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Associations between exposure to polycyclic aromatic hydrocarbons and biomarkers of acute kidney injury among Chilean agricultural workers

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ABSTRACT

Polycyclic aromatic hydrocarbon (PAH) exposures from agricultural and household woodburning may adversely impact kidney health, but studies are limited in Latin America where these practices are prevalent. We aimed to characterize PAH exposures and examine their associations with kidney injury biomarkers among agricultural workers in Chile.

Among 43 male agricultural workers from the Maule Cohort, we quantified urinary concentrations of five kidney injury biomarkers (IL-18, KIM-1, MCP-1, NGAL, YKL-40) and nine hydroxy-PAHs. Additionally, we measured 23 parent PAHs in wristbands, worn 8-11 days. We estimated percent differences in kidney biomarker concentrations and odds ratios of subclinical kidney injury (defined by two or more kidney biomarkers in the highest tertile) per interquartile range increase in PAH exposure concentration.

All urinary PAH and kidney biomarkers were frequently detected (>70%) as were 13 parent PAH compounds in wristbands. We observed consistent positive associations of urinary IL-18 with select PAH exposures. Specifically, higher urinary IL-18 concentrations were observed in association with higher urinary concentrations of 1-PHE (80.4%; 95%CI: 33.8%, 143.3%), 2&3-PHE (44.1%; 95%CI: 12.7%, 84.2%), and 4-PHE (48.8%; 95%CI: 12.9%, 96.1%). Similarly, IL-18 concentrations were positively associated with higher wristband concentrations of anthracene (46.7%; 95%CI: 9.7%, 96.2%), phenanthrene (32.3%; 95%CI: 5.5%, 65.9%), fluorene (56.9%; 95% CI: 10.2%, 123.3%), and pyrene (34.1%; 95%CI: 3.2%, 74.3%) and among participants with naphthalene detected in their wristbands (51.5%; 95%CI: 1.3%, 126.7%). Wristband concentrations of benzo[e]pyrene, benzo [a]pyrene, and chrysene were associated with higher odds of subclinical AKI but not decreased kidney function.

Our findings suggest that select PAH exposures may be associated with kidney injury, addressing major knowledge gaps and informing future studies of kidney health in agricultural communities.

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Glossary

AKI	acute kidney injury
aOR	adjusted odds ratio
CKD	chronic kidney disease
CKDnt	chronic kidney disease of non-traditional etiology
DEGREE	Disadvantaged Populations eGFR Epidemiology
eGFR	estimated glomerular filtration rate
GC-MS/MS	gas chromatography with tandem mass spectrometry
GM	geometric mean
GSD	geometric standard deviation
IQR	interquartile range
KDIGO	Kidney Disease Improving Global Outcome
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOD	limit of detection
MAUCO	Maule Cohort Study
MDL:	method detection limit
PAH	polycyclic aromatic hydrocarbon
SG	specific gravity
UCr	urinary creatinine
95% CI	95% confidence interval
%CV	percent coefficient of variation

AKI Biomarkers

IL-18	interleukin 18
KIM-1	kidney injury molecule-1
MCP-1	monocyte chemoattractant protein-1
NGAL:	neutrophil gelatinase-associated lipocalin
YKL-40	chitinase-3-like protein 1

Urinary PAH Biomarkers

2-FLU	2-hydroxyfluorene
1-NAP	1-hydroxynaphthalene (1-napthol)
2-NAP	2-hydroxynaphthalene (2-napthol)
1-PHE	1-hydroxyphenanthrene
2&3-PHE	2&3-hydroxyphenanthrene
4-PHE	4-hydroxyphenanthrene
9-PHE	9-hydroxyphenanthrene
1-PYR	1-hydroxypyrene

1. Introduction

Globally, acute kidney injury (AKI) affects an estimated 13.3 million people each year and is responsible for more than two million deaths (Mehta et al., 2015). Defined by an abrupt and typically reversible decline in kidney function, AKI is also a risk factor for chronic kidney disease (CKD), which can only be treated with dialysis or transplantation at its most advanced stages (Kurzhagen et al., 2020). In Chile, where this study was conducted, there are several factors suspected to increase the public health burden of kidney diseases, including the country's aging population, rising rates of comorbidities such as hypertension, diabetes, and obesity, and regional and socioeconomic disparities in access to nephrology care and renal replacement therapies (Walbaum et al., 2020; Pedreros-Rosales et al., 2025; Toro et al., 2025; Celis et al., 2025). As the etiology of CKD is undefined in 47% of patients in Chile, environmental and occupational exposures are poorly understood as potential risk factors (Toro et al., 2025). The application of non-invasive, urinary biomarkers holds promise for improving early detection and prevention of AKI and CKD (Zhang and Parikh, 2019; Puthumana et al., 2021). However, there is a paucity of epidemiologic studies characterizing these biomarkers in understudied populations, and even fewer studies that have examined their potential associations with environmental and occupational risk factors.

Polycyclic aromatic hydrocarbons (PAHs) are hazardous chemicals released from the combustion of organic materials, including wood, coal, oil, and various types of waste (Patel et al., 2020). Human exposure to PAHs is ubiquitous and occurs via multiple routes, including inhalation of particulate matter, dietary ingestion of grilled or smoked foods, and dermal contact with contaminated soil and other materials (Mallah et al., 2022). Many rural communities face elevated exposures to PAHs, especially those with prevalent residential woodburning and agricultural burning for crop residue clearance and land management (Akinrinade and Rosa, 2025; Bai et al., 2024). Emissions from biomass combustion are predominantly composed of low molecular weight PAHs (i.e., those with less than four rings), with phenanthrene being a particularly dominant compound in wood smoke (Pozo et al., 2015, 2023; Cereceda-Balic et al., 2012). In the ongoing Maule Cohort study in central Chile, 77% of participants reported wood or coal as their primary fuel for household heating (Ferreccio et al., 2020). Previous monitoring in Chile has also quantified high atmospheric concentrations of PAHs, which have been positively linked to residential woodburning, especially in the winter (Pozo et al., 2015, 2023; Jorquera et al., 2021; Villalobos et al., 2017). While woodburning pollution is a public health threat in the region, existing studies are limited by their use of environmental monitoring for health risk assessments.

Multiple approaches have been employed to assess personal exposure to PAHs, including biomonitoring of urinary PAH metabolites and wearable sampling devices like silicone wristbands (Hamzai et al., 2022; Li et al., 2012; Dixon et al., 2018, 2022). Urinary PAH biomarkers have been validated in several studies, but they exhibit high temporal variability, making them susceptible to measurement error (Li et al., 2012). Additionally, standard methods used for correcting spot urine sample dilution, such as adjusting for urinary creatinine or specific gravity, may be influenced by a person's existing kidney function, potentially resulting in biased exposure estimates (Kuiper et al., 2021; Lee et al., 2025; Weaver et al., 2014). Overcoming this limitation by continually absorbing organic chemicals via passive diffusion (i.e., representing a time-weighted average of exposure), silicone wristbands have been increasingly used in epidemiologic investigations to characterize personal exposures to individual and complex mixtures of PAHs (Hamzai et al., 2022). However, more research is needed to examine the relationship between PAH concentrations measured in wristbands with their respective urinary biomarkers – as existing evidence is limited to pregnant women (Dixon et al., 2018, 2022)– and to determine their utility for kidney health studies.

Existing literature has reported associations between PAH exposures and adverse kidney health outcomes. Among adults from the general U. S. population, higher urinary PAH biomarkers have been associated with increased odds of CKD (Rahman et al., 2022), higher prevalence of kidney stones (Zhou et al., 2022), and higher urinary albumin-creatinine ratios, indicative of kidney damage (Li et al., 2020). Similarly, among U. S. adolescents, higher urinary PAHs were associated with decreased kidney function and higher urinary concentrations of oxidative stress biomarkers (Farzan et al., 2016). Studies of indigenous populations in Mexico, for whom household woodburning is common, have also reported positive correlations between PAH exposures and urinary biomarkers of kidney damage among adults but not children (Flores-Ramírez et al., 2021; Díaz de León-Martínez et al., 2021a). Although the exact mechanisms remain unknown, existing data suggest that PAHs may induce kidney damage by triggering oxidative stress and inflammation, interfering with glomerular filtration, or directly inducing tubular damage (Farzan et al., 2016; Liu et al., 2025; Everett et al., 2010; Nsonwu-Anyanwu et al., 2022; Sun et al., 2021). Despite this evidence, further studies are needed to examine PAH exposures in

relation to kidney health outcomes in vulnerable populations, including residents of communities with prevalent burning practices.

