Silicone Wristbands: Personal Exposure Monitors to Help Support Research on the Exposome

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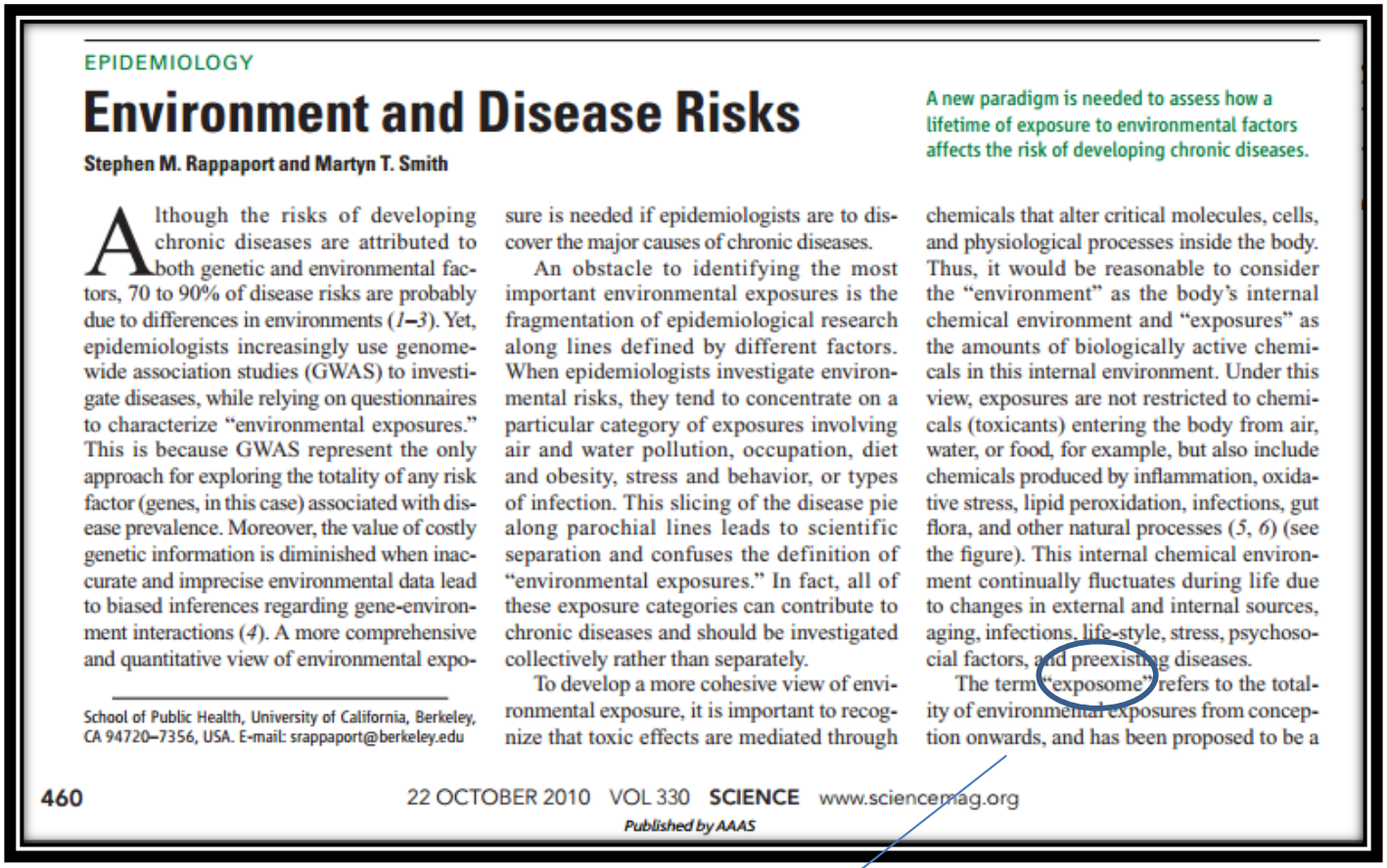
DUKE UNIVERSITY
forging a sustainable future

"…70-90% of disease risks are probably due to differences in environments"



EPIDEMIOLOGY

Environment and Disease Risks

A new paradigm is needed to assess how a lifetime of exposure to environmental factors affects the risk of developing chronic diseases.

Stephen M. Rappaport and Martyn T. Smith

Although the risks of developing chronic diseases are attributed to both genetic and environmental factors, 70 to 90% of disease risks are probably due to differences in environments (*1*–*3*). Yet, epidemiologists increasingly use genome-wide association studies (GWAS) to investigate diseases, while relying on questionnaires to characterize "environmental exposures." This is because GWAS represent the only approach for exploring the totality of any risk factor (genes, in this case) associated with disease prevalence. Moreover, the value of costly genetic information is diminished when inaccurate and imprecise environmental data lead to biased inferences regarding gene-environment interactions (*4*). A more comprehensive and quantitative view of environmental exposure is needed if epidemiologists are to discover the major causes of chronic diseases.

An obstacle to identifying the most important environmental exposures is the fragmentation of epidemiological research along lines defined by different factors. When epidemiologists investigate environmental risks, they tend to concentrate on a particular category of exposures involving air and water pollution, occupation, diet and obesity, stress and behavior, or types of infection. This slicing of the disease pie along parochial lines leads to scientific separation and confuses the definition of "environmental exposures." In fact, all of these exposure categories can contribute to chronic diseases and should be investigated collectively rather than separately.

To develop a more cohesive view of environmental exposure, it is important to recognize that toxic effects are mediated through chemicals that alter critical molecules, cells, and physiological processes inside the body. Thus, it would be reasonable to consider the "environment" as the body's internal chemical environment and "exposures" as the amounts of biologically active chemicals in this internal environment. Under this view, exposures are not restricted to chemicals (toxicants) entering the body from air, water, or food, for example, but also include chemicals produced by inflammation, oxidative stress, lipid peroxidation, infections, gut flora, and other natural processes (*5*, *6*) (see the figure). This internal chemical environment continually fluctuates during life due to changes in external and internal sources, aging, infections, life-style, stress, psychosocial factors, and preexisting diseases.

The term "exposome" refers to the totality of environmental exposures from conception onwards, and has been proposed to be a

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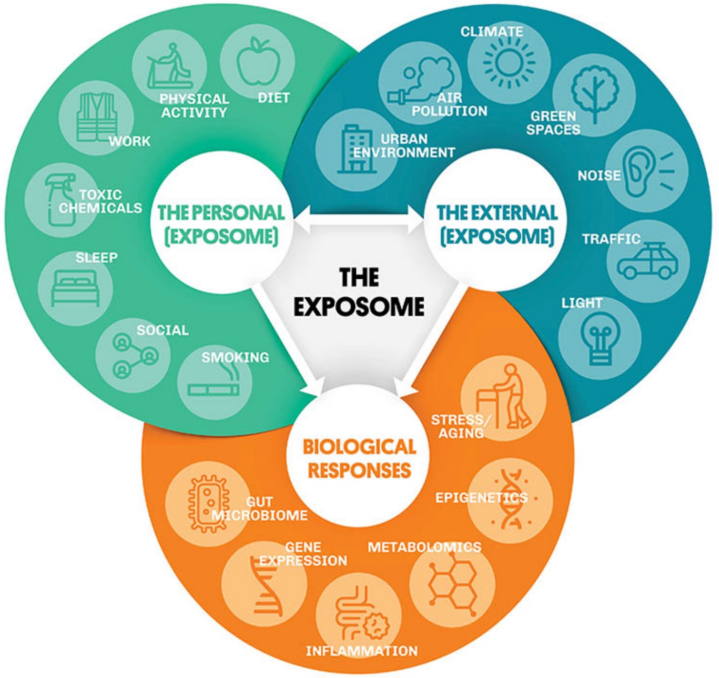
"Exposome"

Challenges with Exposome Research

- The Exposome is complicated & dynamic
- How do we measure everything at once? Most analyses look at a few dozen chemicals at a time, yet we're exposed to thousands each day.
- How do we evaluate changes in our exposure over time? Many studies are cross-sectional in design and may not be measuring exposure at the right time point.

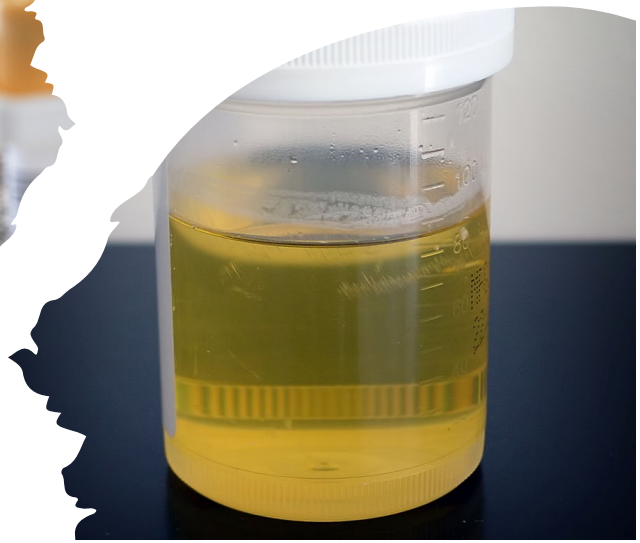


Source: www.isiglobal.com

Exposure to chemical mixtures: what type of samples are best?

- Historically, exposure to mixtures has been assessed using:
  - Blood
  - Urine
  - House Dust

- However, each sample has its own limitations



Blood vs Urine

Blood

Ideal for chemicals with long half-lives in body (months to year)
Examples: PCBs, PFAS, PBDEs, metals

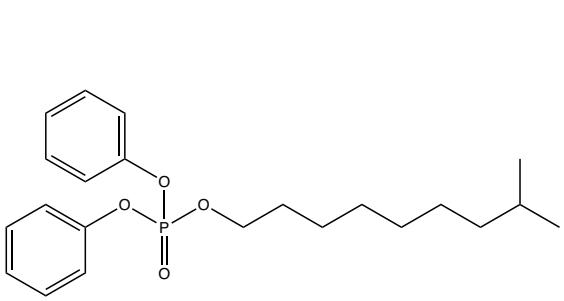
Limitations: -volume available
-collection challenges

Urine

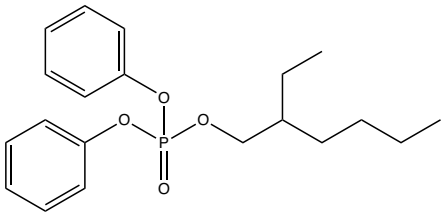
Ideal for chemicals with short half-lives in body (hours to days)
Examples: PAHs, phenols, tobacco

Limitations: - Variability over time?
- Is metabolite known?
- Is metabolite specific to parent?

