Chemical Suspect Screening as a New Approach to Biomonitoring: An Application in Firefighters and Office Workers

Presentation to the Scientific Guidance Panel
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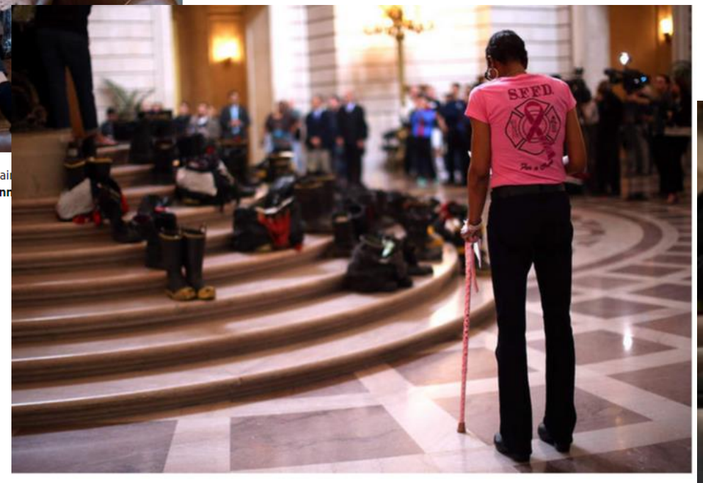
Mounting concern about rates of premenopausal breast cancer among women firefighters in San Francisco

Concern grows in firefighters, others after cancer-causing flame retardants found in test subjects

HIGHLIGHTS

San Francisco firefighters Casey McElheney and Karen Heald with their German short-hai
Nahiku at their home in Davis, are sitting on a couch with flame retardant chemicals. **Mann**
mcrisostomo@sacbee.com



Former San Francisco firefighter and cancer survivor Denise Elarms waits Wednesday to speak during a remembrance ceremony held for San Francisco firefighters who have died of cancer. (Photo by Justin Sullivan/Getty Images)

MIKE KOOZMIN/THE S.F. EXAMINER

Fighting: San Francisco Fire Department firefighter Jeanine Nicholson, seen at her Berkeley home, has undergone a double mastectomy and chemotherapy.

Studies show firefighters have higher exposures to:

Flame retardants
- Burning furniture, protective clothing, etc.

Perfluorinated chemicals
- Chemical in firefighter turnouts & firefighting foams

Polycyclic aromatic hydrocarbons (PAHs)
- Products of combustion

Diesel exhaust – nitro-PAHs
- Fire equipment

Dioxins and furans
- Combustion by-products during fire events

Studies almost exclusively on men.

Photo: Terray Sylvester / The Chronicle
Lieutenant Patty Lui
http://www.sfgate.com/health/article/S-F-Fire-Department-joins-study-into-breast-5833837.php#photo-7019384

Environmental Factors in Breast Cancer

Supplement to ***Cancer***

Chemicals Causing Mammary Gland Tumors in Animals Signal New Directions for Epidemiology, Chemicals Testing, and Risk Assessment for Breast Cancer Prevention

Ruthann A. Rudel, MS
Kathleen R. Attfield, BS
Jessica N. Schifano, BA
Julia Green Brody, PhD

Identifying chemical carcinogens in animal studies is currently the primary means of anticipating cancer effects in humans. Animal studies to evaluate potential chemical carcinogenicity are particularly important for breast cancer because environmental and occupational epidemiologic research is sparse.

Many of these chemicals have been shown to be mammary carcinogens in animal toxicology studies and warrant further study.

- Characterize exposures in humans.
- Inform regulatory, occupational and individual actions to reduce exposures.