In the present pilot study, we characterized exposure to select PAHs in two matrices, urine and silicone wristbands, and explored their associations with biomarkers of acute kidney injury among male agricultural workers in Chile. We hypothesized that PAH exposures would be positively associated with higher AKI biomarker concentrations.

2. Methods

2.1. Study population

We recruited a convenience sample of 43 male agricultural workers from the ongoing Maule Cohort (MAUCO) study who were participating in a nested investigation of kidney disease, conducted according to the Disadvantaged Populations eGFR Epidemiology (DEGREE) protocol (Caplin et al., 2017). Briefly, the MAUCO study is based in Molina (35°06′52″S 71°16′57″W), an agricultural community of approximately 45,000 residents in central Chile. The MAUCO study was initiated in 2014 and is the first prospective study of population-level chronic health conditions, including cardiovascular diseases and cancer in Chile (Ferreccio et al., 2016, 2020). For the present pilot study, which we have described in detail previously (DeSantiago et al., 2026), eligible adult male participants met the following criteria: enrolled in MAUCO between 2017 and 2020, continued residence in Molina, participation in the nested kidney disease investigation, and current employment in the agricultural industry. Based on a list of participants meeting eligibility criteria, study staff contacted and enrolled eligible participants until the target sample size was met. The original aim of this pilot study focused on occupational pesticide exposures, so we enrolled workers involved in crop production, including wine grapes and other fruits (e.g., apples, cherries, kiwis, raspberries). We limited enrollment to male participants, as they represent the majority of agricultural workers in the region. Due to logistic constraints, data collection occurred between July and August 2023, which does not represent top growing or harvest seasons for Chilean agriculture. Nonetheless, this period reflects peak winter months wherein exposure to PAHs from residential woodburning is expected to be high in the study area. Study protocols were reviewed and approved by the Scientific Ethics Committee of Health Sciences at the Pontifical Catholic University of Chile (Pontificia Universidad Católica de Chile) and each participant provided written consent to enroll in the study.

2.2. Study design and sample collection procedures

Each participant completed an initial study visit during which they responded to an interviewer-administered exposure questionnaire to capture data on occupational and residential characteristics, tasks, and behaviors (Table 1). During the same visit, participants were given a silicone wristband to wear as a passive sampler to assess personal exposure to PAHs. The wristbands (24hourwristbands.com, Houston, TX, USA) were cleaned and stored in oven-baked aluminum foil prior to deployment, following established protocols described previously (Baker et al., 2024). Participants wore their wristband for approximately 8-11 days during all routine activities, including while working, eating, bathing, and sleeping. At the end of the wear period, trained study staff collected the wristbands from participants, wrapped them in oven-baked (combusted at 450 °C) aluminum foil, and stored them in a sealed plastic bag. Upon returning their wristbands to study staff, each participant provided a spot urine sample, which was collected in a propylene container. Within 2 h of collection, urinary specific gravity was measured in each sample using an Atago 3741 Digital "Pen" Urine Refractometer (Atago U.S.A., Inc., Bellevue, WA, USA). Both the silicone wristbands and urine samples were stored at −80 °C at the Molina Hospital within 2 h of collection prior to shipment for analysis of PAHs and kidney injury biomarkers. All samples were shipped on dry ice in a

Table 1
Participant demographic characteristics and factors related to PAH exposures overall and by subclinical kidney injury status (n = 43).

	Overall (n = 43)	Subclinical Kidney Injury		p-value
		No (n = 24)	Yes (n = 19)	
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	53.2 (5.7)	52.6 (6.40)	52.6 (6.40)	0.55
Estimated glomerular filtration rate (eGFR)[a]	94.7 (14.2)	94.3 (14.5)	95.1 (14.5)	0.86
Serum creatinine (mg/dL)	0.94 (0.17)	0.94 (0.17)	0.94 (0.17)	0.99
Urinary creatinine (g/L)	1.10 (0.44)	1.14 (0.44)	1.06 (0.45)	0.56
Urinary specific gravity (no units)	1.019 (0.006)	1.019 (0.006)	1.017 (0.005)	0.14
Demographic Characteristics	**N (%)**	**N (%)**	**N (%)**	**p-value**
Ethnicity				
Chilean	41 (95.3%)	23 (95.8%)	18 (94.7%)	0.99
Mapuche	2 (4.7%)	1 (4.2%)	1 (5.3%)	
Education Level				
Less than 8 years	22 (51.2%)	13 (54.2%)	9 (47.4%)	0.76
Equal to or more than 8 years	21 (48.8%)	11 (45.8%)	10 (52.6%)	
Practices Related to PAH Exposures[b]	**N (%)**	**N (%)**	**N (%)**	**p-value**
Current Smoker	12 (27.9%)	7 (29.2%)	5 (26.3%)	0.99
Primary Work Environment				
Indoor	7 (16.3%)	6 (25.0%)	1 (5.3%)	0.11
Outdoor	36 (83.7%)	18 (75.0%)	18 (94.7%)	
Indoor Wood Burning at Home	38 (88.4%)	23 (95.8%)	15 (78.9%)	0.15
Purpose for Indoor Wood Burning				
Primary or supplementary heating	37 (86.0%)	22 (91.7%)	15 (78.9%)	–
Does not burn wood indoors or missing	6 (14.0%)	2 (8.3%)	4 (21.5%)	
Outdoor Wood Burning at Home	10 (23.3%)	6 (25.0%)	4 (21.1%)	0.99
Purpose for Outdoor Wood Burning				
Cooking, pleasure, or supplementary heating	8 (18.6%)	5 (20.8%)	3 (15.8%)	–
Does not burn wood outdoors at home	35 (81.4%)	19 (79.2%)	16 (84.2%)	
Exposed to Burning in the Past 7 Days	37 (86.0%)	22 (91.7%)	15 (78.9%)	0.38

(continued on next page)

Table 1 (*continued*)

	Overall (n = 43)	Subclinical Kidney Injury		p-value
		No (n = 24)	Yes (n = 19)	
	Mean (SD)	Mean (SD)	Mean (SD)	
Trash Burning at Home	10 (23.3%)	6 (25.0%)	4 (21.1%)	0.99
Protein Consumption, at least once per week				
Low-Fat White Meat	39 (90.7%)	23 (95.8%)	16 (84.2%)	0.31
High-Fat White Meat	17 (39.5%)	9 (37.5%)	8 (42.1%)	0.99
Red Meat	18 (41.9%)	14 (58.3%)	4 (21.1%)	0.03
Other Meat Products	26 (60.5%)	14 (58.3%)	12 (63.2%)	0.77
Seafood	25 (58.1%)	16 (66.7%)	9 (47.4%)	0.22

[a] Estimated glomerular filtration rate (eGFR) was calculated with each participant's serum creatinine concentration using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

[b] Select variables were summarized based on their potential association with participants' exposure to polycyclic aromatic hydrocarbons (PAHs) through personal, occupational, residential, and dietary practices.

single batch to Johns Hopkins University for interim storage. Urine aliquots were sent to the Translational Research in Biomarker Endpoints and Applications in Kidney Disease (TRIBE-AKD) lab at Johns Hopkins University (Baltimore, MD, USA) for analysis of AKI biomarkers and urinary creatinine. An additional aliquot was sent to the National Sanitation Foundation (NSF) International laboratory (Ann Arbor, MI, USA) to quantify urinary hydroxylated-PAHs, and the wristbands were sent to the Duke Environmental Analysis Laboratory (Durham, NC, USA) for analyses of PAHs. Of the 43 deployed wristbands, 40 (93%) wristbands were returned for analysis, and all 43 (100%) participants provided a spot urine sample.