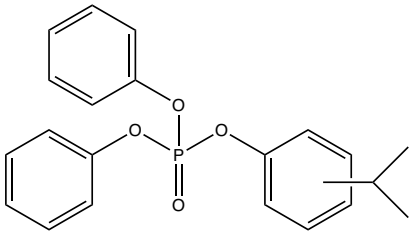
Problem: Who is the parent?



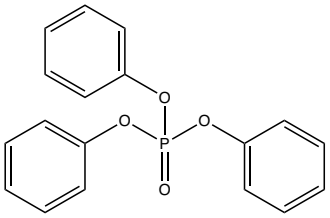
Isodecyl diphenyl phosphate



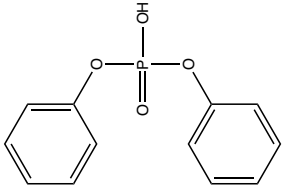
2-ethylhexyl
diphenyl phosphate



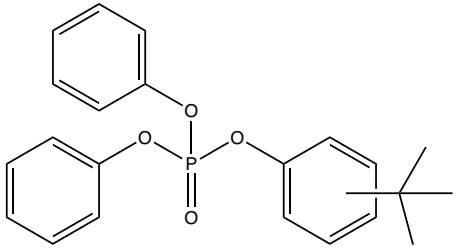
Isopropyl phenyl diphenyl phosphate
(Multiple Isomers)



triphenyl phosphate

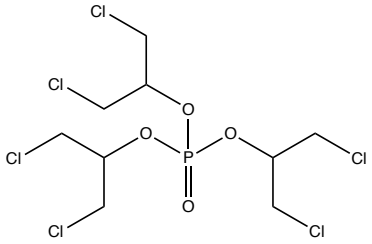


Diphenyl Phosphate
(urinary metabolite)

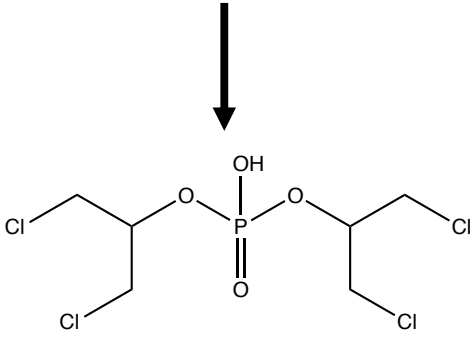


Tertbutyl phenyl diphenyl phosphate
(Multiple Isomers)

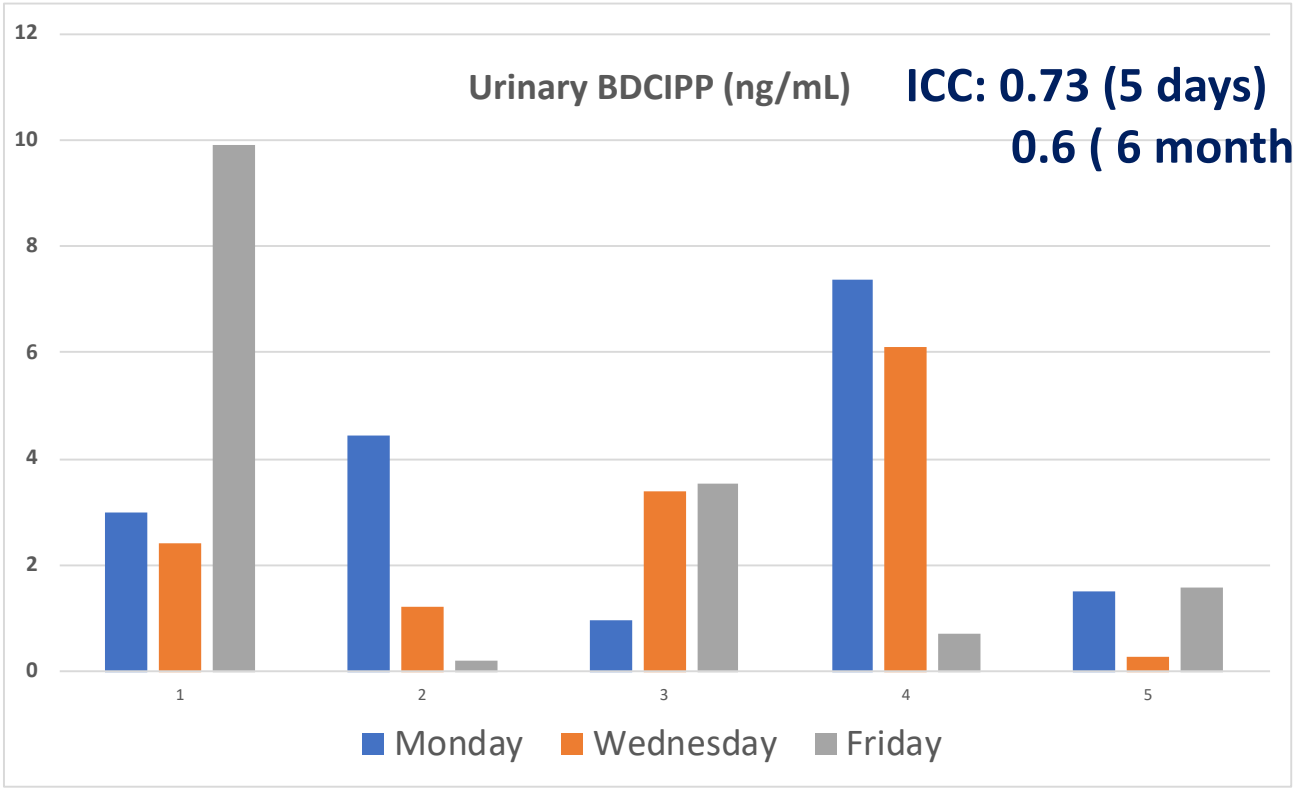
Problem: How variable are levels over time?



Tris (1,3-dichloro-2-propyl) phosphate
(TDCIPP)



Bis (1,3-dichloro-2-propyl) phosphate
(BDCIPP)



First morning urine samples collected from five individuals on Monday, Wednesday & Friday

What type of samples are best to characterize chemical exposures?

To support the “exposome” we need **cumulative** measures of exposure

Source: www.dohadfordoctors.com

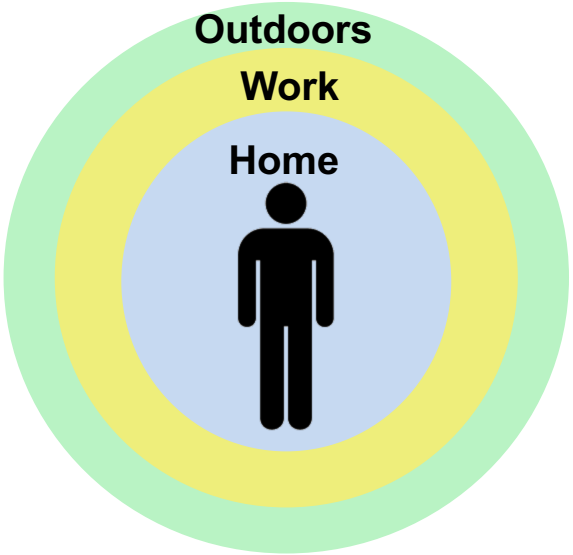
Radiation Badge

Source: www.med-pro.net

Characterization of the External Exposome

Need Approaches/Tools that:

- Integrate exposure measurements over time
- Integrate exposure measures across various micro-environments
- Low participant burden; easy to use

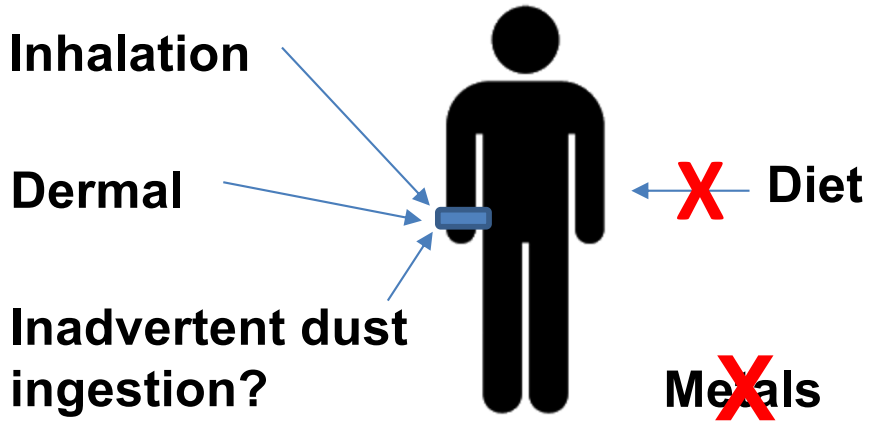


Wearable Samplers:
The Silicone Wristband

- **Wristbands first introduced as a wearable personal passive sampler to measure ambient exposure in occupational settings and in the general population**
  (O'Connell et al., 2014)

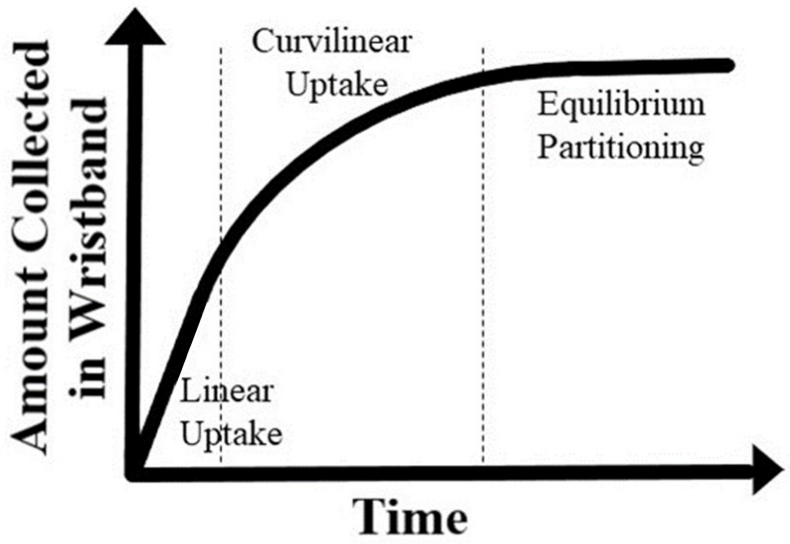
Polydimethylsiloxane (PDMS)