Women Firefighter Biomonitoring Collaborative

Women Firefighters Biomonitoring Collaborative

UNITED FIRE SERVICE WOMEN SAN FRANCISCO

SAN FRANCISCO FIREFIGHTERS CANCER PREVENTION FOUNDATION

THE UNIVERSITY OF CALIFORNIA BERKELEY LET THERE BE LIGHT 1868

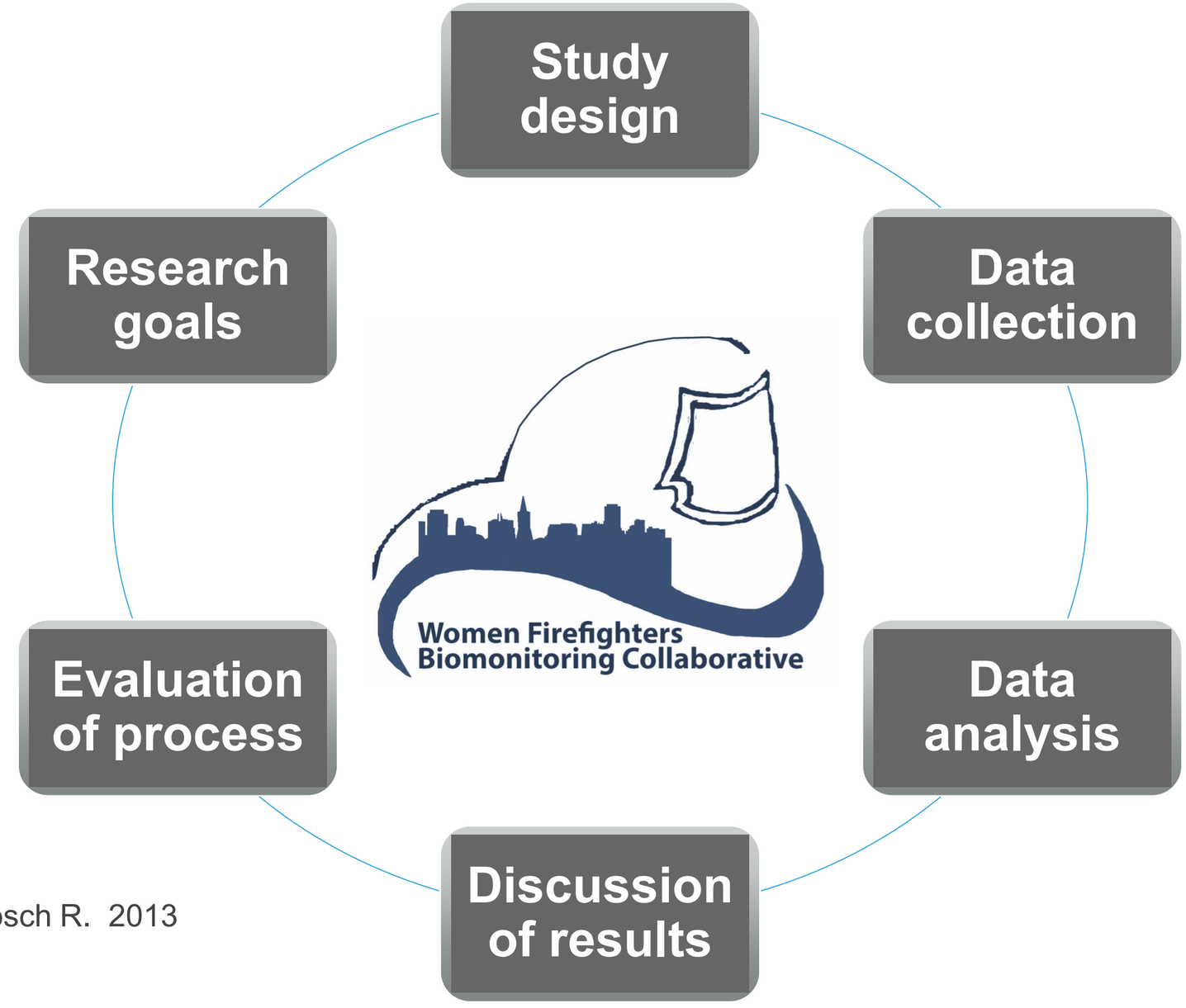
UCSF University of California San Francisco *advancing health worldwide*

SILENT SPRING INSTITUTE Researching the Environment and Women's Health

Breast Cancer Prevention Partners Exposing The Cause Is The Cure

COMMONWEAL

Community-Based Participatory Research



Balazs CL, Morello-Frosch R. 2013

Study Aims:

1. Characterize chemical exposures among women firefighters
2. Assess potential impacts on upstream biomarkers of effect

Office Workers

Firefighters

Exposure after a fire event

Women Firefighter Biomonitoring Collaborative

Inclusion criteria:

- Over 18 years old
- Non-smokers
- Minimum of 5 years with SFFD (FF only)
- On “active” duty (FF only)

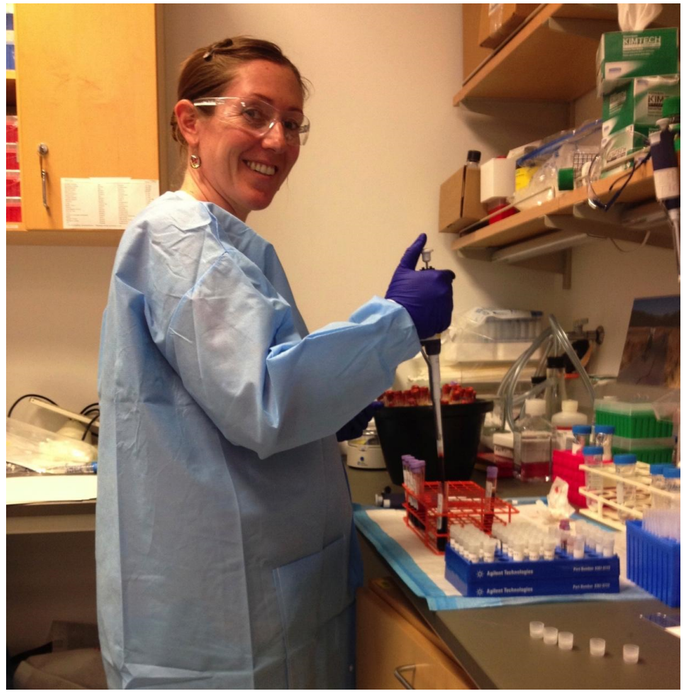
Study activities:

- Exposure assessment interview
- Biospecimen collection (blood and urine)

Number of participants included in chemical suspect screening:

- Female firefighters: 83
- Female officer workers: 79

Collection of Biospecimens (serum, urine, and whole blood)



Emily O’Rourke (Firefighter, UFSW), processing samples

Chemical exposures

- Perfluoroalkyl and polyfluoroalkyl substances (PFASs)
- Flame retardants (OPFRs)
- Non-targeted chemical analysis

Biomarkers of effect

- Thyroid hormones
- Telomere length

Exposure Assessment Interview

- Occupational position and work activities
- Fast food, take-out food, and frozen foods
- Personal care product use
- Consumer products, furniture, and carpets

Women Firefighter Bio-archive

170 WFBC participants agreed to bank samples for future studies.

Approximate milliliters of sample archived per participant by study group

Work Group	N*	Serum	Whole Blood	Plasma	Buffy Coat**	RBCs	Urine (spot)	Urine (MV***)
Firefighters	83	4.00	2.20	1.10	0.50	2.00	7.00	7.00
Office Workers	79	4.00	2.20	1.10	0.50	2.00	7.00	7.00

*Five participants declined to bank their samples
**Buffy coat samples include one aliquot with RNAlater and one without
***Morning void urine