2.3. Exposure assessment: Quantification of polycyclic aromatic hydrocarbons in wristbands

Following previously described methods, small segments of each silicone wristband were extracted for targeted analyses to assess personal environmental exposures to 23 PAHs: naphthalene (NAP); acenaphthene (ACE); acenaphthylene (ACY); anthracene (ANT); phenanthrene (PHE); fluorene (FLE); fluoranthene (FLA); benz[a]anthracene (B[a]A); benzo(c)phenanthrene (B[c]Ph); chrysene (CHRY); pyrene (PYR); benzo[a]pyrene (B[a]P); benzo[e]pyrene (B[e]P); perylene (PER); benzo[j,b,k]fluoranthene (B[j,b,k]F); 7,12-dimethylbenz(a)anthracene (DMBA); 3-methylcholanthrene (3-MC); indeno(1,2,3-cd)pyrene (IP); dibenz(a,h)anthracene (DB[a,h]A); benzo(g,h,i)perylene (BghiP); dibenz[a,l]pyrene (DB[a,l]P); dibenz[a,i]pyrene (DB[a,i]P); dibenz[a,h]pyrene (DB[a,h]P) (Baker et al., 2024). Briefly, a 1g segment was cut from each band, transferred to a clean glass centrifuge tube and spiked with a mixture of isotopically labeled internal standards. Extraction was conducted using sonification and a 1:1 mixture of hexane and acetone. Each extract was concentrated with a SpeedVac Concentrator (Thermo Fisher Scientific, Waltham, MA, USA), cleaned using a dispersive Florisil (Fisher Scientific, Pittsburgh, PA, USA), concentrated to ~0.5 mL using a Nitrogen evaporation system (N-Evap) and loaded into auto sampler vials for analysis. Samples were spiked with a second and different set of isotopically labeled standards prior to analysis to monitor recovery of the internal standards. The samples were analyzed using a Q Exactive GC hybrid quadrupole-Orbitrap gas chromatography-tandem mass spectrometry (GC–MS/MS) system (Thermo Scientific, Waltham, MA, USA) under full scan electron ionization mode. Analyses yielded mass concentrations (ng/g) of the PAHs assayed, which were blank subtracted for any PAHs detected in the three lab blanks (Table S1). Since participants wore their wristbands for different amounts of time, we assumed linear uptake of PAHs in wristbands over time and standardized concentrations by dividing the mass concentration (ng/g) of a given PAH absorbed by the fractional number of days of wristband wear, resulting in time-weighted concentrations (ng/g-day). Method detection limits (MDLs) ranged from 0.04 to 7.54 ng/g.

2.4. Exposure assessment: Quantification of urinary polycyclic aromatic hydrocarbon biomarkers

Urinary concentrations (ng/L) of nine PAH monohydroxylated biomarkers were quantified, including one fluorene biomarker: 2-hydroxyfluorene (2-FLU); two naphthalene biomarkers: 1-hydroxynapthalene

Table 2
Summary statistics for parent polycyclic aromatic hydrocarbon (PAH) concentrations on **wristbands** (ng/g/day) normalized to the individual wear period (n = 40)[a,b,c].

Category[d]	Parent Compound	Abbreviation	MDL	%>MDL	GM (GSD)	Min	Median (IQR)	Max
Low Molecular Weight PAHs	Naphthalene	NAP	7.54	45	1.24 (3.11)	<MDL	<MDL (<MDL - 2.32)	178.95
	Acenaphthene	ACE	0.25	93	0.17 (2.34)	<MDL	0.18 (0.12 - 0.30)	0.67
	Acenaphthylene	ACY	0.67	98	1.27 (2.65)	<MDL	1.25 (0.81 - 2.11)	10.35
	Anthracene	ANT	0.12	100	1.07 (2.08)	0.16	1.04 (0.65 - 1.84)	3.96
	Phenanthrene	PHE	1.34	100	9.50 (1.65)	3.71	9.32 (6.86 - 12.09)	24.24
	Fluorene	FLE	1.13	100	1.47 (1.82)	0.56	1.35 (0.86 - 2.38)	4.36
High Molecular Weight PAHs	Fluoranthene	FLA	0.12	100	2.99 (1.96)	0.68	2.95 (2.16 - 4.80)	11.59
	Benz[a]anthracene	B[a]A	0.05	100	0.34 (2.54)	0.04	0.38 (0.23 - 0.63)	1.82
	Benzo(c)phenanthrene	B[c]Ph	0.07	85	0.09 (4.01)	<MDL	0.13 (0.05 - 0.27)	0.53
	Chrysene	CHRY	0.04	100	0.67 (2.24)	0.09	0.67 (0.46 - 1.07)	3.57
	Pyrene	PYR	0.24	100	3.08 (2.10)	0.63	2.88 (2.05 - 5.35)	14.31
	Benzo[a]pyrene	B[a]P	0.12	90	0.11 (3.10)	<MDL	0.13 (0.08 - 0.23)	1.05
	Benzo[e]pyrene	B[e]P	0.13	93	0.15 (2.90)	<MDL	0.18 (0.12 - 0.28)	1.04
	Perylene	PER	0.07	48	0.02 (3.86)	<MDL	<MDL (<MDL - 0.05)	0.29
	Benzo[j,b,k]fluoranthene	B[jbk]F	0.19	100	0.38 (2.15)	0.06	0.45 (0.27 - 0.59)	2.02

Abbreviations: MDL: method detection limit; %>MDL: percentage detected above the MDL; GM: geometric mean; GSD: geometric standard deviation; Min: minimum; IQR: interquartile range; Max: maximum.

[a] Summary statistics were calculated after replacing values < LOD (i.e., <MDL) with the respective LOD/$\sqrt{2}$ and were not calculated for biomarkers with %>MDL <50%.

[b] Normalized concentrations (ng/g/day) were determined by dividing total concentrations (ng/g) by the fractional days each participant wore their wristband.

[c] Three participants lost their wristbands during work activities and were excluded from these analyses.

[d] Low molecular weights PAHs are considered those with less than four aromatic rings, while high molecular weight PAHs are those with four or more rings.

(1-NAP) and 2-hydroxynapthalene (2-NAP); five phenanthrene biomarkers: 1-hydroxyphenanthrene (1-PHE), 2- and 3-hydroxyphenanthrene together (2- and 3-PHE), 4-hydroxyphenanthrene (4-PHE), and 9-hydroxyphenanthrene (9-PHE); and one pyrene biomarker: 1-hydroxypyrene (1-PYR). Each PAH biomarker was measured using liquid chromatography with tandem mass spectrometry (LC-MS/MS) following a validated method at NSF International (Ann Arbor, MI, USA), which was developed based on Onyemauwa et al. (Onyemauwa et al., 2009) Briefly, biomarker analysis was conducted with a Thermo Scientific Transcend TXII Turbulent Flow system interfaced with a Thermo Scientific Vantage triple quadrupole mass spectrometer with multiple reaction monitoring in negative ionization mode. Following this method, urinary concentrations of 2- and 3-hydroxyphenanthrene (2- and 3-PHE) were jointly quantitated as they can be difficult to separate. Limits of detection (LODs) ranged between 10 and 50 ng/L (Table 3). We determined method precision (% coefficient of variation, %CV) using five replicate measurements of low-, medium-, and high-quality control samples for each analyte, which captures both intraday and interday variability. Across all analytes, the %CV ranged from 0.7 to 16.8% (Table S2).

2.5. Outcome assessment: Quantification of urinary acute kidney injury biomarkers

We measured concentrations (pg/mL) of five urinary acute kidney injury (AKI) biomarkers: interleukin 18 (IL-18), kidney injury molecule-1 (KIM-1), monocyte chemoattractant protein-1 (MCP-1), chitinase-3-like protein 1 (YKL-40), and neutrophil gelatinase-associated lipocalin (NGAL). The targeted biomarkers are released in the urine following injury (NGAL, KIM-1), inflammation (IL-18, MCP-1), and repair (YKL-40) processes in the kidneys and were selected based on their potential for the early detection of acute kidney injury and to predict its progression (Zhang and Parikh, 2019; Puthumana et al., 2021). All biomarker concentrations were quantified using patterned arrays

Table 3
Summary statistics for PAH biomarker concentrations in **urine samples** (n = 43).

