phenols or suspect phthalate metabolites detected.

Table 1. Relationship between number of suspects detected and daily consumer product use (Y/N)^a

Outcome:	N suspect phenols			N suspect phthalate metabolites		
	<i>b</i>	<i>p</i>	<i>p(adj)</i>	<i>b</i>	<i>p</i>	<i>p(adj)</i>
PCP daily use						
Sun screen	0.78	0.56	0.89	-0.62	0.45	0.99
Make up	0.58	0.65	0.89	0.01	0.98	0.99
Lotion	3.44	0.01	0.08	0.18	0.82	0.99
Lip balm/moisturizers	0.81	0.52	0.89	-0.11	0.89	0.99
Hair gel/spray	-0.25	0.89	1.00	0.05	0.96	0.99
Deodorant	0.07	0.97	1.00	1.16	0.22	0.97
HCP daily use						
Scented candles/incense	-3.43	0.02	0.13	-1.13	0.23	0.97
Cleaning sprays	-1.27	0.40	0.89	1.03	0.26	0.97
Cleaning solvents	0.00	1.00	1.00	0.06	0.94	0.99
Bleach	1.24	0.51	0.89	0.64	0.58	0.99
Air freshener	-1.72	0.26	0.89	-0.66	0.48	0.99

^aOnly categories with frequency of daily use greater than 10 was tested. Linear regression models were used with adjustment for race/ethnicity. Multiple comparisons were adjusted using the FDR method.

Stage 1 results:

When daily use of consumer product categories were examined on an individual basis, only daily use of lotion or scented candles/incense were marginally associated with the number of suspect phenols detected in serum.

Stage 2 results:

- The detection (Y/N) of three suspect phenols (out of 14 suspects tested) were associated with daily use of lotion or scented candles/incense but such association were no longer significant (at 0.1 level) after FDR correction.
- We tested the relative concentration of 8 suspect phenols that were detected over 80% of the participants and did not find differences by daily use of lotion nor scented candles/incense.

Conclusion

- Our exploratory analysis suggest potential demographic differences in consumer product use and the presence of suspect phenols and phthalate metabolites in maternal serum.
- Daily consumer product use may be associated with the presence of suspect phenols and phthalate metabolites in maternal serum.
- Follow-up study with larger sample size is needed to examine exposures to these compounds among certain race/ethnicity and income groups.

Funding

This work is supported in part by the NIEHS grant PO1ES022841 and the US EPA grant 83543301 [TJW, RMF, AW, JMS, RRG and TL], the March of Dimes Prematurity Research Center at Stanford, Burroughs Wellcome Fund, and K01LM012381 [MS and AW].

Acknowledgement

The authors thank all CiOB participants and staff for their contribution to the study.

Contact: aolin.wang@ucsf.edu
<https://prhe.ucsf.edu>