Exposure Routes



Chemical Accumulation in Wristbands

- Wristbands must be cleaned first
- Stored airtight until worn
- Typically worn for 5-7 days
- Wear continuously; chemicals sorb, but do not rapidly desorb
- Slope of uptake reflects:
  - Concentration gradient
  - Phys/chem properties (Log Koa)



Samon et al. 2022

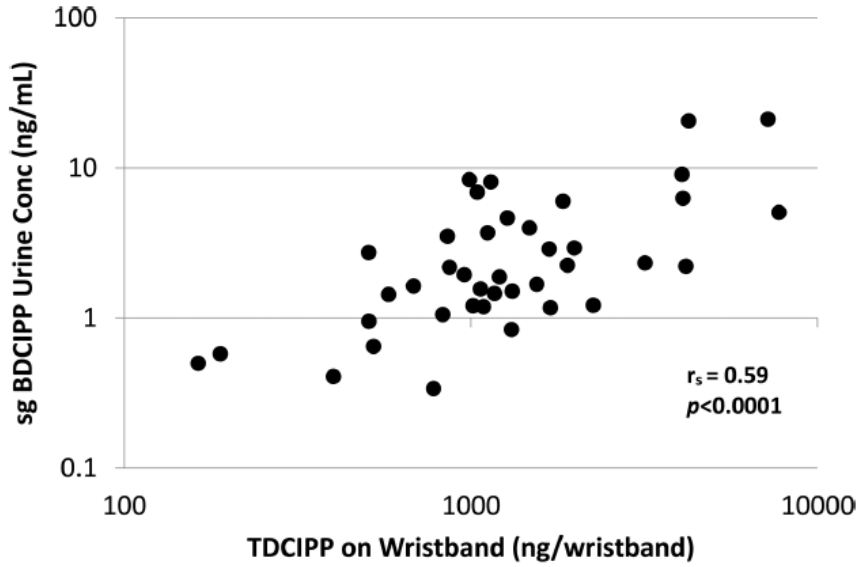
Are measurements of chemicals on wristbands correlated with internal dose?

Do Wristband Measurements Correlate with Internal Dose?

Environmental Science & Technology
Article
pubs.acs.org/est

Measuring Personal Exposure to Organophosphate Flame Retardants Using Silicone Wristbands and Hand Wipes

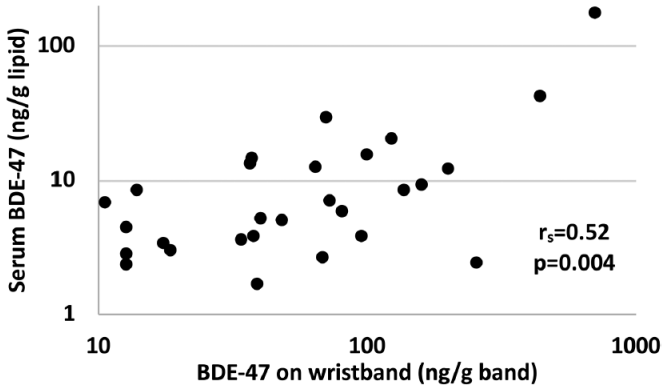
Stephanie C. Hammel,[†] Kate Hoffman,[†] Thomas F. Webster,[‡] Kim A. Anderson,[§] and Heather M. Stapleton*[,†]



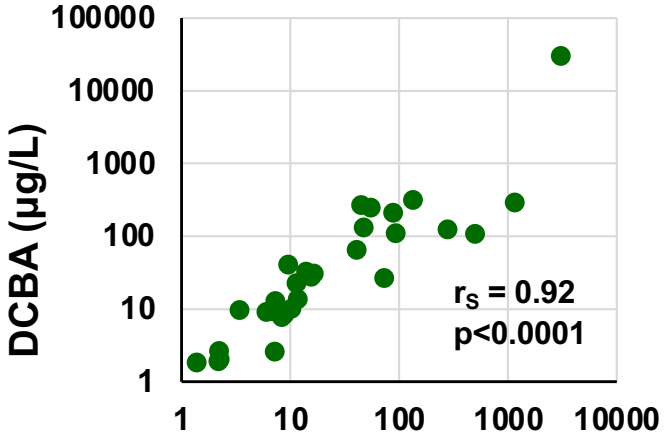
- 40 participants
- Wore a pre-cleaned wristband for 5 days. (24 hours a day; while sleeping and bathing/showering)
- Provided first morning void urine:
  Days 1, 3, 5

Do Wristband Measurements Correlate with Internal Dose? - Yes

Blood



Urine



Environmental Science & Technology

Article

Cite This: *Environ. Sci. Technol.* 2018, 52, 11875−11885

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Evaluating the Use of Silicone Wristbands To Measure Personal Exposure to Brominated Flame Retardants

Stephanie C. Hammel, Allison L. Phillips, Kate Hoffman, and Heather M. Stapleton*

Nicholas School of the Environment, Duke University, Durham, North Carolina 27708, United States

Supporting Information

Environmental Science & Technology

pubs.acs.org/est

Article

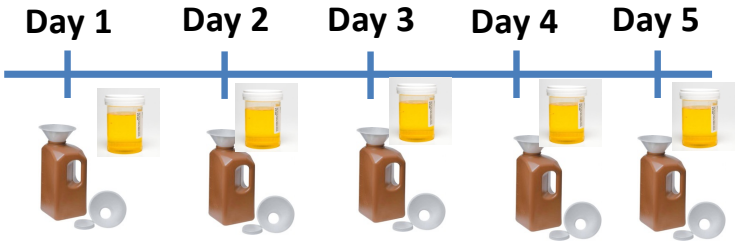
Comparative Assessment of Pesticide Exposures in Domestic Dogs and Their Owners Using Silicone Passive Samplers and Biomonitoring

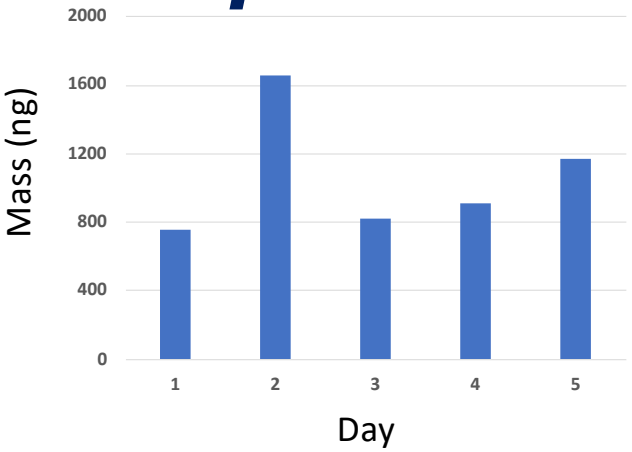
Catherine F. Wise, Stephanie C. Hammel, Nicholas J. Herkert, Maria Ospina, Antonia M. Calafat, Matthew Breen, and Heather M. Stapleton*

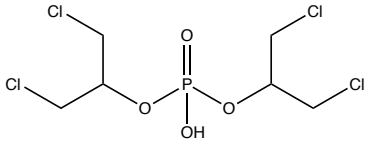
Are Wristbands Better Than Relying on a Single or Spot Urine Sample?

OR

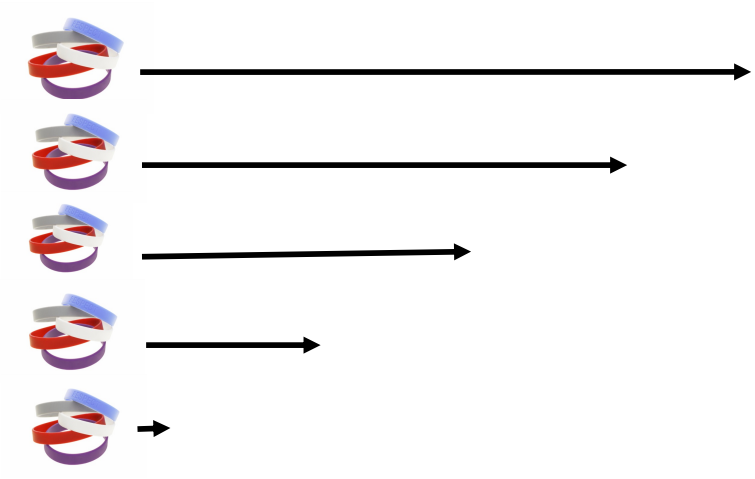
Wristbands or Spot Urine?