Environmental Science & Technology

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Article

Integrating Exposure Knowledge and Serum Suspect Screening as a New Approach to Biomonitoring: An Application in Firefighters and Office Workers

Rachel Grashow, Vincent Bessonneau, Roy R. Gerona, Aolin Wang, Jessica Trowbridge, Thomas Lin, Heather Buren, Ruthann A. Rudel,* and Rachel Morello-Frosch*

Cite This: https://dx.doi.org/10.1021/acs.est.9b04579

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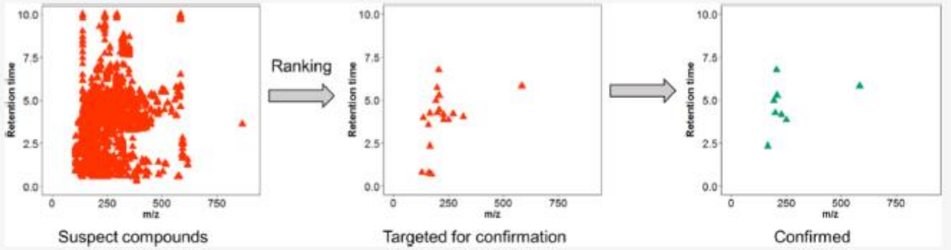

Environmental Science & Technology

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Article

Exposure to Perfluoroalkyl Substances in a Cohort of Women Firefighters and Office Workers in San Francisco

Jessica Trowbridge, Roy R. Gerona, Thomas Lin, Ruthann A. Rudel, Vincent Bessonneau, Heather Buren, and Rachel Morello-Frosch*

Cite This: https://dx.doi.org/10.1021/acs.est.9b05490

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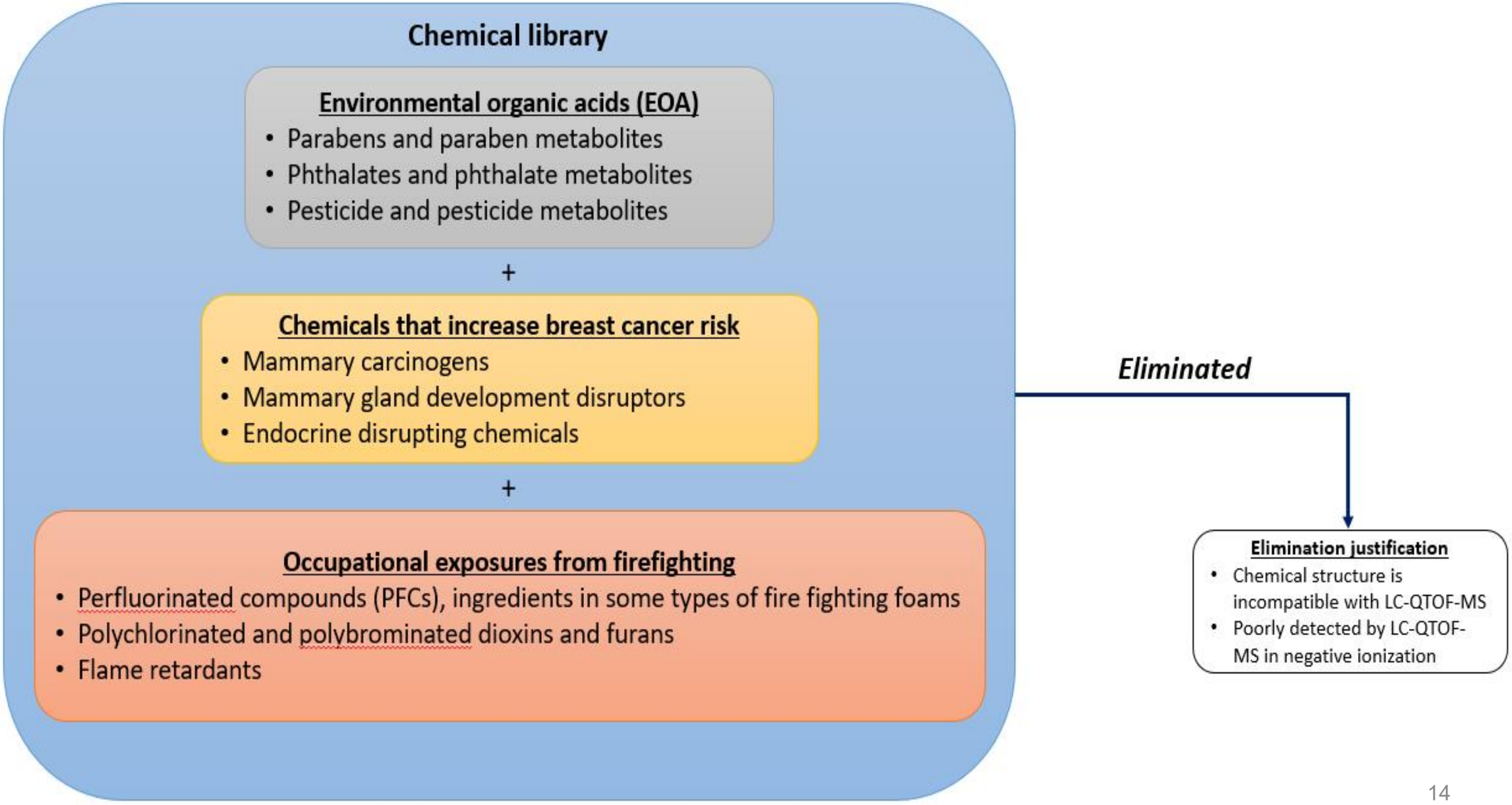
Study Demographics