	Parent Compound	Biomarker Name	Acronym	LOD	%> LOD	GM (GSD)	Min	Median (IQR)	Max
Creatinine Corrected Concentrations (ng/g)	Fluorene	2-Hydroxyfluorene	2-FLU	10	100	415.73 (2.04)	163.37	397.52 (258.53 - 549.73)	2502.96
	Naphthalene	1-Hydroxynapthalene	1-NAP	50	100	812.94 (3.04)	67.42	686.86 (352.82 - 1809.80)	9813.31
		2-Hydroxynapthalene	2-NAP	50	100	6458.50 (1.81)	1842.01	6628.36 (4645.96 - 10849.73)	22715.99
	Phenanthrene	1-Hydroxyphenanthrene	1-PHE	10	100	238.75 (1.68)	106.45	246.79 (157.59 - 327.37)	977.43
		2&3-Hydroxyphenanthrene	2&3-PHE	20	100	329.75 (1.95)	116.47	303.06 (223.19 - 447.07)	3924.86
		4-Hydroxyphenanthrene	4-PHE	10	84	30.01 (2.16)	<LOD	31.43 (17.53 - 43.59)	240.61
		9-Hydroxyphenanthrene	9-PHE	10	88	31.89 (2.69)	<LOD	26.12 (16.60 - 53.72)	350.46
	Pyrene	1-Hydroxypyrene	1-PYR	10	100	198.38 (2.10)	54.11	169.78 (121.23 - 294.04)	2137.72
Specific Gravity Corrected Concentrations (ng/L)	Fluorene	2-Hydroxyfluorene	2-FLU	10	100	451.18 (2.08)	151.50	424.22 (278.66 - 686.23)	2461.12
	Naphthalene	1-Hydroxynapthalene	1-NAP	50	100	882.25 (2.93)	76.71	837.62 (422.63 - 1813.82)	10816.13
		2-Hydroxynapthalene	2-NAP	50	100	7009.20 (1.89)	2028.74	7607.26 (4292.85 - 12132.83)	23964.49
	Phenanthrene	1-Hydroxyphenanthrene	1-PHE	10	100	259.11 (1.74)	83.01	284.85 (154.58 - 394.48)	867.64
		2&3-Hydroxyphenanthrene	2&3-PHE	20	100	357.86 (1.98)	139.69	334.53 (211.59 - 523.62)	3315.35
		4-Hydroxyphenanthrene	4-PHE	10	84	32.57 (2.21)	<LOD	35.25 (18.81 - 52.78)	204.65
		9-Hydroxyphenanthrene	9-PHE	10	88	34.60 (2.64)	<LOD	28.27 (17.05 - 62.09)	493.62
	Pyrene	1-Hydroxypyrene	1-PYR	10	100	215.30 (2.10)	62.44	192.42 (130.74 - 332.12)	1805.74
Uncorrected Concentrations (ng/L)	Fluorene	2-Hydroxyfluorene	2-FLU	10	100	417.35 (2.39)	60.46	383.89 (253.30 - 671.37)	2757.49
	Naphthalene	1-Hydroxynapthalene	1-NAP	50	100	816.11 (2.82)	95.21	717.29 (400.08 - 1520.08)	9808.40
		2-Hydroxynapthalene	2-NAP	50	100	6483.70 (2.25)	810.89	6189.85 (3450.32 - 11962.14)	26850.30
	Phenanthrene	1-Hydroxyphenanthrene	1-PHE	10	100	239.69 (2.02)	26.51	271.37 (159.09 - 402.84)	976.94
		2&3-Hydroxyphenanthrene	2&3-PHE	20	100	331.03 (2.27)	45.07	322.58 (215.03 - 534.71)	3922.89
		4-Hydroxyphenanthrene	4-PHE	10	84	30.13 (2.43)	<LOD	35.83 (16.21 - 53.09)	240.49
		9-Hydroxyphenanthrene	9-PHE	10	88	32.01 (2.93)	<LOD	27.67 (13.21 - 72.36)	250.17
	Pyrene	1-Hydroxypyrene	1-PYR	10	100	199.16 (2.49)	32.36	196.82 (113.54 - 358.74)	2136.65

[a]Summary statistics were calculated using instrument read values when available or after replacing values < LOD (ng/L) with the respective LOD/$\sqrt{2}$.
[b]Raw (uncorrected) urinary concentrations of each biomarker were corrected for each participant's respective urinary creatinine concentration or specific gravity.
Abbreviations: LOD: limit of detection; %>LOD: percentage detected above the LOD; GM: geometric mean; GSD: geometric standard deviation; IQR: interquartile range.

coupled with electrochemiluminescence on the MesoScale Discovery platform (MesoScale Diagnostics, LLC, Gaithersburg, MD, USA). Two multiplex plates were used to assay biomarkers simultaneously (plate 1: IL-18, KIM-1 and MCP-1; plate 2: YKL-40 and NGAL). A summary of assay sensitivity and precision parameters are included in the supplemental materials (Table S3). As clinical thresholds do not exist, we created a composite outcome for subclinical kidney injury, defined as the presence of two or more biomarkers in the highest tertile of concentrations, as done previously (Leibler et al., 2021). This outcome does not reflect established cutoffs for the biomarkers, which may represent different types of kidney injury, but seeks to better capture the potential for multidimensional risk of subclinical damage.

2.6. Outcome assessment: Quantification of kidney function

Serum was collected from each participant, on average, 16 (range: 0-28) days prior to urine collection. Using serum creatinine concentration, which was measured at the Molina Hospital in Chile, we calculated estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equation (Inker et al., 2021). Briefly, $eGFR = 142 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.200} \times 0.9938^{Age}$, where S_{cr} is standardized serum creatinine (mg/dL), κ is 0.9 for males, α is −0.302 for males, $\min(S_{cr}/\kappa, 1)$ is the minimum of S_{cr}/κ or 1.0, $\max(S_{cr}/\kappa, 1)$ is the maximum of S_{cr}/κ or 1.0, and age is expressed in years.

2.7. Accounting for urinary dilution

Accounting for dilution in spot urine samples is important to reduce measurement error of biomarker concentrations, but applying standard methods in this study, using either urinary creatinine or specific gravity, is complicated by the potential relation of these factors to the main outcome of interest, AKI (Kuiper et al., 2021; Lee et al., 2025; Weaver et al., 2014; Wen et al., 2022). Furthermore, endogenous proteins (AKI biomarkers) and metabolites of xenobiotic chemicals (PAH biomarkers) may be excreted differently in the urine, leading to additional potential for measurement error when accounting for urinary dilution. Acknowledging these uncertainties, we included urinary creatinine as a covariate in our main models and also examined the impact of alternative dilution correction methods in sensitivity analyses. Specifically, we built additional models that: (1) included specific gravity as a covariate, (2) directly corrected exposure and outcome biomarker concentrations for urinary creatinine or specific gravity, and (3) models that did not account for urinary dilution. For these sensitivity analyses and to facilitate comparison with other studies, we calculated both urinary creatinine- (UCr) and specific gravity- (SG) corrected concentrations of the AKI and PAH biomarkers. For urinary creatinine correction, biomarker concentrations were normalized by dividing the raw biomarker concentration by the UCr concentration, resulting in units of pg/mg-UCr for AKI biomarkers and ng/g-UCr for PAH biomarkers. For specific gravity, we applied the Boeniger method (Boeniger et al., 1993), which was calculated as $E_{sg} = E_o \times (SG_{median}–1)/(SG_o–1)$, where E_{sg} is the SG-corrected biomarker concentration, E_o is the observed biomarker concentration, SG_{median} is the median specific gravity of the study sample and SG_o is each participant's observed specific gravity. The median specific gravity among our study sample was 1.019.

2.8. Statistical analyses

We calculated summary statistics for participants' demographic characteristics and behaviors related to PAH exposures. For AKI biomarkers and PAH exposures with a detection frequency (DF) ≥80%, we retained machine-read values, when available, and otherwise imputed the concentration using the respective $LOD/\sqrt{2}$. For two participants, urinary concentrations of 2-NAP were above the calibration curve, so the samples were diluted to retrieve valid measurements. We calculated descriptive statistics for all concentrations, including the geometric mean (GM) and standard deviation (GSD), based on the right-skewed distributions of the AKI biomarkers and PAH exposures in both matrices. For all urinary biomarkers, we calculated descriptive statistics of the UCr-corrected, SG-corrected, and uncorrected concentrations. To determine the degree to which urinary PAH biomarkers, which represent internal dose, corresponded to wristband concentrations of parent PAH compounds, we calculated Spearman correlation coefficients. We also evaluated whether the direction or strength of correlation of concentrations between matrices varied by duration of wristband deployment (less or greater than the median wear time, 9.4 days) or among samples collected on Mondays (assumed to be reflective of recent weekend exposure, n = 19) vs. other weekdays (assumed to reflective of recent weekday exposure, n = 21). Similarly, we used Spearman correlations to assess the strength of the monotonic relationships between uncorrected concentrations of the five AKI biomarkers, urinary creatinine, specific gravity, and eGFR.

To assess independent associations of the AKI biomarker concentrations and PAH exposures, we fit crude (unadjusted) and multivariable linear regression models. For parent PAH compounds with multiple urinary biomarkers (i.e., naphthalene and phenanthrene), we calculated the molar sum of their metabolites to quantify the total exposure to the parent compound. Calculations were as follows: $\Sigma NAP\ (nmol/mL) = (C_{1\text{-}NAP} + C_{2\text{-}NAP}) \times (1/144.17\ g/mol) \times (1/1000)]$ and $\Sigma PHE\ (nmol/mL) = (C_{1\text{-}PHE} + C_{2\&3\text{-}PHE} + C_{4\text{-}PHE} + C_{9\text{-}PHE}) \times (1/194.23\ g/mol) \times (1/1000)]$ where $C_{1\text{-}NAP}$, for example, is the participant's urinary concentration of 1-NAP (ng/mL), and 144.17 and 194.23 are the molecular weights (g/mol) for the naphthalene and phenanthrene biomarkers, respectively. In all models, both the AKI biomarker and PAH exposure variables were included as log-transformed concentrations, except wristband measures of naphthalene and perylene, which were dichotomized (detect vs. non-detect) as they were less frequently detected (DF < 80%). As clinical guidelines are not well established, we estimated the percent difference in urinary AKI biomarker concentrations associated with an interquartile range (i.e., the difference between the 75th and 25th percentiles) increase for each wristband or urinary PAH concentration. Similarly, we assessed the association between interquartile range increases of the PAH exposures and estimated glomerular filtration rate (eGFR) as a continuous outcome. All main models were adjusted for participants' age in years (continuous), primary work environment (outdoors vs. indoors), reported red meat consumption (at least once per week vs. less than once per week), and urinary creatinine concentration (g/L, continuous). Covariate selection was based on *a priori* knowledge of factors associated with PAH exposures or observed associations with subclinical kidney injury (i.e., two or more biomarkers in the highest tertile), or both. Finally, we modeled associations between binary outcomes [i.e., subclinical kidney injury and reduced kidney function ($eGFR<90\ mL/min/1.73\ m^2$)] and PAH exposures using multivariable logistic regression.