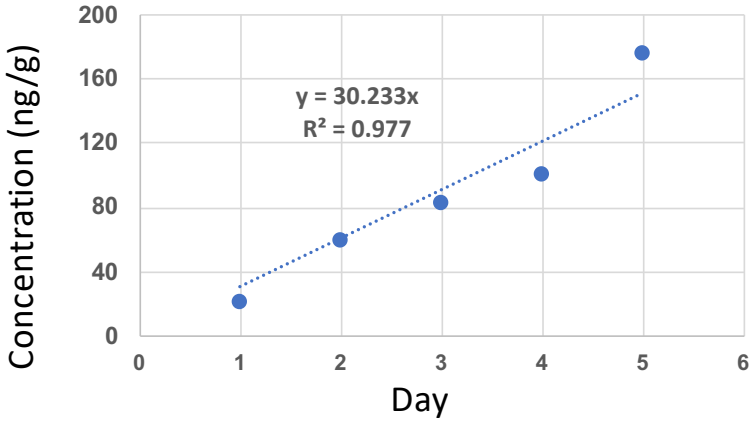




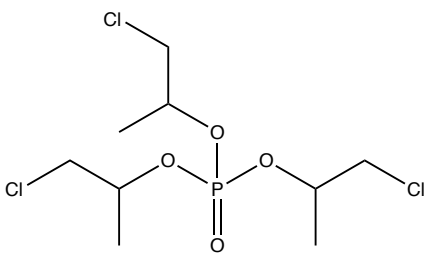


Urinary Metabolite

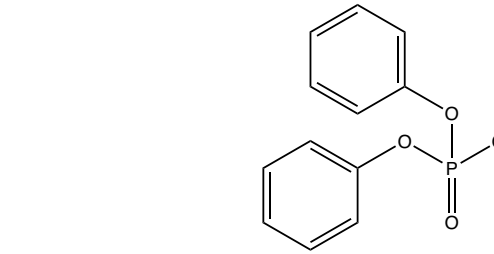




Chemical Accumulation on Wristbands

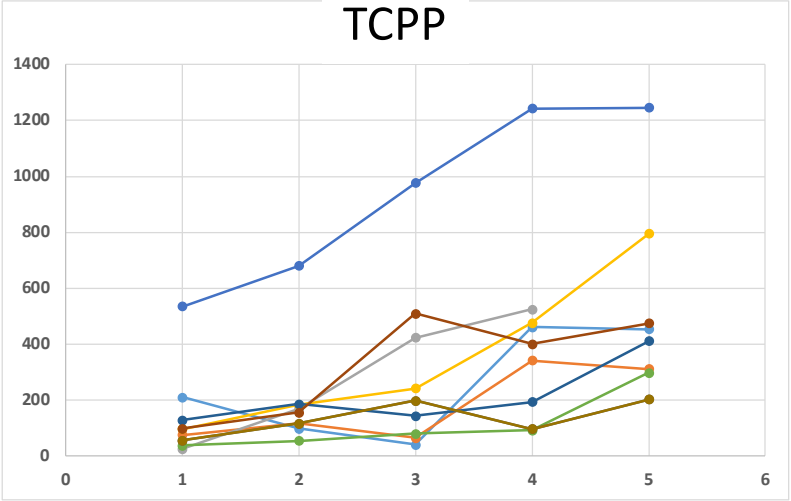


TCPP

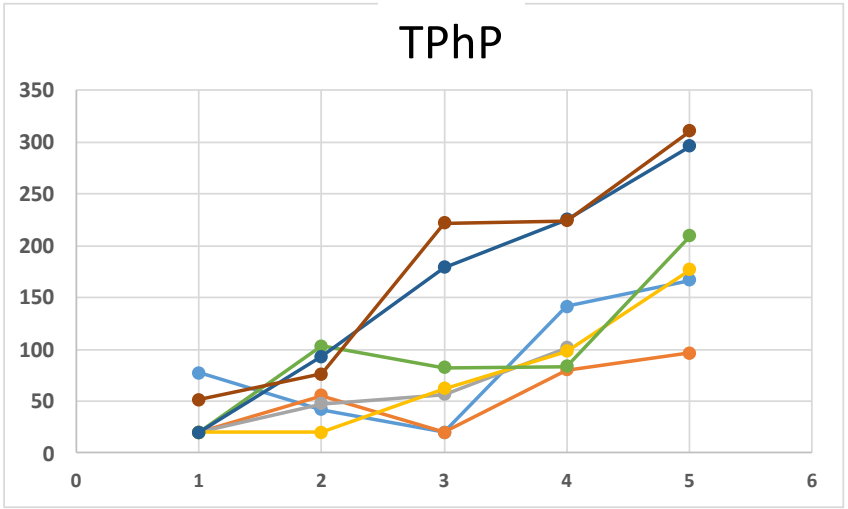


TPhP

Parts per billion(ng/g)



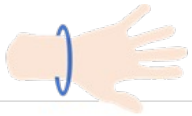
Sampling Days

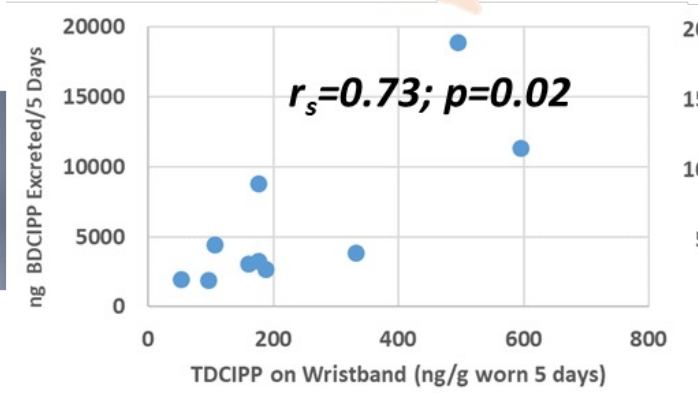


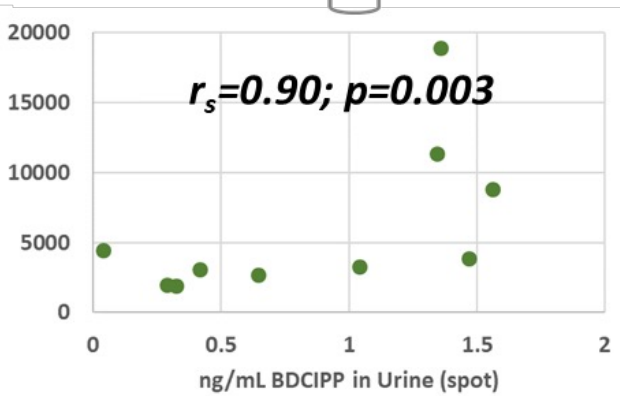
Sampling Days

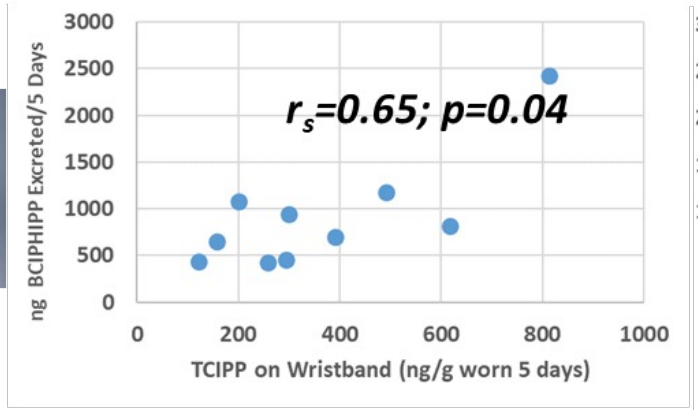
*Chemicals still accumulate despite showering daily.

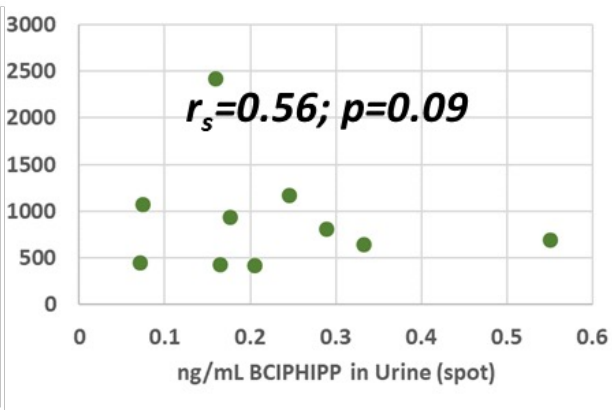
Wristbands or Spot Urine?











Major Findings:

Wristband's ability to predict the total mass excreted (over 5 days) was equivalent or better than a spot urine sample for some OPEs

Hoffman et al. 2021

Will chemical measurements on wristbands better predict internal dose compared to house dust? Handwipes?

Exposure in our Homes

- People spend a majority of time indoors
- Building materials and furnishings can be treated with semi-volatile organic chemicals (SVOCs)
- A large proportion of SVOC exposures occur in our homes
- Most studies measure indoor air/dust- should we use wristbands?

Toddler's Exposure to SVOCs in the Indoor Environment (TESIE)

- 203 children aged 3-6 years were recruited from 190 homes in central North Carolina between 2014-2016

- Children provided samples of blood, urine, and a handwipe during a home visit by the study team. A house dust sample was collected from the main living area, and a questionnaire was administered

House Dust

Foam Cushion

Hand Wipe

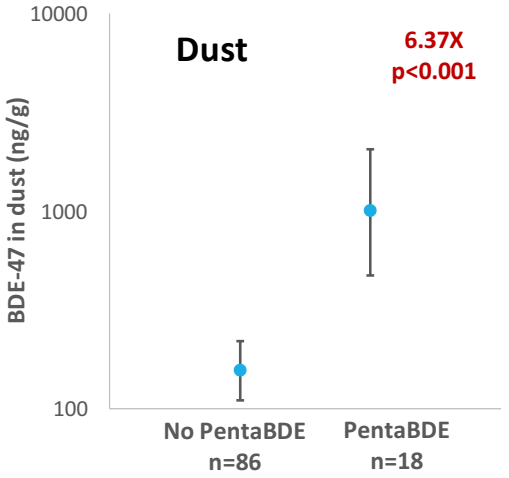
Wristband

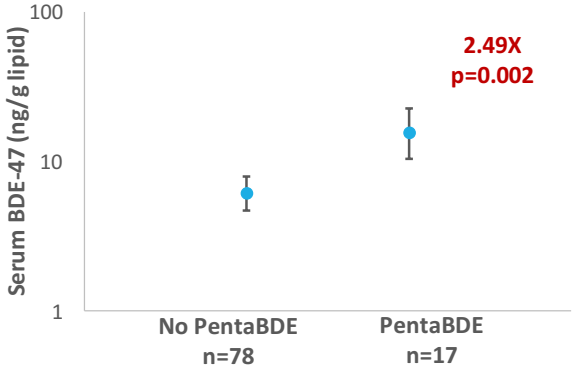
Serum

Urine

Sofas and Flame Retardant Exposure

- PentaBDE is a commercial FR mixture commonly applied to furniture foam until 2005 (banned from use due to concerns about persistence and toxicity)
- If PentaBDE was positively identify in the sofa (via GC-MS), levels in indoor dust were 6.4X higher than homes without PentaBDE in their sofa
- If PentaBDE was present in the sofa, blood levels of PBDEs were ~2.5X higher in people with PentaBDE in their sofa compared to people without PentaBDE in their sofa
- ONE item in the home was a significant predictor of exposure



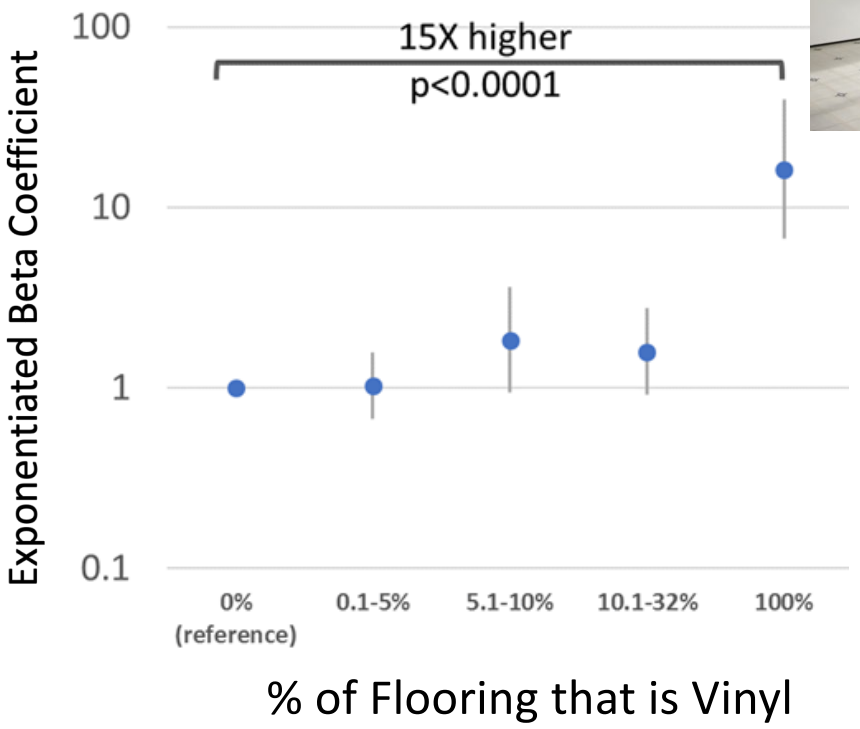


Stephanie Hammel PhD student

Hammel et al. 2017

Vinyl Flooring and Phthalate Exposure

- Flooring square footage measured in the home; categorized by % of vinyl floor in the home
- Benzyl butyl phthalate metabolite measured in children's pooled urine samples
- Higher levels (15X) were measured in children living in homes with 100% vinyl flooring



Statistical models adjusted for race, ethnicity, age, sex and outdoor temperature

Hammel et al. 2019

Correlations with Biomarkers of Exposure

Which samples have the highest correlation with urinary biomarkers?