characteristic	OWs (n = 79)	FFs (n = 83)	p-value[b]
Age			
mean ± SD	48.1 ± 10.6	47.9 ± 8.4	0.4
Race/Ethnicity *n* (%)			
non-Hispanic Asian	17 (22)	13 (16)	0.3
non-Hispanic blacks	5 (6)	9 (11)	
Hispanics of all races	7 (9)	8 (9)	
multiracial	10 (13)	16 (19)	
non-Hispanic whites	40 (50)	37 (45)	
Education *n* (%)			
high school or less	5 (6)	6 (7)	<0.001
some college	10 (13)	40 (48)	
college graduates or higher	64 (81)	37 (45)	
BMI			
mean (SD)	25.8 (5.2)	26.2 (3.5)	0.2
Household Income *n* (%)			
<$99,999	23 (29)	1 (1)	<0.001
$100,000–174,999	18 (23)	29 (35)	
$175,000–199,999	12 (15)	17 (20)	
>$200,000	26 (33)	36 (44)	

OW=office worker
FF= firefighter

Developing an in-house chemical mass spectra database

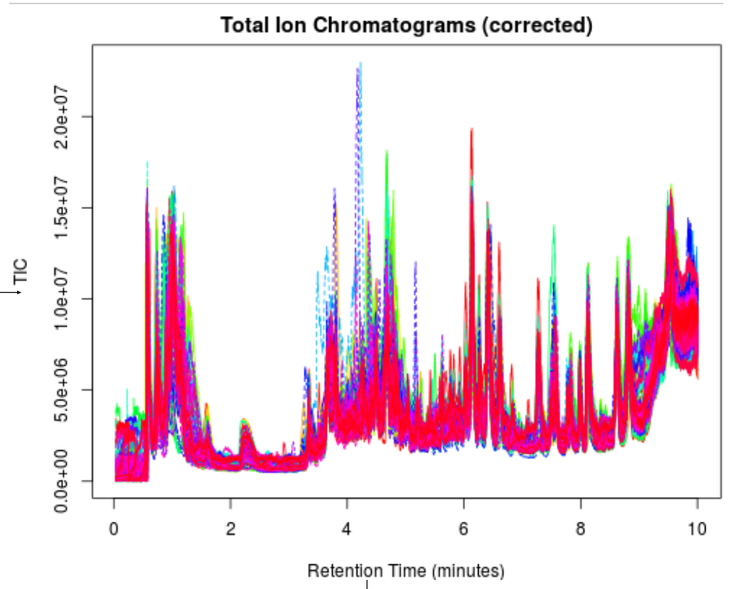


Identification of novel chemical exposures in study

83 serum samples from women firefighters

79 serum samples from women office workers

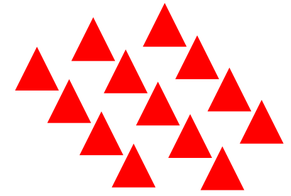
Liquid Chromatography with Quadrupole Time-Of-Flight Mass Spectrometry (LC-QTOF/MS) ESI-



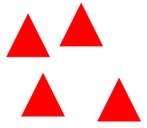
In-house MS library of 722 chemical formulas
- Phenols
- Phthalate metabolites
- Pesticide metabolites
- Per- poly-fluorinated chemicals
- Flame retardants