While our main models were adjusted for urinary creatinine as a covariate, we evaluated the robustness of our results by implementing alternative methods to account for urine dilution. Specifically, we examined models adjusted for specific gravity as a covariate (Model 2 for both wristband and urine) and those in which the AKI and PAH biomarker variables were UCr- or SG-corrected before being entered in the model (Models 3-4 for wristbands and Models 3-5 for urine); we also evaluated the models without accounting for urinary dilution (Model 5 for wristbands and Model 6 for urine). Given the exploratory nature of this work, we assessed the consistency of associations between the PAH exposures and AKI biomarkers. Given the small sample size, we did not adjust for multiple comparisons and interpreted results in the context of overall patterns rather than relying solely on p-values; significance was assessed at $\alpha = 0.05$. All analyses were completed in R (4.4.2).

3. Results

3.1. Study sample characteristics

Demographic characteristics of study participants are displayed in Table 1. Among the 43 study participants, the mean age was 53.2 years (SD: 5.7), 41 (95.3%) reported Chilean ethnicity, and 22 (51.2%) completed less than 8 years of formal education. Participants had a mean eGFR of 94.7 mL/min/1.73 m^2 (SD: 14.2), which did not differ by subclinical kidney injury status ($p = 0.86$), but 16 (37.2%) participants had an eGFR <90 mL/min/1.73 m^2 (not displayed), or mildly reduced kidney function according to 2024 Kidney Disease Improving Global Outcome (KDIGO) guidelines (Stevens et al., 2024). Considering potential sources of PAH exposures, 12 (7.9%) participants were current smokers, 38 (88.4%) and 10 (23.3%) reported burning wood indoors and outdoors at home, respectively, and 10 (23.3%) reported burning their trash. All participants who burned wood inside reported that it was their primary or supplementary source of household heat. Participants reported outdoor woodburning for cooking, recreation, and supplementary heating. Participants with potential subclinical kidney injury (i.e., two or more AKI biomarkers in the highest tertile) tended to work primarily outdoors (94.7% vs. 75.0%, $p = 0.11$) and were less likely to consume red meat at least once weekly (21.1% vs. 58.3%, $p = 0.03$).

3.2. Wristband PAH concentrations

On average, participants wore their wristbands for 9.4 days (range: 8.0-11.3 days). Of the 23 PAHs analyzed, we detected 15 in at least 45% of wristbands (NAP: 45%; PER: 48%), with 13 of these detected in >80% (Table 2). We have also reported raw PAH concentrations (ng/g), unadjusted for length of wear (Table S4). Among the remaining eight PAHs, two were detected in only one wristband each (3-methylcholanthrene and dibenz(a,h)anthracene) and six (7,12-dimethylbenz(a)anthracene, indeno(1,2,3-cd)pyrene, benzo(g,h,i)perylene, dibenz[a,l]pyrene, dibenz[a,i]pyrene, and dibenz[a,h]pyrene) were not detected in any wristband.

3.3. Urinary PAH Biomarker concentrations

Summary statistics of UCr-corrected, SG-corrected, and uncorrected urinary PAH biomarker concentrations are presented in Table 3. Urinary concentrations of the assayed PAH biomarkers were highly detected (>80% for all biomarkers), and six biomarkers (2-FLU; 1-NAP; 2-NAP; 1-PHE; 2&3-PHE; and 1-PYR) were detected in 100% of participant urine samples. Spearman correlation coefficients within matrices were positive, ranging from 0.42 to 0.95 among wristband PAH concentrations (Table S5) and 0.26–0.86 among SG-corrected urinary PAH biomarkers (Table S6). For PAHs with paired urinary biomarkers and parent compounds in wristbands, strong, positive correlations were observed for fluorene and 2-FLU (0.63, $p < 0.01$), and pyrene and 1-PYR ($\rho = 0.60$, $p < 0.01$) (Table S7). Strong to week positive correlations were observed for phenanthrene with its metabolites: 2&3-PHE ($\rho = 0.67$, $p < 0.01$) > 1-PHE ($\rho = 0.66$, $p < 0.01$) > 4-PHE ($\rho = 0.41$, $p < 0.01$) > 9-PHE ($\rho = 0.22$, $p = 0.17$). The molar sum of urinary phenanthrene metabolites was also positively correlated with wristband concentrations of phenanthrene ($\rho = 0.68$, $p < 0.01$). Spearman correlations remained positive for all parent-biomarker combinations but were stronger among samples collected on Mondays (assumed to be reflective of recent weekend exposure, range: 0.26, 0.79) vs. those collected on other weekdays (assumed to reflective of recent weekday exposure, range: 0.16, 0.58). Similarly, all correlations remained positive when stratified by duration of wristband wear, but stronger correlations were observed for participants with a shorter (range: 0.21, 0.74) vs. longer (range: 0.16, 0.52) wear period (Table S7).

3.4. Urinary AKI Biomarker concentrations

Descriptive statistics of the primary outcomes, urinary concentrations of five biomarkers of acute kidney injury, are presented in Table 4. All AKI biomarkers were detected in the urine of more than 70% of our participants, with three (KIM-1, MCP-1, and NGAL) detected in every sample. Concentrations varied the least for MCP-1 (GSD: 1.84) and most for YKL-40 (GSD: 3.53). Spearman correlation coefficients ranged from 0.12 to 0.67 among the uncorrected AKI biomarker concentrations and from −0.04 to 0.16 between eGFR and each biomarker (Table S8). Significant positive correlations ($p < 0.05$) were observed for all pairwise combinations of AKI biomarkers, except between MCP-1 and NGAL ($\rho = 0.26$, $p = 0.10$). Similarly, excluding NGAL, the other four AKI biomarkers (i.e., IL-18, KIM-1, MCP-1, YKL-40) demonstrated statistically significant positive correlations, ranging from 0.37 to 0.72, with both urinary creatinine concentrations and specific gravity, which were also positively correlated with each other ($\rho_{UCr\text{-}SG} = 0.82$, $p < 0.01$).

3.5. Associations of wristband PAH concentrations with AKI biomarkers

Results from multivariable linear regression models of AKI biomarkers in relation to wristband PAH concentrations are shown in Fig. 1; crude and adjusted effect estimates of percent difference and 95% confidence intervals per interquartile range increase in wristband PAH concentration are also presented in Table S9. In adjusted models, we observed consistent positive associations between select AKI biomarkers and wristband PAH concentrations. Specifically, higher concentrations of urinary IL-18 were associated with anthracene (46.7%; CI: 9.7%, 96.2%), phenanthrene (32.3%; CI: 5.5%, 65.9%), fluorene (56.9%; CI: 10.2%, 123.3%), and pyrene (34.1%; CI: 3.2%, 74.3%), per interquartile range increase in wristband PAH concentration. Moreover, non-significant elevations of urinary IL-18 were observed in relation to wristband concentrations of benzo[a]pyrene (20.5%; CI: 0.2%, 45.0%). Higher urinary IL-18 concentrations were also observed among participants who had naphthalene detected in their wristbands compared to those who did not (51.5%; CI: 1.3%, 126.7%). Similarly, we observed statistically significant positive associations of urinary YKL-40 concentrations with pyrene (67.4 %; CI: 6.8%, 162.5%) and benzo[j,b,k]fluoranthene (47.6%; CI: 4.4%, 109.8%), and a non-statistically significant elevation with fluorene (86.3%; CI: −0.5%, 248.9%). While the majority of our estimates were positive, we did not observe consistent trends of association between the other PAHs measured in wristbands and AKI biomarkers (i.e., KIM-1, MCP-1, and NGAL) (Table S9). In sensitivity analyses using several dilution-correction approaches, estimates shifted slightly toward the null when we used methods other than model adjustment for urinary creatinine. Nonetheless, any model that accounted for urinary dilution produced more conservative estimates than Model 5, which ignored dilution. Importantly, the positive associations of IL-18 with anthracene and fluorene, and of YKL-40 with pyrene, remained statistically significant across all models (Table S10).