Dust

Handwipes

Wristbands

Urine

Serum

Spearman correlation coefficients

(with urine or serum biomarker; n=77)

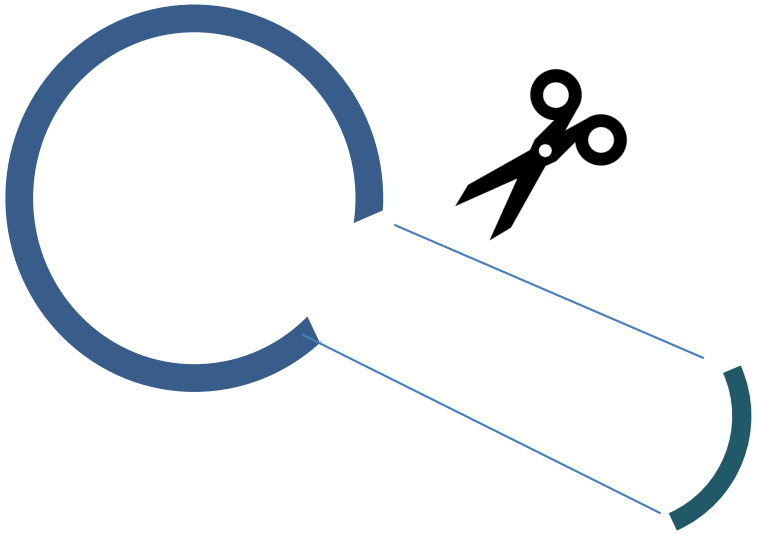
	Analyte Pair	Wristband	Handwipe	House Dust	
Organophosphate Flame retardants/ plasticizers	TDCPP - BDCIPP	0.52*	0.48*	0.13	Urine Correlations
	2IPPDPP – IPPPP	0.22*	0.20	0.13	
	4tBDPP- tbPPP	0.35*	0.16	0.05	
Phthalate Plasticizers	Diethyl phthalate	0.41*	NA	0.17	
	Benzyl butyl phthalate- MBzP	0.56*	0.56*	0.23*	
	Diisononyl phthalate	0.24*	0.22	0.20	
Brominated Flame Retardant	BDE-47 (n=19)	0.73*	0.71*	0.57*	Serum Correlations

* - statistically significant

Wristband Analyses

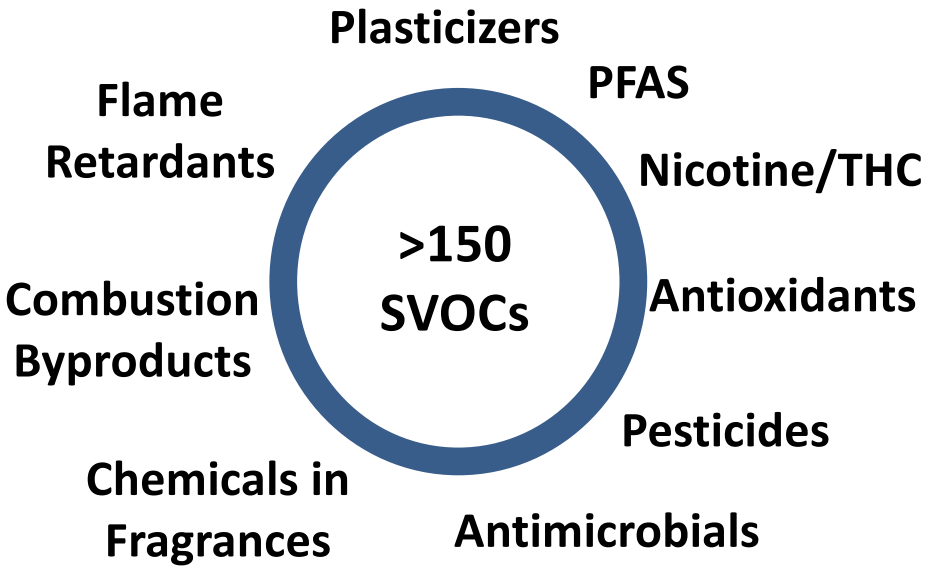
Analytical Details

Wristband (WB)



~1/5 of WB
(~0.7 grams)

Analytical Details

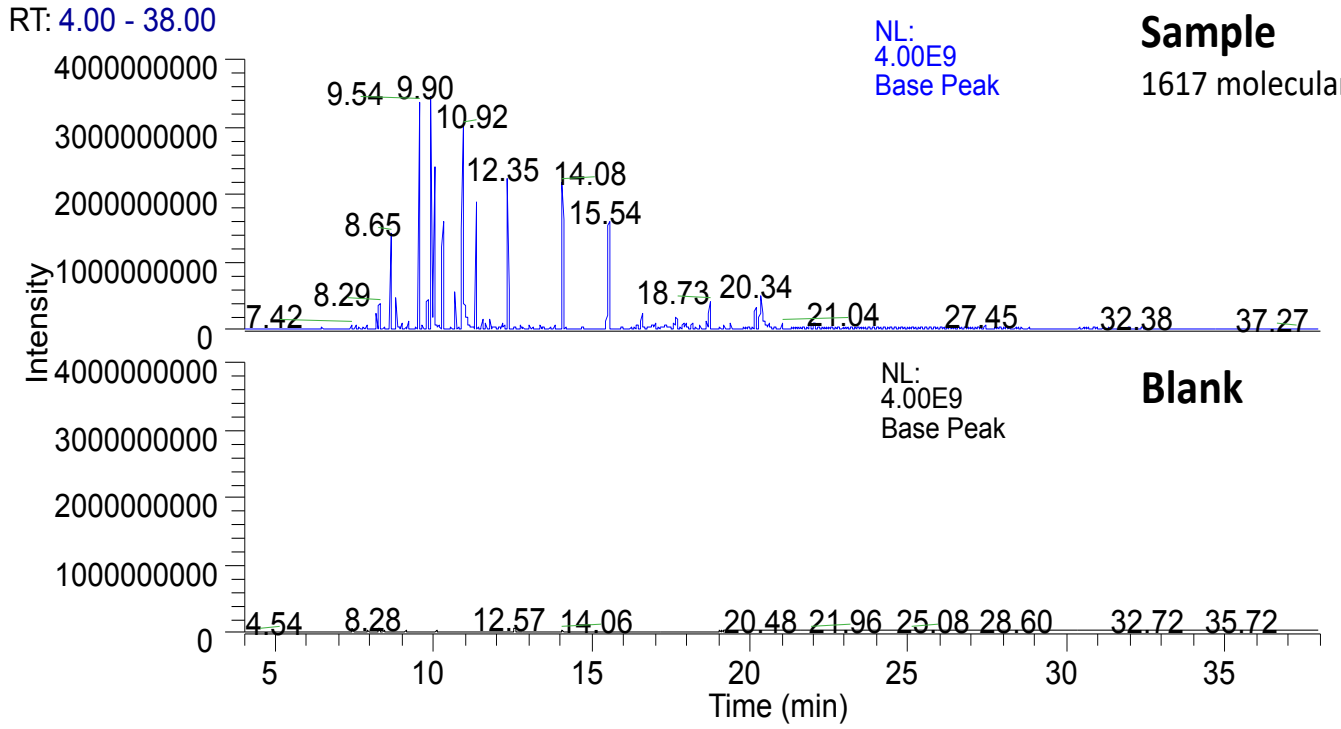


- Wristbands extracted and analyzed using high resolution gas chromatography high resolution mass spectrometry (GC-HRMS)
  - Targeted analysis
  - Untargeted analysis

Thermo Scientific™ Q Exactive™ GC Orbitrap™ GC-MS/MS

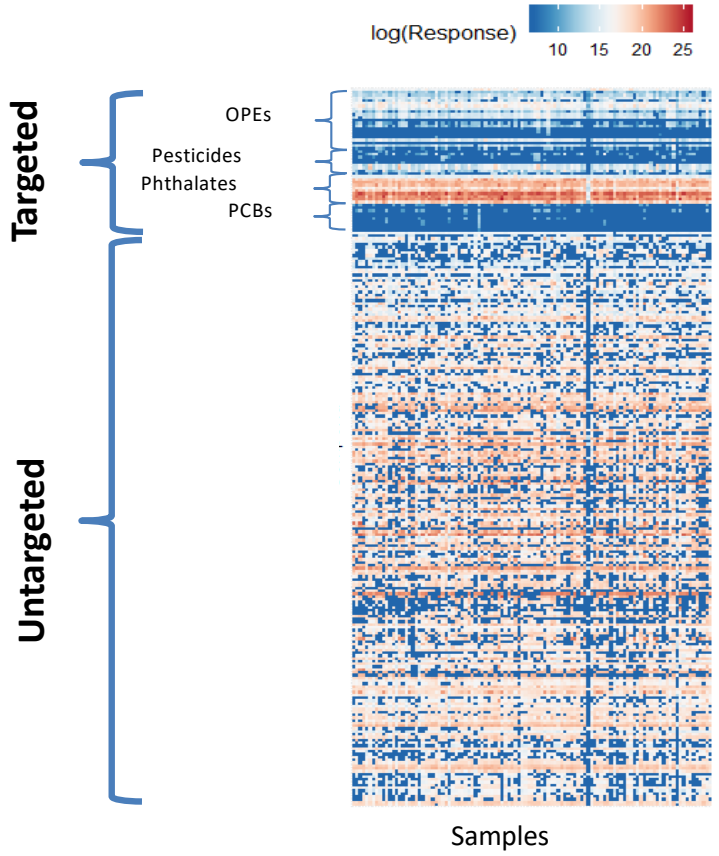
Untargeted Analyses

Nicholas Herkert, PhD



Exposure Data from Wristbands

- Data presented is from a cohort of 110 pregnant women in NYC (unpublished data)
- Untargeted features are much more abundant than targeted features
- Implication: we're not paying attention to the most abundant exposures!