Molecules identification

620 chemicals that matched 300 formulas

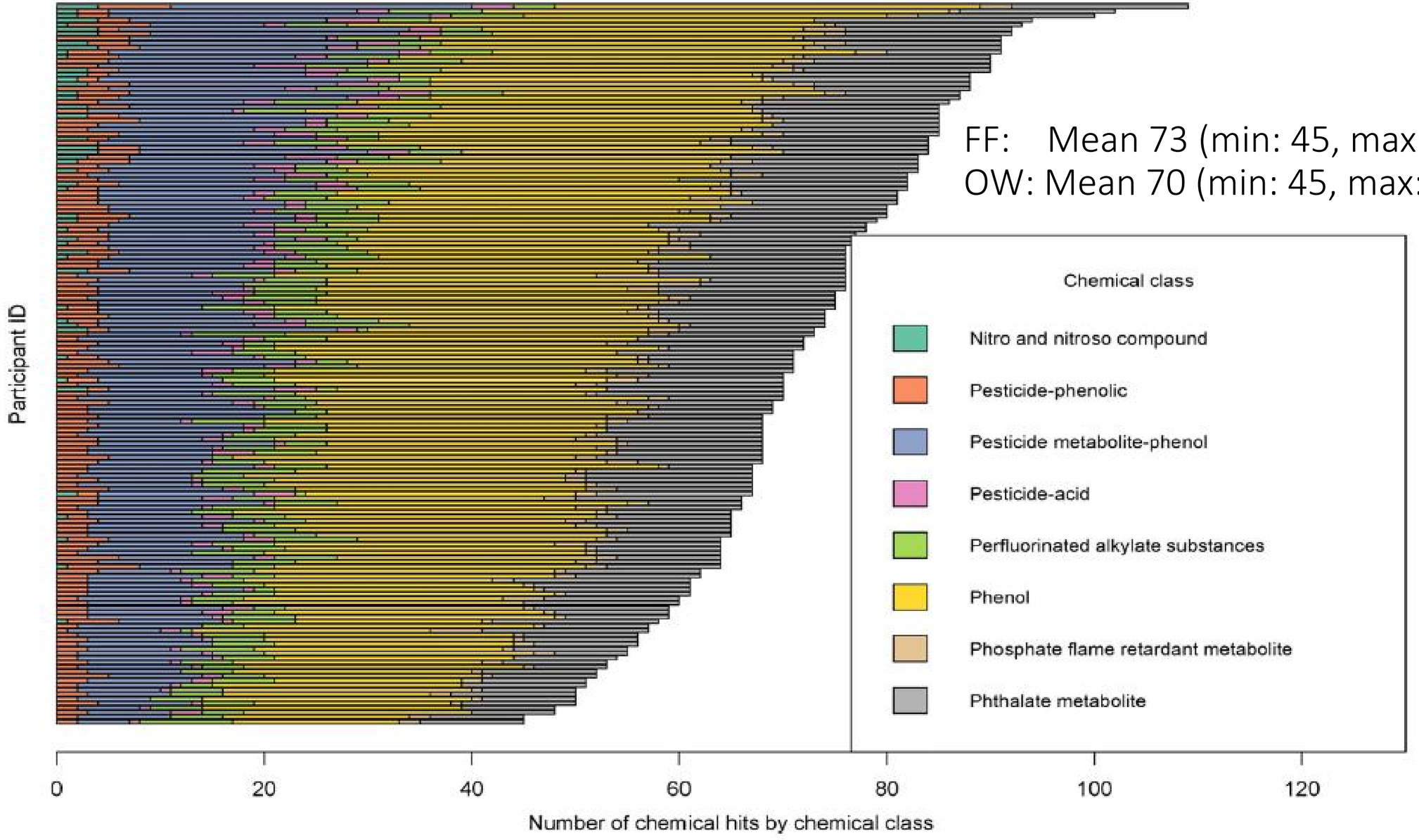


Prioritization based on toxicity and detection frequency



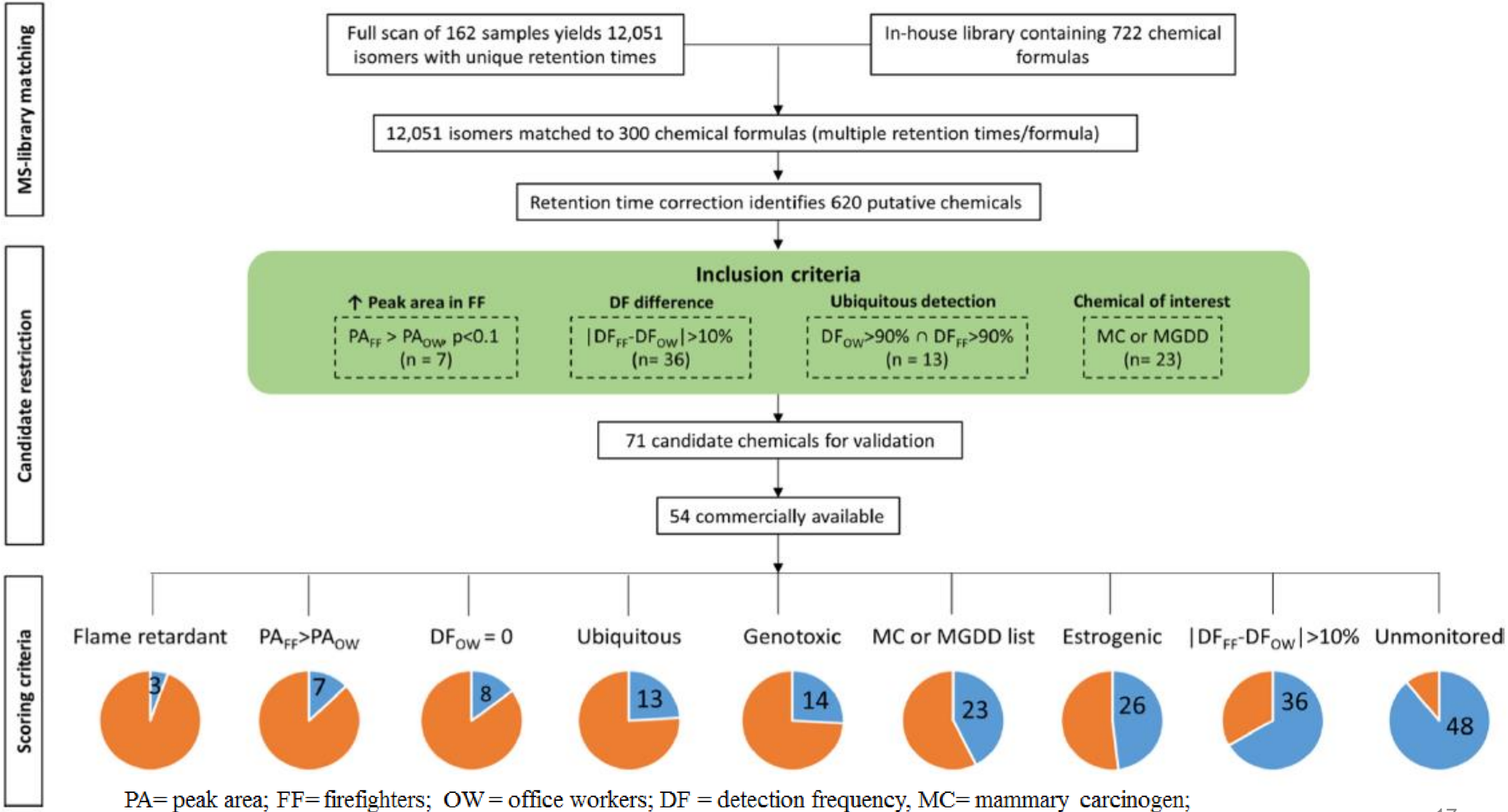
Chemicals selected for further biomonitoring studies

Cumulative number of environmental chemicals detected with LC-QTOF/MS ESI- in serum samples from women firefighters and office workers (N=162)



FF: Mean 73 (min: 45, max: 109)
OW: Mean 70 (min: 45, max: 100)

Scoring and ranking of chemicals detected by chemical suspect screen



PA= peak area; FF= firefighters; OW = office workers; DF = detection frequency, MC= mammary carcinogen; MGDD = mammary gland developmental disruptor