3.6. Associations of urinary PAH Biomarker concentrations with AKI biomarkers

Associations between urinary PAH and AKI biomarker concentrations estimated by multivariable linear regression are displayed in Fig. 2; effect estimates (95% CIs) of the percent difference in AKI biomarker concentration per interquartile range increase in the PAH biomarker concentration from crude and adjusted models are summarized in Table S11. We observed consistent positive associations between urinary concentrations of IL-18 and select urinary PAH biomarkers. Specifically, higher urinary IL-18 concentrations were associated with higher urinary concentrations of 1-PHE (80.4%; CI: 33.8%, 143.3%), 2&3-PHE (44.1%; CI: 12.7%, 84.2%), and 4-PHE (48.8%; CI: 12.9%, 96.1%). An interquartile range increase in the urinary molar sum of phenanthrene metabolites was also associated with higher concentrations of IL-18

Table 4
Summary statistics for concentrations of acute kidney injury biomarkers in **urine samples** (n = 43).

	Urinary AKI Biomarker	LLOD	% >LLOD	GM (GSD)	Min	Median (IQR)	Max
Creatinine Corrected Concentrations (pg/mg)	Interleukin 18 (IL-18)	4.6	97	28.36 (1.85)	<LLOD	28.64 (17.91 - 36.98)	121.41
	Kidney Injury Molecule-1 (KIM-1)	4.6	100	656.72 (2.09)	62.44	776.07 (454.28 - 1013.96)	3504.03
	Monocyte Chemoattractant Protein-1 (MCP-1)	1.7	100	123.06 (1.60)	55.18	115.01 (96.93 - 150.82)	596.26
	Chitinase-3-Like Protein 1 (YKL-40)	34.1	72	79.67 (3.26)	<LLOD	96.46 (47.65 - 142.59)	919.23
	Neutrophil Gelatinase-Associated Lipocalin (NGAL)	35.8	100	8514.13 (2.55)	1404.97	8658.54 (4719.38 - 14994.43)	93097.40
Specific Gravity Corrected Concentrations (pg/mL)	Interleukin 18 (IL-18)	4.6	97	29.05 (2.06)	<LLOD	25.47 (17.65 - 40.81)	139.75
	Kidney Injury Molecule-1 (KIM-1)	4.6	100	672.75 (2.29)	70.693	710.89 (500.93 - 1091.84)	7598.48
	Monocyte Chemoattractant Protein-1 (MCP-1)	1.7	100	126.06 (1.84)	30.082	117.66 (87.39 - 172.20)	1292.99
	Chitinase-3-Like Protein 1 (YKL-40)	34.1	72	81.62 (3.53)	<LLOD	96.39 (<LLOD - 131.19)	1993.34
	Neutrophil Gelatinase-Associated Lipocalin (NGAL)	35.8	100	8722.02 (2.70)	1254	7517.77 (4605.66 - 14792.23)	201881.40
Uncorrected Concentrations (pg/mL)	Interleukin 18 (IL-18)	4.6	97	26.87 (2.22)	<LLOD	26.75 (17.66 - 40.72)	171.15
	Kidney Injury Molecule-1 (KIM-1)	4.6	100	622.31 (2.70)	33.51	689.36 (416.66 - 1191.75)	7439.37
	Monocyte Chemoattractant Protein-1 (MCP-1)	1.7	100	116.61 (2.10)	17.17	115.42 (75.11 - 182.73)	1265.92
	Chitinase-3-Like Protein 1 (YKL-40)	34.1	72	75.50 (3.66)	<LLOD	78.52 (<LLOD - 146.15)	1951.60
	Neutrophil Gelatinase-Associated Lipocalin (NGAL)	35.8	100	8068.11 (2.86)	1305.47	8252.87 (4631.56 - 12450.15)	197654.03

Abbreviations: LLOD: lower limit of detection; %>LLOD: percentage detected above the LLOD; GM: geometric mean; GSD: geometric standard deviation; Min: minimum; IQR: interquartile range; Max: maximum.
[a]Summary statistics were calculated using instrument read values when available or after replacing values < LOD with the respective LOD/$\sqrt{2}$.
[b]Raw urinary concentrations of each biomarker were corrected for each participant's respective urinary creatinine concentration or specific gravity.

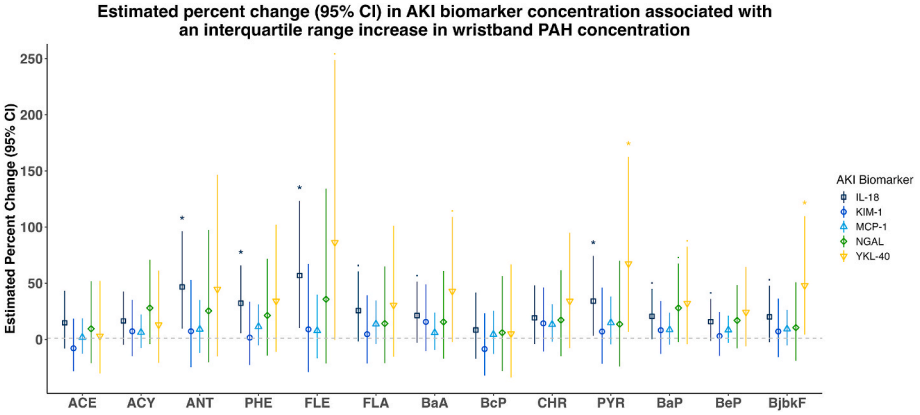

Fig. 1. Forest plots of estimated percent change (95% confidence interval) in acute kidney injury (AKI) biomarker concentrations associated with an interquartile range increase in parent polycyclic aromatic hydrocarbon (PAH) wristband concentrations (n = 40). Wristband concentrations of PAHs (exposure) and urinary concentrations of AKI (outcome) biomarkers were natural log-transformed and treated as continuous variables. Associations were modeled using linear regression models adjusting for age (years); primary work environment (outdoors vs. indoors [ref]); indoor woodburning at home (yes vs. no [ref]); red meat consumption (at least once per week vs. not [ref]); and urinary creatinine (g/L). **Abbreviations**: 95% CI: 95% confidence interval. **PAHs**: ACE: acenaphthylene; ACY: acenaphthylene; ANT: anthracene; PHE: phenanthrene; FLE: fluorene; FLA: fluoranthene; BaA: benz[a]anthracene; BcP: benzo(c)phenanthrene; CHR: chrysene; PYR: pyrene BaP: benzo[a]pyrene; BeP: benzo[e]pyrene; BjbkF: benzo[j,b,k]fluoranthene. **AKI Biomarkers**: IL-18: interleukin 18; KIM-1: kidney injury molecule-1; MCP-1: monocyte chemoattractant protein-1; YKL-40: chitinase-3-like protein 1; NGAL: neutrophil gelatinase-associated lipocalin. Statistically significant estimates are marked: · ($p < 0.10$); * ($p < 0.05$); and ** ($p < 0.01$). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(62.5%; CI: 25.2%, 110.9%). In our main models, the other four AKI biomarkers (KIM-1, MCP-1, NGAL and YKL-40) were not associated with urinary PAH biomarker concentrations (Table S11). The adjusted associations between urinary PAH and AKI biomarker concentrations were most conservative in our main models (i.e., those with urinary creatinine as a covariate); the observed associations were similar when using UCr-corrected exposure and outcome biomarker concentrations (Model 3). Using three other approaches, which all included specific gravity (Models 2, 4, and 5) to account for urinary dilution, we observed evidence of additional positive associations of IL-18 with 2-FLU and 1-PYR, of KIM-1 with 1-PHE, and of MCP-1 with 1-NAP (Table S12). Furthermore, in the model that did not account for urinary dilution, IL-18, KIM-1 and MCP-1 all demonstrated statistically significant positive associations with six of the urinary PAH biomarkers evaluated (2-FLU, 2-NAP, 1-PHE, 2&3-PHE, 4-PHE, and 1-PYR); in the same models, NGAL and YKL-40 were also elevated in relation to 1-PHE concentrations.