Case Studies with Wristbands

1. **Occupational (Firefighters)**
2. **One Health (Companion canines)**
3. **Regional differences in exposure**

Characterizing Exposures in Firefighters

Jessica Levasseur
PhD candidate

- Research collaboration with firefighters in Durham, NC
- Each firefighter was asked to wear silicone wristbands for 6 days while during the following three periods:

Home

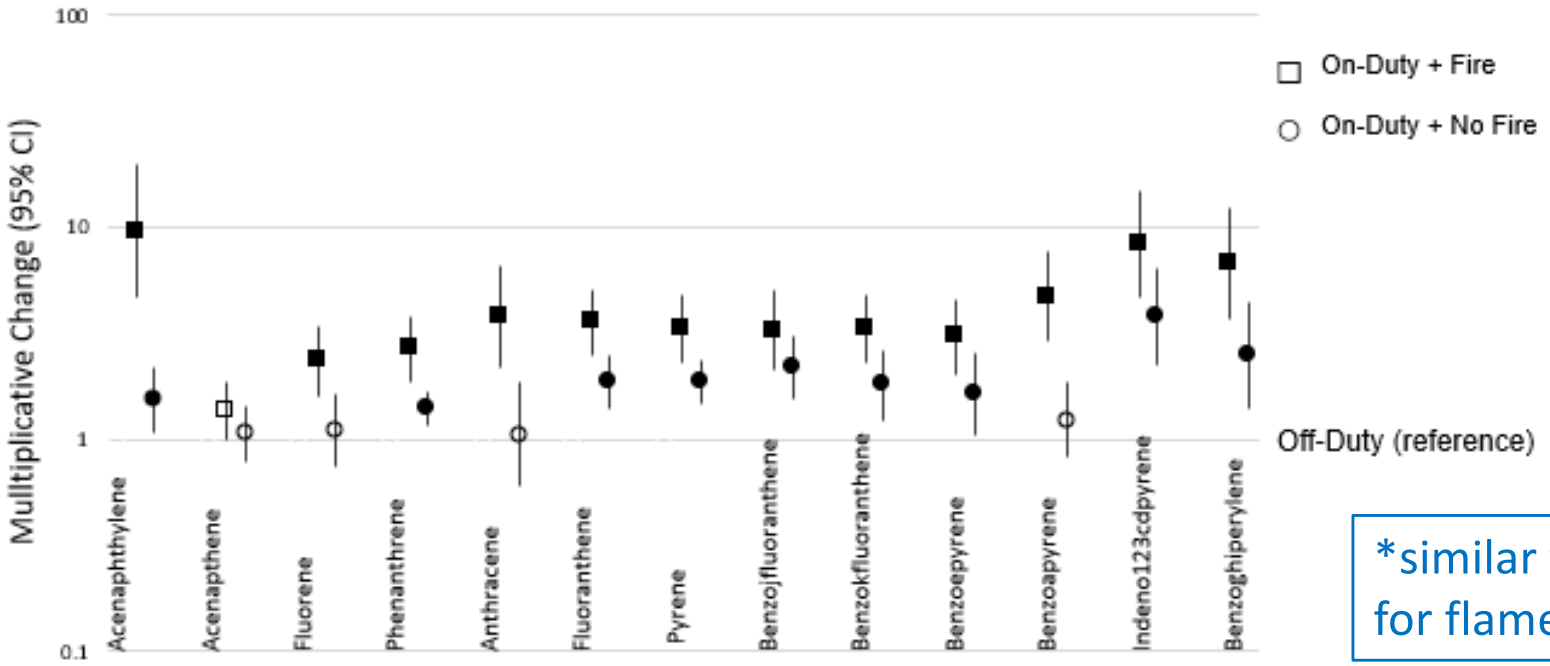
Work
(no fire event)

Work
(fire event)

Question: How do chemical exposures change on-duty vs off-duty? When responding to a fire?

Levasseur et al., 2022

PAH Exposures in Firefighters

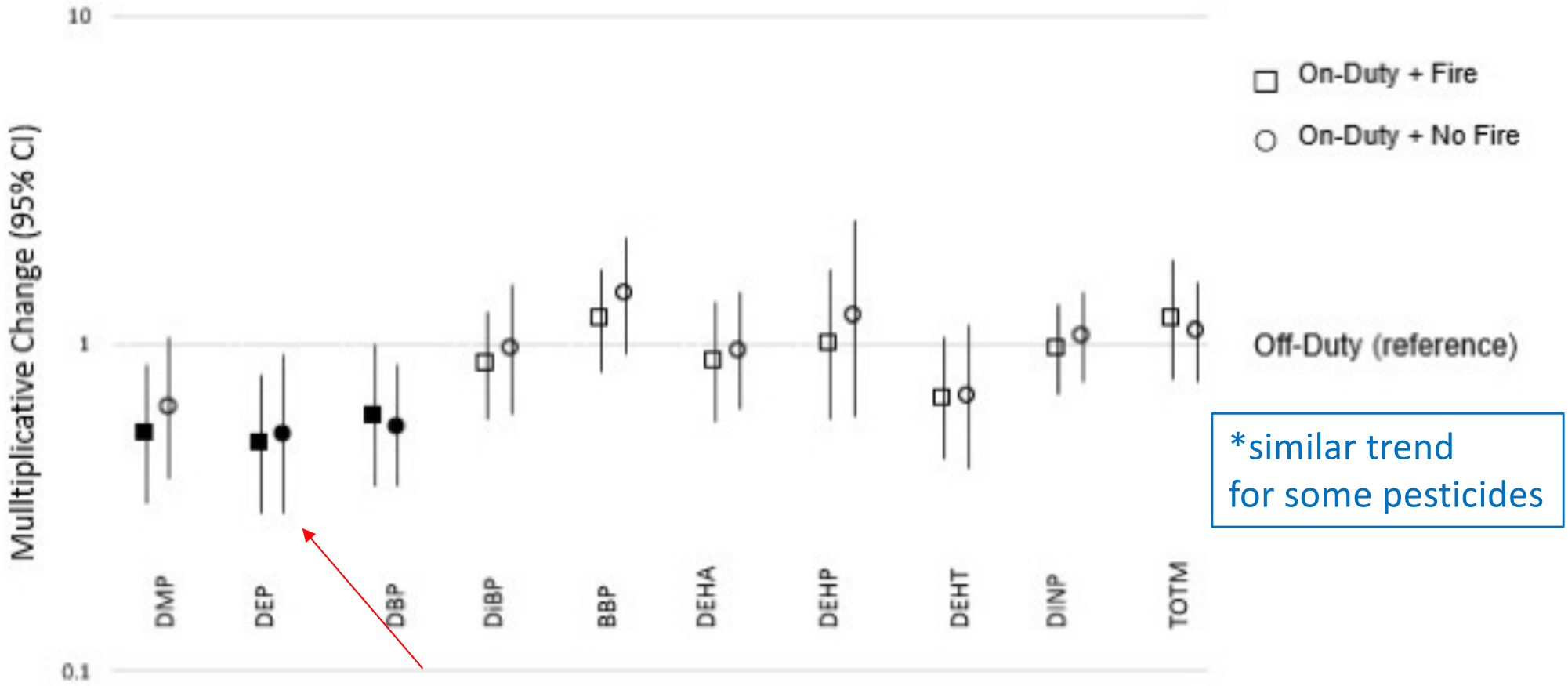


*similar trend
for flame retardants

Figure 1. Multiplicative change (10^{β}) in silicone wristband PAH measurements while on-duty (with fire event and without fire event) as compared to off-duty. Exponentiated beta coefficients from these regression analyses represent the multiplicative change in $\log_{10}$-transformed mass of chemical(s) found on on-duty wristbands relative to the reference category of off-duty wristbands. Filled shapes indicate $p<0.05$.

Levasseur et al., 2022

Phthalate Exposures in Firefighters



*similar trend
for some pesticides

Used in personal care products

Levasseur et al., 2022

Pets & People: A Shared Environment

- Do pets & their owners have similar chemical exposures?
- Can we use silicone dog tags to support canine oncology research?