Partial list of candidate chemicals to be validated

Chemical name	Chemical class	DF FF (%)	DF OW (%)	Mean peak area FF	Mean peak area OW
2,4-bis(1,1-dimethylethyl) phenol	Phenol	82 (100%)	76 (100%)	9.17E+05*	7.66E+05
benzyl p-hydroxybenzoate (PHBB) OR 2-hydroxy-4-methoxybenzophenone (BP-3))	Phenol	16 (19.5%)	6 (7.9%)	2.98E+04	2.12E+04
bisphenol F	Phenol	10 (12.2%)	0 (0%)	4.98E+05	NA
perfluorooctanesulfonamidoacetate (PFOSAA)	PFAS	16 (19.5%)	25 (32.9%)	3.94E+04	4.56E+04*
diphenyl phosphate (DPP)	Phosphate FR metabolite	45 (54.9%)	39 (51.3%)	1.57E+04	1.68E+04
ethyl-p-hydroxybenzoate (ethyl paraben)	Phenol	52 (63.4%)	35 (46.1%)	1.10E+05	1.57E+05§
benzyl p-hydroxybenzoate (PHBB) OR 2-hydroxy-4-methoxybenzophenone (BP-3))	Phenol	30 (36.6%)	38 (50%)	6.04E+04	9.68E+04
4-hexyloxyphenol	Phenol	31 (37.8%)	21 (27.6%)	6.60E+04	6.87E+04
4-butoxyphenol	Phenol	77 (93.9%)	71 (93.4%)	7.21E+04	8.58E+04*
2,3,6-trimethylphenol	Phenol	18 (22%)	7 (9.2%)	2.04E+04	1.15E+04
4-phenethylphenol	Phenol	82 (100%)	76 (100%)	1.35E+05	1.43E+05*
4-heptyloxyphenol	Phenol	51 (62.2%)	55 (72.4%)	2.89E+05	2.55E+05
1-allyl-1-nitrosourea	Nitro and Nitroso compound	12 (14.6%)	5 (6.6%)	7.25E+04	3.96E+04

§ p<0.1; *p<0.05; **p<0.01; FF=firefighter; OW=office worker; DF=detection frequency; PA=peak area; RT=retention time

Scoring chemical candidates based on *a priori* criteria for confirmation

Chemical name	Chemical class	DF FF (%)	DF OW (%)	Mean peak area FF	Mean peak area OW	Flame retardent	DF > 90% in FF and OW	|DF_FF - DF_OW| greater than 10%	T-test PA p<0.1	Unmonitored	Genotoxic	Estrogenic	OW non-detect	MC list	Score
2,4-bis(1,1-Dimethylethyl)phenol	Phenol	82 (100%)	76 (100%)	9.17E+05*	7.66E+05	0	1	0	1	1	1	1	0	0	5
Benzyl p-hydroxybenzoate (PHBB) or 2-Hydroxy-4-methoxybenzophenone -2	Phenol	16 (19.5%)	6 (7.9%)	2.98E+04	2.12E+04	0	0	1	0	1	1 0	1	0	0	5
Benzyl p-hydroxybenzoate (PHBB) or 2-Hydroxy-4-methoxybenzophenone -2	Phenol	30 (36.6%)	38 (50%)	6.04E+04	9.68E+04	0	0	1	0	1	1 0	1	0	0	4
Bisphenol F	Phenol	10 (12.2%)	0 (0%)	4.98E+05	NA	0	0	1	0	1	0	1	1	0	4
Perfluorooctanesulfonamidoacetate (PFOSAA)	PFC	16 (19.5%)	25 (32.9%)	3.94E+04	4.56E+04*	0	0	1	1	1	0	0	0	0	3
Diphenyl phosphate (DPP)	Phosphate Flame Retardant metabolite	45 (54.9%)	39 (51.3%)	1.57E+04	1.68E+04	1	0	0	0	0	0	0	0	0	1
Ethyl-p-hydroxybenzoate (Ethyl paraben)	Phenol	52 (63.4%)	35 (46.1%)	1.10E+05	1.57E+05§	0	0	1	1	0	0	1	0	0	3
Pentachlorophenol	Phenol	57 (69.5%)	44 (57.9%)	2.54E+04	3.01E+04	0	0	1	0	0	1	1	0	0	3
Perfluorooctylethanoic acid	FC	65 (79.3%)	53 (69.7%)	1.54E+04	1.64E+04	0	0	1	0	1	0	0	0	0	2
Dinoseb	Pesticide-phenolic	82 (100%)	75 (98.7%)	5.52E+04	6.47E+04§	0	0	0	1	0	1	1	0	0	3
Dipropyl phosphate	Phosphate Flame Retardant metabolite	37 (45.1%)	22 (28.9%)	2.25E+04	2.26E+04	1	0	1	0	1	0	0	0	0	3
Methyl eugenol	Phenol	77 (93.9%)	70 (92.1%)	3.30E+04	3.19E+04	0	0	0	0	0	0	1	0	1	2