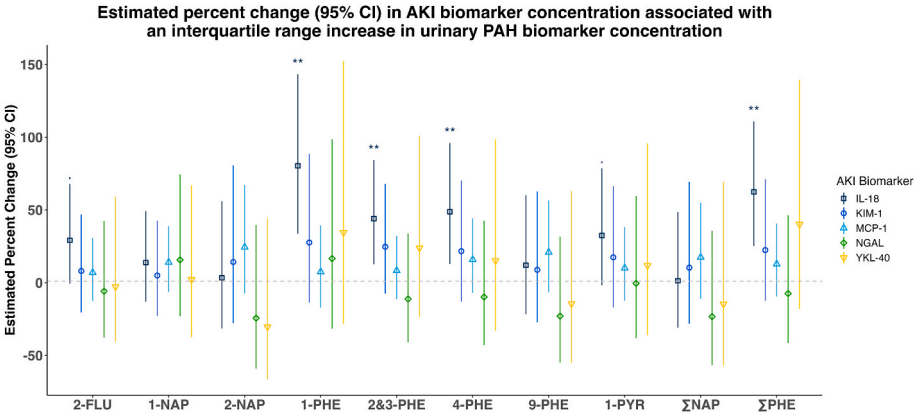

Fig. 2. Forest plots of estimated percent change (95% confidence interval) in acute kidney injury (AKI) biomarker concentrations associated with an interquartile range increase in urinary polycyclic aromatic hydrocarbon (PAH) biomarker concentration (n = 43). Urinary concentrations of both PAH (exposure) and AKI (outcome) biomarkers were natural log-transformed and treated as continuous variables. Associations were modeled using linear regression models adjusting for age (years); primary work environment (outdoors vs. indoors [ref]); indoor woodburning at home (yes vs. no [ref]); red meat consumption (at least once per week vs. not [ref]); and urinary creatinine (g/L). **Abbreviations**: 95% CI: 95% confidence interval. **PAH Biomarkers**: 2-FLU: 2-hydroxyfluorene; 1-NAP: 1-hydroxynapthalene; 2-NAP: 2-hydroxynapthalene; 1-PHE: 1-hydroxyphenanthrene; 2&3-PHE: 2&3-hydroxyphenanthrene together; 4-PHE: 4-hydroxyphenanthrene; 9-PHE: 9-hydroxyphenanthrene; 1-PYR: 1-hydroxypyrene; ∑NAP: molar sum of naphthalene metabolites (1-NAP, 2-NAP); ∑PHE: molar sum of naphthalene metabolites (1-PHE, 2&3-PHE, 4-PHE, 9-PHE). **AKI Biomarkers**: IL-18: interleukin 18; KIM-1: kidney injury molecule-1; MCP-1: monocyte chemoattractant protein-1; YKL-40: chitinase-3-like protein 1; NGAL: neutrophil gelatinase-associated lipocalin. Statistically significant estimates are marked: · ($p < 0.10$), and * ($p < 0.05$). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.7. Associations of PAH exposures with subclinical kidney injury and kidney function

Wristband concentrations of select parent PAH compounds were associated with higher odds of subclinical kidney injury (defined as two or more of the biomarkers in the highest tertile) including benzo[e]pyrene (aOR: 5.58; 95% CI: 1.12, 27.72), benzo[a]pyrene (aOR: 4.82; 95% CI: 1.10, 21.07), and chrysene (aOR: 3.16; 95% CI: 1.00, 9.93). Elevated odds of subclinical kidney injury were also observed with higher concentrations of benzo[j,b,k]fluoranthene (aOR: 2.92; 95% CI: 0.94, 9.06), benz[a]anthracene (3.72; 95% CI: 0.99, 14.08), and pyrene (aOR: 3.99; 95% CI: 0.94, 16.94), albeit these estimates were not statistically significant; Table S13. Conversely, we did not observe consistent associations of subclinical AKI with the other wristband PAH concentrations or the urinary PAH biomarkers assessed. Similarly, eGFR and reduced kidney function (eGFR <90 mL/min/1.73 m^2) were not associated with PAH exposures in our study.

4. Discussion

In this study, we observed widespread exposure to PAHs, characterized through both silicone wristbands and urinary biomarkers, among our sample of male agricultural workers in a Chilean community with prevalent household woodburning. We also quantified five biomarkers of acute kidney injury among most participants and identified positive associations of those biomarkers with exposure to select PAHs. Specifically, IL-18, a biomarker of kidney inflammation, was consistently associated with higher exposure to select PAHs, including phenanthrene, fluorene and pyrene, as measured though their concentrations in both silicone wristbands and their respective urinary biomarkers. These results underscore the need for biomonitoring in larger populations exposed to PAHs and their potential contribution to kidney health effects.

An increasing number of studies have employed silicone wristbands to assess exposure to multiple environmental contaminants, including PAHs, among highly exposed groups (Hamzai et al., 2022; González-Quiroz et al., 2025). Still, results can be challenging to compare between studies due to differences in reporting and study design, including variable length of wear. Consistent with results among firefighters, we observed higher wristband concentrations of lower molecular weight PAHs (i.e., those with two or three aromatic rings) compared to higher molecular weight PAHs, many of which were infrequently or not detected in our wristbands (Baum et al., 2020). Like another firefighter study, phenanthrene, pyrene, and fluoranthene were the most abundant compounds by mass in wristbands worn by our participants, as was naphthalene in the wristbands in which it was detected (Levasseur et al., 2022). The detection frequency of most PAHs, except for naphthalene, was similar to that observed among high school students in Santiago, Chile (Manzano et al., 2019), but higher than those reported among community residents of Alto Mayo, Peru (Bergmann et al., 2017), schoolchildren in Montevideo, Uruguay (Running et al., 2024), and women in rural Guatemala (Butler-Dawson et al., 2025). Similarly, detection rates of several PAHs was greater in our study sample than among residents of an Appalachian mining community, except for phenanthrene, which was nearly ubiquitous in wristbands from both studies (Hendryx et al., 2020). Compared to Uruguayan children who each wore a wristband for a week, concentrations of select PAHs, including acenaphthylene and benz[a]anthracene, were lower, but median concentrations in this study were two to three times higher for fluorene, fluoranthene, chrysene, and pyrene, and more than 20-fold higher for phenanthrene (Running et al., 2024). Although participants in this study wore their wristbands for two days longer on average than the residents of the mining community, mean concentrations were nearly two-fold greater for multiple PAHs, including phenanthrene, fluorene, fluoranthene, and pyrene, and lower for only for benz[a]anthracene (Hendryx et al., 2020). Our results also align with previous work in Alto Mayo, Peru, where the detection of PAHs in wristbands was more frequent in three rural communities compared to the regional capital, suggesting potential urban-rural exposure disparities (Bergmann et al., 2017). Among adult women in rural Guatemala, higher concentrations of PAHs were observed in wristbands worn by community residents compared to those employed as sugarcane seeders, possibly attributable to higher exposure to indoor biomass burning (Butler-Dawson et al., 2025). Finally, when considering the relationship between parent PAHs detected in wristbands to their corresponding urinary biomarkers, our results are consistent with previous evidence among pregnant women that observed strong to weak positive correlations between concentrations in the two matrices, depending on the specific PAH (Dixon et al., 2018, 2022).

Traditionally, urinary biomonitoring has been used to measure PAH

exposures, but studies among agricultural workers are limited. For example, among 45 studies in Europe that assessed occupational PAH exposures using urinary biomarkers, none represented agricultural workers despite their potential for elevated exposure (Louro et al., 2022). Among adults sampled for the Second Korean National Environmental Health Survey, those employed in agriculture, forestry, and fisheries had higher odds of elevated exposure for 1-hydroxypyrene compared to the reference group (Hong et al., 2023). Similarly, among respondents in the Australian Workplace Exposures Study, workers in the agricultural industry had the highest probability of exposure to PAHs (Driscoll et al., 2016). Urinary concentrations of several PAH biomarkers, including 2-FLU, 1-PHE, 2&3-PHE, 4-PHE, and 1-PYR, were generally higher in our study than those observed in the U.S. general population (Centers for Disease Control and Prevention, 2024) and among adults from Australia (Thai et al., 2016, 2020), Canada (Health Canada, 2017), and Italy (Tombolini et al., 2018), but lower than concentrations reported in Chinese adults (Sun et al., 2017). Similarly, concentrations of 2-NAP were higher among our study population compared values reported by studies in Australia (Thai et al., 2016, 2020), Canada (Health Canada, 2017), Italy (Tombolini et al., 2018), and Korea (Hong et al., 2023), but lower than those observed in China (Sun et al., 2017), Spain (Peris-Camarasa et al., 2024), and among Hispanic adults from the U.S. general population (Centers for Disease Control and Prevention, 2024). We also observed lower urinary 1-NAP concentrations compared to previously reported values. Compared to studies of indigenous workers and children in Mexico, for whom household woodburning is common, urinary PAH biomarkers were observed at lower concentrations among our study sample but more frequently detected (Flores-Ramírez et al., 2021; Díaz de León-Martínez et al., 2021a, 2021b).