n = 30 pairs

Wristband

Dog-tag

Cathy Wise, PhD

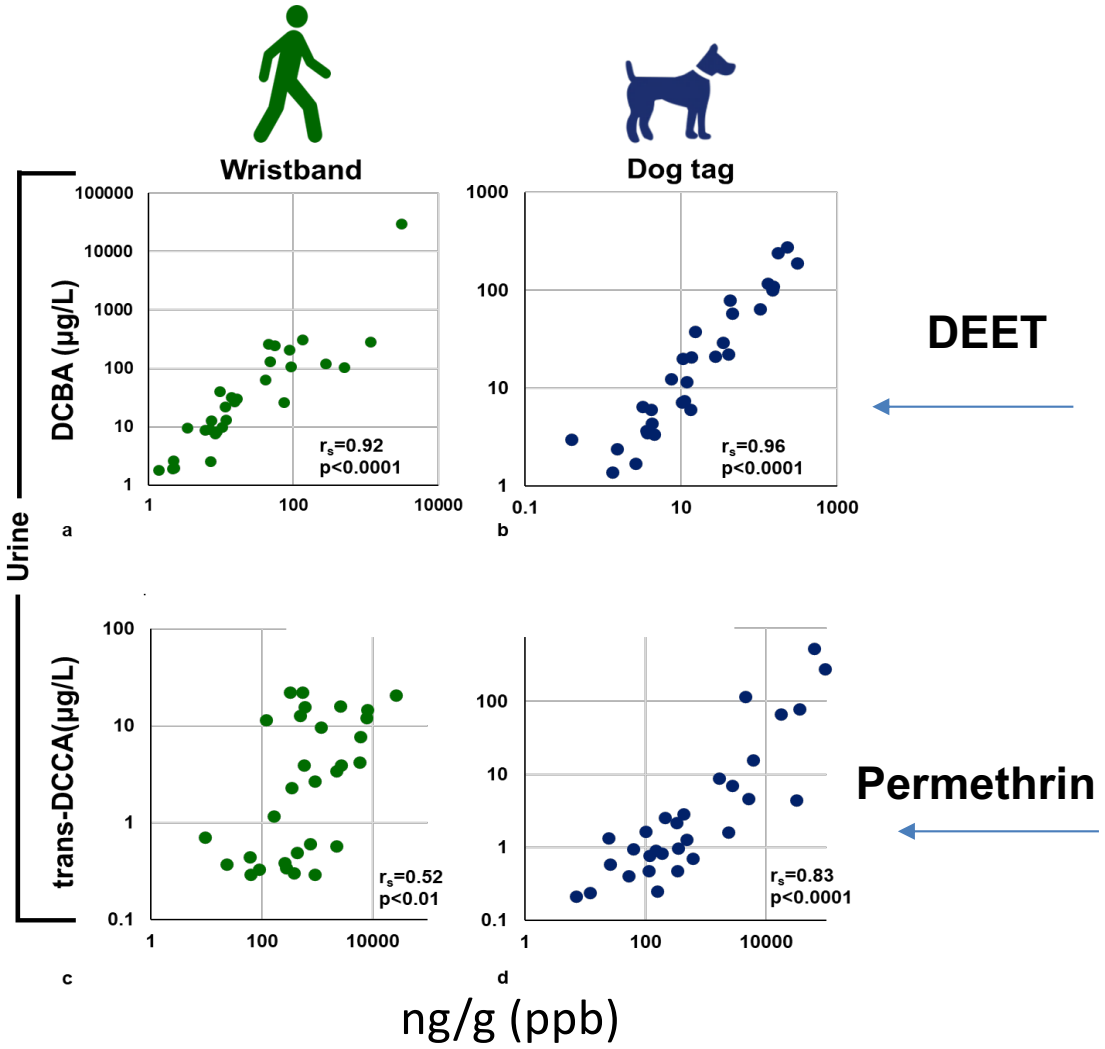
Day 1 → Day 3 → Day 5

Urine



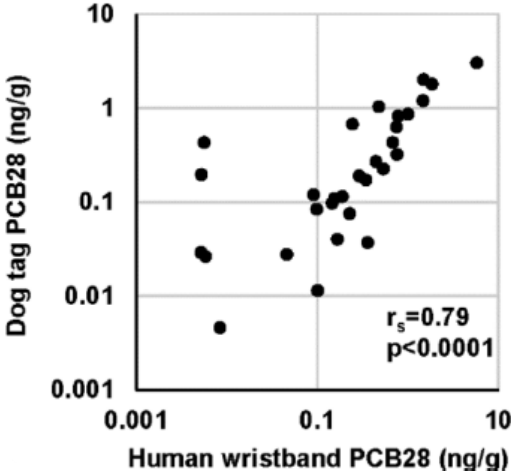
Pooled Urine

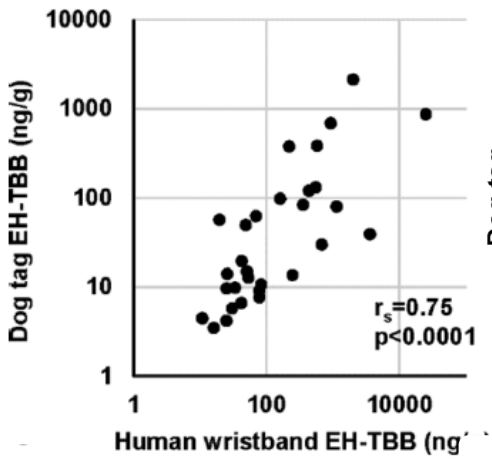
- Several OPE and pesticides were significantly correlated in silicone tags and pooled urine
- Correlations often stronger in dogs compared to humans

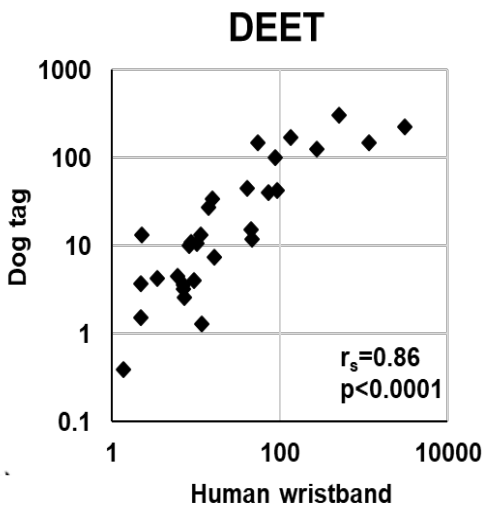


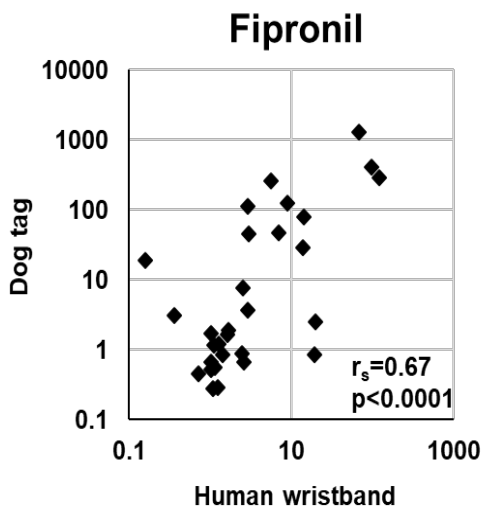
Wise et al. 2020, 2022

Dog & Owners Have Shared Exposures









PCB 28
A Legacy Contaminant

EH-TBB
A Novel BFR

Pesticide Exposures

Wise et al. 2020, 2022

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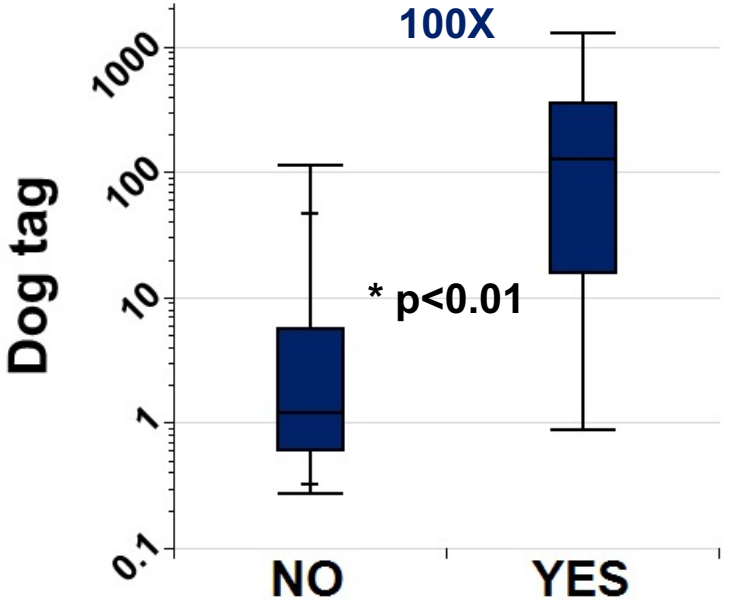
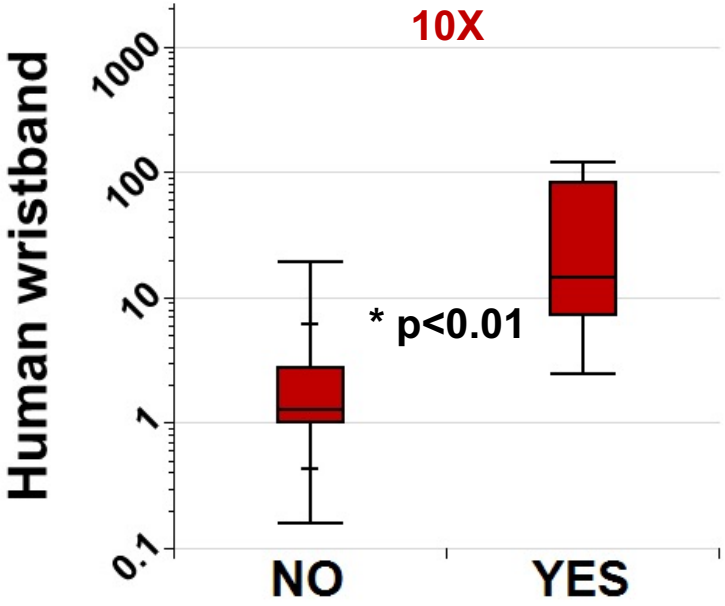
Fipronil Exposure

Reported use of flea and tick product containing fipronil

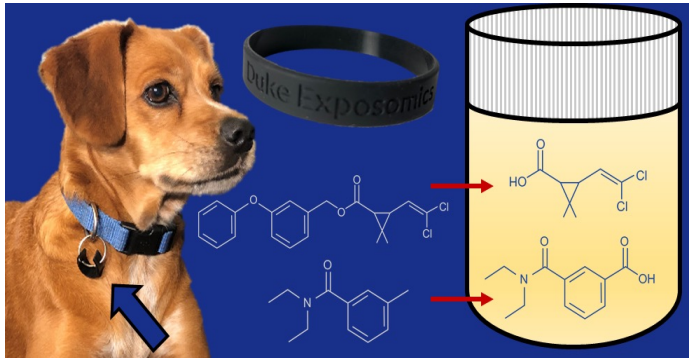
YES n=9
NO n=21





Wise et al. 2022

Investigating Exposures Associated with Bladder Cancer



Matthew Breen, PhD
NC State Vet School

Cathy Wise, PhD
Duke

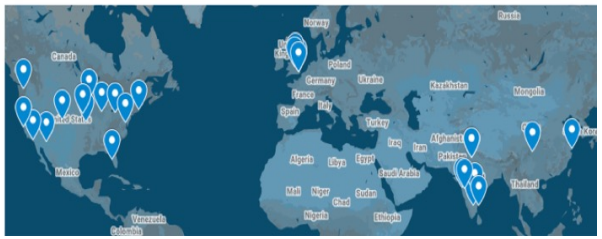
- Our research team (Duke & NC State) is currently conducting a case-control study using silicone samplers to examine gene-environment risk factors for bladder cancer:

  "**A Canine Model for Human High-Risk Non-Muscle Invasive Human Bladder Cancer: Molecular and Environmental Considerations**"

- 25 Cases, 75 Controls (age, sex and breed matched; recruited 2020-2021 using AKC resources)
- Cases have a specific BRAF mutation detected in urine suggesting they have high risk for developing bladder cancer (<5% FA; no clinical symptoms of disease)
- Silicone tags analyzed using both targeted and untargeted approaches