Retention time and exact mass for chemicals selected for validation

Chemical name	Chemical class	# of isomers	Mean RT for serum samples	RT lab standard	Validation status
2,4-bis(1,1-dimethylethyl) phenol	Phenol	4	4.33, 5.25, 5.48, 6.73	6.72	✓
2-hydroxy-4-methoxybenzophenone (BP-3))	Phenol	2	4.33, 5.25	5.30	✓
bisphenol F	Phenol	2	3.91	4.00	✓
perfluorooctanesulfonamidoacetate (PFOSAA)	PFC	1	5.93	5.95	✓
diphenyl phosphate (DPP)	Phosphate Flame Retardant metabolite	1	3.86	3.90	✓
ethyl-p-hydroxybenzoate (ethyl paraben)	Phenol	2	2.21, 3.80	2.30	✓
benzyl p-hydroxybenzoate (PHBB)	Phenol	2	4.33, 5.25	4.40	✓
4-hexyloxyphenol[1]	Phenol	1	5.81	5.80	✓[a]
4-butoxyphenol	Phenol	1	4.19	5.10	×[b]
2,3,6-trimethylphenol	Phenol	2	3.97	4.25	×[b]
4-phenethylphenol	Phenol	1	5.71	6.02	×[b]
4-heptyloxyphenol (2 isomers)	Phenol	1	5.09	6.22	×[b]
1-allyl-1-nitrosourea	Nitro and Nitroso compound	1	0.76	1.20	×[b]

[a] validated but with high LOD, [b] not validated because of retention time mismatch

Descriptive statistics of select chemicals measured from NTA.						
				Percentile		
Chemical name	LOD	Occupation	Detection Frequency %	50th	95th	Max
Benzophenone 3 (BZP3)	0.2					
		FF	25.9	<LOD	7.24	16.47
		OW	34.2	<LOD	19.2	100.56
Dinoseb	0.01					
		FF	8.2	<LOD	0.2	8.98
		OW	2.4	<LOD	0.01	0.36
Diphenyl Phosphate (DPP)	0.01					
		FF	48.2	<LOD	0.19	1.72
		OW	40.2	<LOD	0.24	0.77
Ethyl Paraben (EP)	0.01					
		FF	81.2	0.06	0.68	4.53
		OW	65.9	0.04	0.92	3.98
Perfluoro-1-octanesulfonamidoacetic acid (PFOSAA)	0.01					
		FF	69.4	0.03	0.13	0.72
		OW	80.5	0.04	0.12	0.27

WWBC
Women Workers Biomonitoring Collaborative

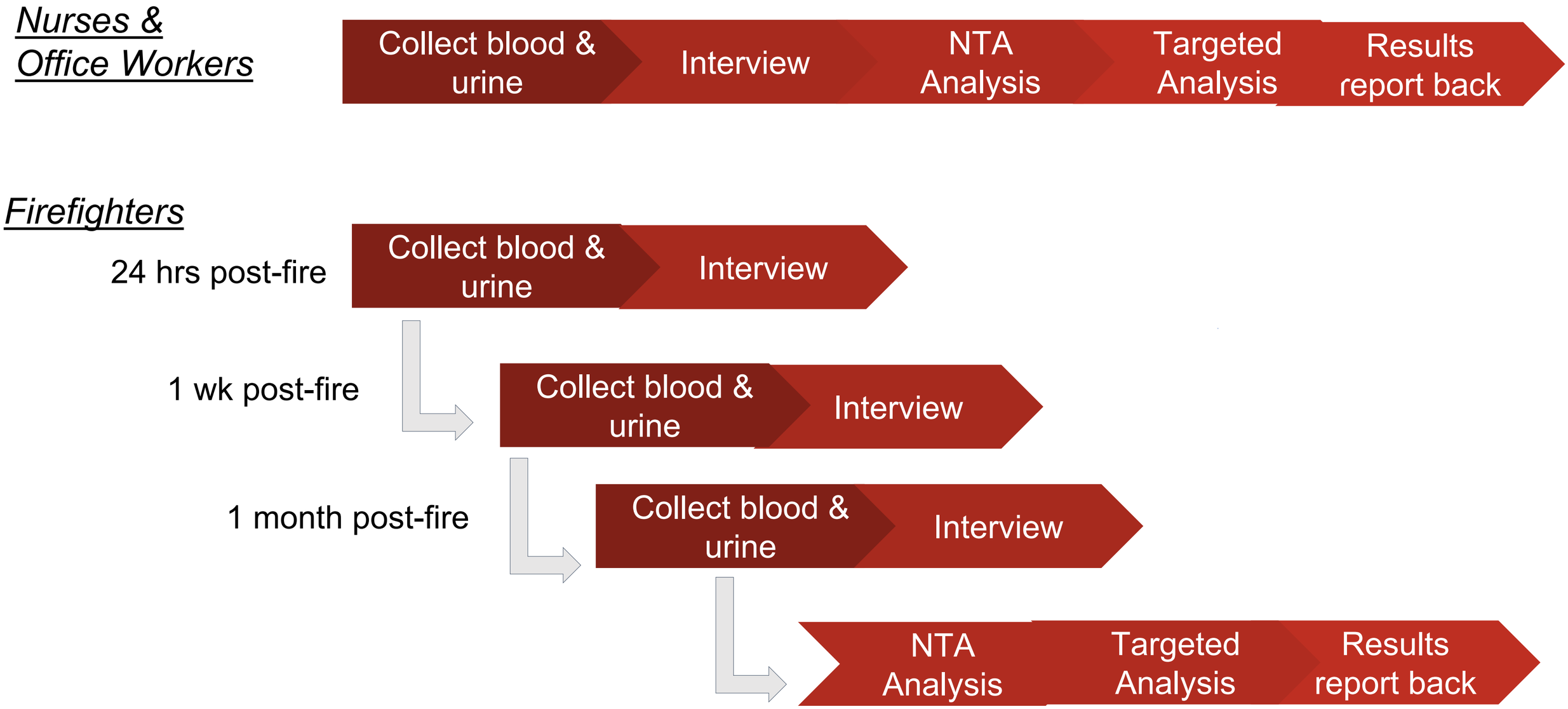
EXPANDING COHORT TO NURSES

60 UCSF inpatient nurses

40 CCSF employees

20 SFFD firefighters

WWBC Methods: NTA drives discovery/prioritization of novel chemicals for targeted analysis



Digital Exposure Report-back Interface (DERBI)

Landing page

This web site provides your study results from the Women Firefighters Biomonitoring Collaborative Study. It shows:

+ The levels of chemicals found in your samples.
+ How your levels compare with other people.
+ Where these chemicals come from.
+ How they can affect health.
+ How you can reduce levels of these chemicals in your body, your home, and at work.