Urinary biomarkers have also been increasingly used in epidemiological studies to predict the diagnosis, progression, and severity of kidney diseases (Canki et al., 2024; Strauβ et al., 2024; Claure-Del Granado et al., 2022). In the context of CKD of nontraditional etiology (CKDnt), in which traditional risk factors (i.e., hypertension, diabetes, advanced age) are absent, KIM-1 and NGAL are the two most frequently measured urinary biomarkers (Claudel et al., 2024). Previously reported urinary concentrations of KIM-1 and NGAL vary but are consistent with those observed among our study sample. We observed a median urinary NGAL concentration that was comparable to previous studies among Nicaraguan youth and sugarcane workers in CKDnt endemic regions (Leibler et al., 2021; Wesseling et al., 2016; Laws et al., 2016; Petropoulos et al., 2020) and slightly higher but still within the same order of magnitude as studies among farmers (Abdul et al., 2021), other occupational groups (Ekanayake et al., 2022), and youth in Sri Lanka (De Silva et al., 2021; Tdksc et al., 2022), sugarcane harvesters in Guatemala (Butler-Dawson et al., 2022), and indigenous women in Mexico (Díaz de León-Martínez et al., 2019). KIM-1, a biomarker of proximal tubular damage, is not found in the urine of individuals with healthy kidneys (Canki et al., 2024) but was detected in all participants in the present study. The median KIM-1 concentration was similar those reported among youth from Mexico and Nicaragua (Ferreccio et al., 2016; Butler-Dawson et al., 2022), but lower than workers and CKDnt cases in Nicaragua and Sri Lanka (Ekanayake et al., 2022; Wijkström et al., 2018; Hansson et al., 2022). However, we observed higher concentrations of urinary KIM-1 compared to indigenous women in Mexico and youth in Sri Lanka (De Silva et al., 2021; TDKSC et al., 2022; Díaz de León--Martínez et al., 2019). Few studies have measured the other AKI biomarkers evaluated in the present study, but we observed similar concentrations of urinary IL-18 and MCP-1 as those reported among Nicaraguan adolescents and patients with chronic kidney disease, but lower concentrations of YKL-40 (Leibler et al., 2021; Zhang et al., 2018; Parikh et al., 2020).

Existing evidence on PAH exposures and kidney health is limited, with very few studies having examined associations between exposure to multiple PAHs and kidney injury biomarkers. A study of male kitchen workers in India observed positive correlations between urinary PAH and kidney injury biomarkers, including KIM-1 (Singh et al., 2018). Similarly, although urinary PAHs were not measured, a study of Italian adults observed higher levels of urinary NGAL among Italian factory workers compared to office workers and general population controls (Lacquaniti et al., 2012). Among adult indigenous populations in Mexico, where household woodburning is prevalent, elevated exposure to PAH exposures has also been positively correlated with urinary biomarkers of kidney damage, including NGAL (Flores-Ramírez et al., 2021). The results of this study are in accord with hypotheses that PAHs may induce kidney damage via pro-inflammatory pathways. For example, exposure to select PAHs, including phenanthrene, fluorene, and pyrene, was positively associated with urinary concentrations of IL-18, which is a cytokine responsible for upregulating interferon gamma and enhancing natural killer cell activity and has been associated with several inflammatory kidney diseases (Hirooka and Nozaki, 2021). Similarly, urinary naphthalene biomarker concentrations were associated with higher MCP-1, a chemokine involved in the promotion of renal fibrosis via a series of signaling cascades and activation of inflammatory cells (Liu et al., 2024). While we did not observe consistent associations between PAH exposure and estimated glomerular filtration rate, it is possible subclinical kidney damage can occur before significant declines in kidney function take place. Further studies are needed to corroborate our findings and elucidate the underlying pathways by which PAHs may induce kidney dysfunction.

We acknowledge the limitations of the present study. The majority of agricultural workers in the region are male; thus our results are not generalizable to females, who may face even higher risk of PAH exposures, especially due to the high prevalence of residential woodburning in the study area. The cross-sectional design of this work does not allow us to establish a temporal relationship between exposure to PAHs and the kidney biomarkers assessed, but it is unlikely that existing damage to the kidneys would lead to higher PAH exposures as measured in the silicone wristbands. The relatively short periods of exposure assessment may also fail to capture true temporal variability of exposures over time, potentially biasing associations with more stable outcomes (e.g., estimated glomerular filtration rate or eGFR), toward the null. Furthermore, urinary PAH biomarkers are rapidly eliminated and primarily reflect exposures occurring within the previous 24–48 h. Nevertheless, prior investigations have demonstrated that spot urine samples can provide valid estimates of exposure, particularly when exposure is recurrent, as is typical with daily household woodburning (Dixon et al., 2018; Barr et al., 2005; Aylward et al., 2014). While the aim of the present study was to characterize PAH exposures and examine their associations with parameters of kidney health, it will be important for future studies to evaluate the sources of exposures in our study area, as well as concomitant exposures. Specifically, agricultural workers may face a dual burden of exposure to PAHs in both occupational and residential environments, which may require different interventions to reduce exposures. Additionally, we cannot dismiss the possibility of unmeasured confounding from other environmental and occupational exposures prevalent in our study area, such as particulate matter, pesticides and heat stress, which may induce similar negative responses in the kidneys. Nonetheless, it is likely that participants in our study are exposed to multiple environmental and occupational hazards simultaneously, and further work is needed to examine the cumulative impacts of these exposures on the kidneys and other adverse health outcomes. Additional studies with larger sample sizes are needed to employ advanced statistical methods for analyzing complex environmental mixtures and discovering shared metabolic pathways that link environmental exposures to adverse kidney health outcomes.

Despite the noted limitations, the present study has several strengths. To our knowledge, this is the first study to evaluate PAH exposures using silicone wristbands in a population exclusively comprised of agricultural workers and only one of a few studies in Latin America. In studies of kidney health, wristbands have several advantages as an exposure

matrix. Not only are they less invasive and easier to store than urine samples, but they also overcome the potential for reverse causation as wristband concentrations are not dependent on existing kidney function, which can impact the excretion of urinary biomarkers. Additionally, many studies have relied solely on 1-PYR to evaluate occupational exposure to PAHs, but we were able to quantify urinary concentrations of nine PAH biomarkers, representing four parent compounds. While the urinary biomarkers of kidney injury measured in the present study do not have established clinical guidelines, previous studies support their translational potential for predicting the incidence, progression, and severity of acute kidney injury and other renal health outcomes. They are also less invasive than measuring kidney function, which requires a serum sample to estimate glomerular filtration rate, and may be able to detect kidney dysfunction not captured in routine testing. Our results were consistent between both exposure matrices and when comparing multiple methods applied to account for urinary dilution, an assumption that is often made but not always tested in epidemiologic studies, increasing our confidence that the observed results did not arise due to chance alone. Rather, our results support the validity of multiple methods for measuring PAH exposures and that those measures will yield consistent results, which is especially important in resource-constrained settings. Still, these results should only be applied to the assessment of PAHs, as there may be different exposure pathways and excretion profiles for other environmental contaminants.

In summary, this study demonstrated the feasibility of using silicone wristbands, which showed positive correlations (strong to weak) with urinary biomarkers, as tools to assess PAH exposures among agricultural workers. We measured multiple PAHs, in both wristbands and urine, and biomarkers of kidney injury, all of which were widely detected in our study population. Our analysis indicated that exposure to select PAHs, including phenanthrene, fluorene, and pyrene may be associated with increased urinary concentrations of IL-18. Still, further research is warranted in populations at high risk of environmental and occupational exposures and with low access to kidney health care resources. This work supports the potential for using urinary biomarkers to detect kidney diseases earlier, which is critical for reducing disparities in settings lacking access to nephrology care. Future studies should also account for potential temporal variation in exposures and consider mixtures of multiple environmental and occupational exposures that may also impact kidney health.

CRediT authorship contribution statement

Grant D. Tore: Writing – review & editing, Writing – original draft, Visualization, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Melissa DeSantiago:** Writing – review & editing, Funding acquisition, Conceptualization. **Heather M. Stapleton:** Writing – review & editing, Resources, Methodology, Investigation. **Wassim Obeid:** Writing – review & editing, Resources, Methodology, Investigation. **Chirag R. Parikh:** Writing – review & editing, Resources, Methodology, Investigation. **Jordan R. Kuiper:** Writing – review & editing, Methodology. **Margarita Valenzuela:** Writing – review & editing, Investigation. **Catterina Ferreccio:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Louis Fazen:** Writing – review & editing. **Aisha S. Dickerson:** Writing – review & editing. **Sandra Cortés:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Lesliam Quirós-Alcalá:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2026.114791.

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