Regional Differences in Chemical Exposures

Wristbands in Offices Worldwide



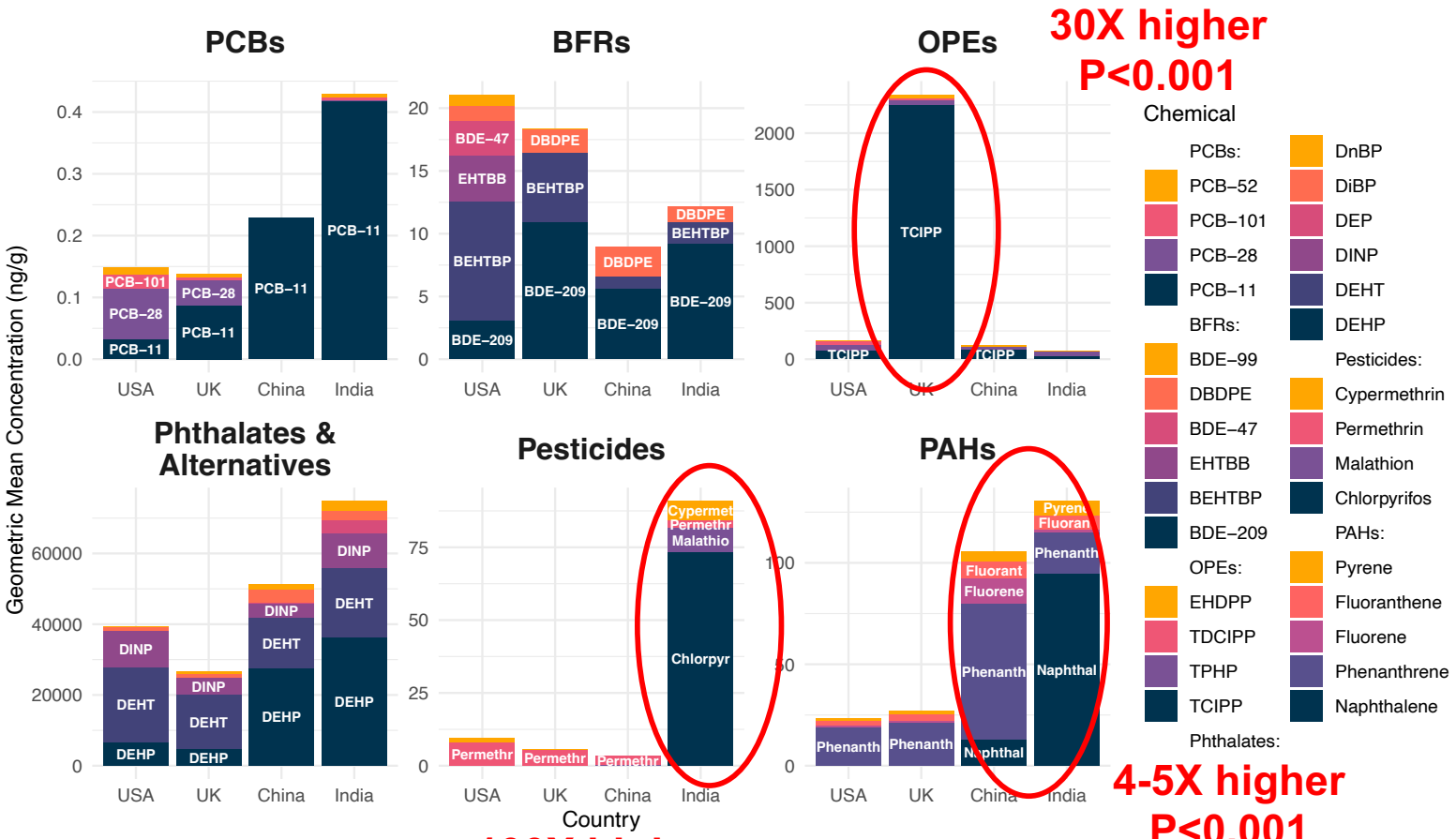
Goal: Explore exposure differences by region.

N= 251 people

Anna Young, PhD
Postdoctoral Researcher
Harvard University

Joe Allen, PhD
Associate Professor
Harvard University

Geographic Differences in Exposure



Young et al., 2022

Using Wristbands in Toxicology Research

Environmental Science & Technology

pubs.acs.org/est

Article

https://pubs.acs.org/est?ref=pdf

Thyroid Receptor Antagonism of Chemicals Extracted from Personal Silicone Wristbands within a Papillary Thyroid Cancer Pilot Study

Christopher D. Kassotis, Nicholas J. Herkert, Stephanie C. Hammel, Kate Hoffman, Qianyi Xia, Seth W. Kullman, Julie Ann Sosa, and Heather M. Stapleton*

Cite This: *Environ. Sci. Technol.* 2020, 54, 15296−15312 | Read Online

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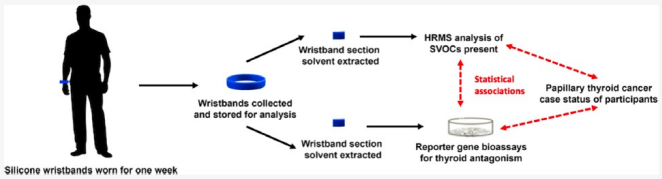

ABSTRACT: Research suggests that thyroid cancer incidence rates are increasing, and environmental exposures have been postulated to be playing a role. To explore this possibility, we conducted a pilot study to investigate the thyroid disrupting bioactivity of chemical mixtures isolated from personal silicone wristband samplers within a thyroid cancer cohort. Specifically, we evaluated TRβ antagonism of chemical mixtures extracted from wristbands (n = 72) worn by adults in central North Carolina participating in a case−control study on papillary thyroid cancer. Sections of wristbands were solvent-extracted and analyzed via mass spectrometry to quantify a suite of semivolatile chemicals. A second extract from each wristband was used in a bioassay to quantify TRβ antagonism in human embryonic kidney cells (HEK293/17) at concentrations ranging from 0.1 to 10% of the original extract (by volume). Approximately 70% of the sample extracts tested at a 1% extract concentration exhibited significant TRβ antagonism, with a mean of 30% and a range of 0−100%. Inhibited cell viability was noted in >20% of samples that were tested at 5 and 10% concentrations. Antagonism was positively associated with wristband concentrations of several phthalates, organophosphate esters, and brominated flame retardants. These results suggest that personal passive samplers may be useful in evaluating the bioactivities of mixtures that people contact on a daily basis. We also report tentative associations between thyroid receptor antagonism, chemical concentrations, and papillary thyroid cancer case status. Future research utilizing larger sample sizes, prospective data collection, and measurement of serum thyroid hormone levels (which were not possible in this study) should be utilized to more comprehensively evaluate these associations.

Kassotis et al. 2020

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

Hormone receptor activities of complex mixtures of known and suspect chemicals in personal silicone wristband samplers worn in office buildings

Anna S. Young [a,*], Nicholas Herkert [b], Heather M. Stapleton [b], Brent A. Coull [a,c], Russ Hauser [a], Thomas Zoeller [d], Peter A. Behnisch [e], Emiel Felzel [e], Abraham Brouwer [e], Joseph G. Allen [a]

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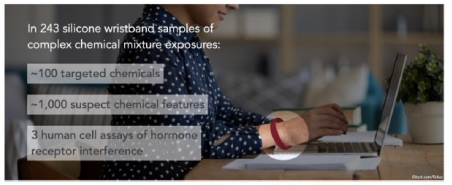
[e] BioDetection Systems, Science Park 406, 1098 XH Amsterdam, Netherlands

HIGHLIGHTS

- Office workers wore silicone wristbands to collect exposures to chemical mixtures.
- We observed 1044 chemical signatures in wristband samples via suspect screening.
- Every wristband extract was hormonally active in human hormone receptor cell assays.
- The chemical mixtures disrupted estrogen, androgen, and thyroid hormone receptors.
- Exposures were influenced by personal care products, buildings, gender disparities.

GRAPHICAL ABSTRACT



Young et al. 2023

Advantages of Using Silicone Samplers to Support Exposomics Research

- Silicone samplers are a non-invasive tool for measuring exposure to hundreds of chemicals.
- Can be easily mailed back and forth (no clinic visit!). Chemical levels are stable at room temperature for several months (stable at -20C for years)
- Provide a measure of *integrated average exposure over time*; can support prospective study designs and complement biomonitoring
- ***However,*** they do not capture dietary exposure and do not provide insight into differences in toxicokinetics

Remaining Uncertainties/Questions

- **Does showering/bathing, swimming, etc impact accumulation?**
- **Right hand vs left hand?**
- **Role of clothing (long sleeved vs short sleeves)**
- **Sweat?**
- **Activity – does greater movement enhance uptake?**

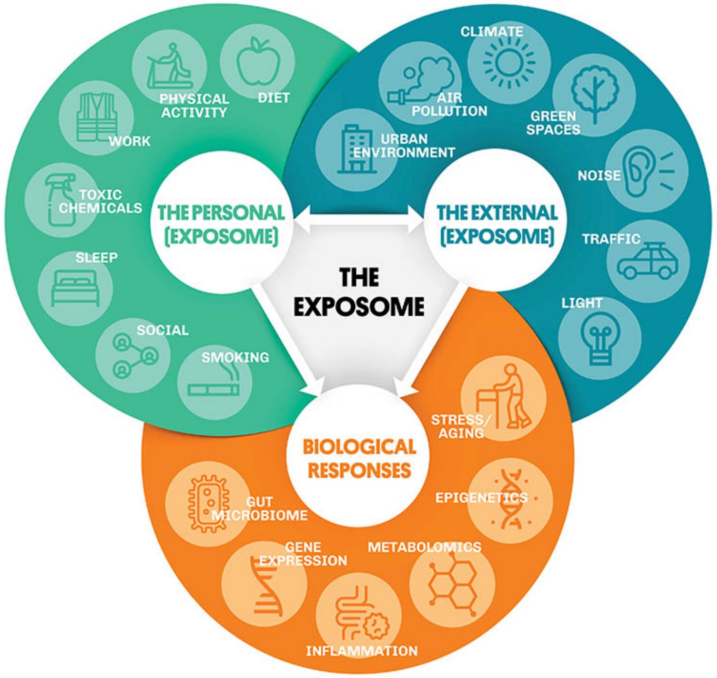
The Future of Exposome Research

1. Need approaches that link the external environment with biological responses

   Deploy wristbands when collecting biological specimens?

2. How does exposure to chemical mixtures change over time?

   Prospective collection of wristbands in cohort studies?



Source: www.isiglobal.com

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- Antonia Calafat
- Andreas Sjodin

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EPA United States Environmental Protection Agency

Children's Health & Discovery Initiative
At Duke University

Michael & Annie Falk Foundation

Thanks to our **participants** for providing samples for these studies!!