Start Here

Context

Firefighters are exposed to chemicals every day — at the fire ground, at the fire station, and in some firefighting equipment. Read more

Chemicals in the study

Your blood samples were tested for chemicals used in flame retardants, non-stick or stain-resistant surfaces, and products of combustion (burning). Read more

This website

This website includes the results of the chemical measurements we did with your samples. By clicking through the website, you can learn more about where these chemicals come from, their links to health, and how to reduce exposures in your home and community. Read more

DERBI Chemicals page

Personal headline

Sources

Health effects

Exposure reduction tips

Your Results: PFASs

Highly fluorinated chemicals

Your sample had a higher level of PFDoA than most others in the study. Scroll down to see all of your results.

Where do these chemicals come from?

PFASs help products resist grease and water. They are applied to stain-resistant textiles (like carpets, furniture, and clothing), waterproof outdoor gear, and grease-repellent food packaging (such as fast food wrappers and microwave popcorn bags). PFAS chemicals are used to produce polytetrafluoroethylene (PTFE or "Teflon"), used on nonstick pots and pans and in some dental flosses and beauty products. PFASs are found in certain firefighting foams, called aqueous film forming foam (AFFF). Some drinking water supplies are contaminated by PFASs.

Why might these chemicals be a health concern?

PFASs tend to persist in the body and the environment. Exposure to these chemicals can affect:

- **Lipid metabolism.** PFASs can alter how the body breaks down and stores fats, which can affect energy, metabolism, and body weight and composition. PFAS exposure is associated with high cholesterol in humans.

How can I reduce my exposure?

At home

- **Wash hands frequently.**
- **Avoid spray treatments** that make rugs, furniture, or other textiles stain- or water-resistant.

During and after a fire incident

- **Use a self-contained breathing apparatus (SCBA) from initial fire attack through the completion of overhaul** at structure, car, and dumpster fires, and whenever AFFF is used.
- **Use wet wipes to clean hands, neck, jaw and face** immediately after being engaged in fire suppression activities, overhaul, or other exposure to smoke.

Personal results graphs

(continued from Chemicals page)

Your Results

Legend

- your chemical level
- A firefighter's chemical level
- An office worker's chemical level
- A firefighter that didn't have a detectable amount of the chemical in their blood
- An office worker that didn't have a detectable amount of the chemical in their blood

ng/mL: nanograms of the chemical per milliliter of blood.

Tip: Mouse over your graphs to learn how to read them.

PFDA

PFOS

PFOA

PFUnDA

Proposed NTA report-back: Aggregate summary

The WFBC screened blood samples for hundreds of chemicals to look for unexpected exposures.

We screened blood samples for more than 700 chemicals **using a new technology that detects a wide range of chemicals without having to measure exact amounts.** We used this tool to **look for chemicals with different exposures between firefighters and office workers, as well as chemicals that have not been measured** in large exposure studies before. The following 6 chemicals were selected for follow-up measurements because they were frequently detected among WFBC participants, were more common in firefighters, or are potentially linked to breast cancer risk:

- **Benzophenone-3** is an ultraviolet (UV) filter used in sunscreens, textiles, plastic bottles, and other products to protect against sun damage.
- **Ethyl paraben** is a preservative added to personal care products (like cosmetics, lotions, and shampoos) and other products like toys and pesticides to prevent the growth of mold and bacteria.
- **Perfluoro-1-octanesulfonamidoacetic acid (PFOSAA)** is a perfluoroalkyl substance (PFAS). PFAS are used in stain-resistant and non-stick coatings as well as certain firefighting foams.
- **Diphenyl phosphate (DPHP)** is a breakdown product of triphenyl phosphate, which has many consumer and industrial uses including as a flame retardant and floor polish.
- **Dinoseb** is a banned pesticide that was previously used to control weeds on farms. However, it is still produced and sold for other purposes. Dinoseb has been found in some weight loss supplements.
- **Pentachlorophenol (PCP)** is commonly used as a wood preservative for industrial applications, such as utility poles.

For most of these chemicals, firefighters and office workers had similar levels of exposure. However, like other flame retardants measured in this study, diphenyl phosphate was detected more frequently in firefighters than office workers, suggesting that workplace exposures may be important. The banned pesticide dinoseb was also found more often in firefighters, but it was detected in very few participants overall. Our scientific paper describing this approach is here.

Considerations for report-back of NTA results

Describing method in meaningful ways

- How NTA differs from targeted methods
- Advantages and disadvantages

Distinguishing between chemical suspects versus confirmed/quantified compounds

Report # of chemical suspects found?

- By chemical group?
- Suspect profile for each participant?

Criteria for choosing chemicals for validation/quantification

Thank you!

Our WFBC Team

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Ruthann Rudel, Vincent Bessenneau, Silent Spring Institute

Heather Buren, United Fire Service Women, San Francisco

Tony Stefani, SF Firefighter Cancer Prevention Foundation

Roy Gerona, UC San Francisco

Sharyle Patton, Commonweal

Connie Engel, Nancy Buermeyer, Breast Cancer Prevention Partners

Our Funders

California Breast Cancer Research Program #19BB-2900

San Francisco Firefighter Cancer Prevention Foundation

International Association of Firefighters, Local 798

NIOSH Targeted Research Training Program

Contact Us

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